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ORIGINAL ARTICLES

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Original Article

Shock Index and Modified Shock Index Might be Reliable for Predicting Morbitidy in Pregnancy-Related Hypertensive Disorders

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Keywords: Mortality; preeclampsia; shock index; the modified shock index.

ABSTRACT

Objective: Maternal Early Warning Criteria including; systolic - diastolic blood pressure, peripheral oxygen saturation and urine output, is a useful marker for predicting postoperative complications. Shock index and the modified shock index were used to determine the need for fluid and transfusion in hypovolemia. The aim of this study is to evaluate the effectiveness of using shock index and modified shock index as a parameter of the early warning system to predict the need for postpartum blood transfusion, complications and mortality in pregnancy-related hypertensive diseases.

Methods: Following the Ethics Committee approval, between 2012-2017, 192 patients between the ages of 13-47, undergoing caesarean section due to preeclampsia, eclampsia, chronic hypertension and gestational hypertension were enrolled in this study.

Results: There was a positive correlation between SI and embolism and arrhythmia at admission and between the modified shock index and Intrauterine Growth Retardation at delivery ($p<0.05$). There is a significant positive correlation between the shock index and modified shock index at admission and fresh frozen plasma and Platelet suspension transfusion. There is a significant positive correlation between the shock index at delivery and packed red blood cells, fresh frozen plasma, and platelet suspension transfusion. There is a significant positive correlation between the modified shock index at delivery fresh frozen plasma and packed red blood cells transfusions ($p<0.05$).

Conclusion: It was concluded that modified shock index and shock index could important markers in predicting maternal and fetal complications in hypertensive diseases due to pregnancy as well as postpartum blood transfusion.

INTRODUCTION

According to the current data published by the World Health Organization (WHO), hypertensive disorders, maternal hemorrhage, and sepsis account for 50% of maternal deaths related to pregnancy.[1] In pregnancy-related hypertensive disorders, there is an increase in the incidence of thromboembolic complications and postpartum hemorrhage in the postoperative period.[2] Therefore, early clinical identification and treatment of conditions such as pregnancy-related hypertensive disorders and postpartum hemorrhage are critical for maternal outcome.

Preeclampsia, a pregnancy-related hypertensive disorder, is diagnosed in 3-5% of pregnancies.[3] Decreased placental perfusion, decreased organ perfusion, and endothelial dysfunction play a role in the development of preeclampsia and cause damage to multiple organs. Infarction, necrosis, and intraparenchymal hemorrhage are observed in the liver and adrenal glands secondary to decreased perfusion. Hypovolemic shock occurs resulting from endocardial necrosis in the heart. While glomerular endotheliosis occurs in the kidney, occlusion occurs in the capillary lumen. Preeclampsia causes various maternal and fetal complications due to poor placental perfusion and vasospasm. The incidence of intrauterine growth retardation (IUGR) elevates among the babies of mothers with preeclampsia, which is responsible for 15% of preterm labors. Insufficiency of prenatal care for preeclamptic patients leads to approximately 5000 maternal deaths annually.[4] Advanced age, obesity, and the presence of multiparity, pulmonary

edema, acute renal failure, and coagulopathy worsen the course of the disease.[5] In cases of preeclampsia accompanied by pregnancy-related hypercoagulopathy, individuals become more susceptible to pulmonary embolism and other embolic complications due to endothelial dysfunction.[6]

Conventional methods such as blood pressure, heart rate, and urine output are frequently used to predict hemodynamic complications such as hemorrhage, shock, and sepsis in the postpartum period.[7,8] In recent years, the shock index (SI) parameter, which is the ratio of heart rate to blood pressure, has started to appear in studies as a new method for hemodynamic monitoring. The normal range of SI has been indicated to vary from 0.5 to 0.7 in healthy individuals. An increased SI value despite normal heart rate and normal systolic blood pressure (SBP) has been associated with the fall of the pressure in the left ventricle.[9] It has been demonstrated that mortality increases if SI is above 1 in patients presenting to the emergency department (ED).[10] Some studies have indicated that SI may be superior to conventional monitoring methods in the early prediction of complications such as hemodynamic insufficiency and associated massive blood transfusion and hysterectomy.[11] It has been shown in studies conducted in pregnant women that the risk of developing postpartum hemorrhage is high and maternal mortality increases in patients with an SI value above 0.9.[12,13]

The modified shock index (MSI) was introduced by Liu et al.[14] in 2012 as the ratio of heart rate and mean arterial pressure, and the normal range was specified as 0.7-1.3. In several studies, MSI has been indicated to be effective in the prediction of blood transfusion need for trauma patients.[15] Liu et al. indicated that an MSI of >1.3 is associated with a higher incidence of hemodynamic insufficiency, mortality in patients applying to ED, and a greater rate of intensive care unit (ICU) admissions.[14] Another study reported that when the MSI cut off value was determined as 1.15 in trauma patients admitted to ED, MSI values above this value were associated with an increase in the need for massive transfusion.[15]

Despite all these studies, there is not enough data regarding the use of maternal SI and MSI in the prediction of maternal and fetal outcomes and the need for transfusion of blood and blood products in the postpartum period. The aim of the present study is to investigate the impact of SI and MSI on feto-maternal morbidity and mortality and to determine a cut off value in the preeclampsia group.

MATERIALS AND METHODS

This retrospective cross-sectional study was conducted following the Ethics Committee approval (protocol number: 09.2018.163, date: 06/01/2018). We analyzed the data of 192 patients undergoing a caesarean section after being admitted due to preeclampsia, eclampsia, chronic hypertension (ChHT), and gestational hypertension (GHT) between 2012 and 2017 at our university hospital. We recorded vital signs, demographic characteristics, and postoperative complications for each patient. The data including age, body mass index (BMI), gestational age, duration of hospital stay, laboratory results (ALT, AST, BUN, creatinine, Hb, Hct, INR, Plt, albumin), fetal weight at birth, and APGAR scores at the 1st and 5th minutes were recorded.

We evaluated pulse rate, systolic and diastolic blood pressure (DBP), SI, and MSI both on admission and during labor, and investigated the association of SI and MSI on admission with IUGR, pulmonary embolism, seizure, and development of postoperative severe arrhythmia. The heart rate and blood pressure values were recorded every 5 minutes during the surgery. The type of anesthesia was determined according to the staff anesthesiologist's decision after the preanesthesia assessment. Either spinal anesthesia or general anesthesia was given. Spinal anesthesia was performed using a pencil point 25G spinal needle at the L4-5 or L3-4 level in a sitting position. General anesthesia patients were administered IV propofol 2-3 mg/kg, fentanyl 1-2 mcg/kg, and rocuronium 0.6 mg/kg during induction and sevoflurane 2% with a 50% oxygen and 50% air mixture as maintenance of anesthesia.

The need for blood transfusion was recorded. Red blood cell transfusion was given if the patient's Hb level was below 9 g/dL. FFP was given when there was oozing and the INR level was higher than 1.5. A platelet transfusion was administered if the platelet count was below 100,000/μL.

Statistical Analysis

While evaluating the data obtained from the study, we used IBM SPSS Statistics 22 for statistical analyses. The One-Way ANOVA test was used for normally distributed quantitative data, and the Kruskal Wallis H test was used for non-normally distributed quantitative data. While the Mann Whitney U test was used for the comparison of non-normally distributed data between two groups, the Chi-square test was used to examine discrete variables. The results were evaluated in a 95% confidence interval and with a significance level of $p<0.05$.

RESULTS

The study included 140 patients with preeclampsia, 15 patients with eclampsia, 24 patients with ChHT, and 13 patients with GHT. The patients were aged from 13 to 47 years (31.93±6.54 years). We observed a statistically significant difference regarding the values of average age and gestational age ($p<0.05$). Hospital stays and BMI values were statistically similar between the groups. There was statistically significant similarity between the groups except for creatinine, albumin, and INR levels ($p>0.05$) (Table 1).

No statistically significant difference was observed between the groups regarding birth weight and APGAR scores (Table 2).

It was observed that postpartum pulse rate, SI, and MSI

measurements were statistically significantly higher than the measurements on admission to the hospital (p<0.05). However, no statistically significant difference was observed regarding blood pressure measurements (Table 3).

The pulse rate, systolic blood pressure, diastolic blood pressure, SI, and MSI values at the time of admission to the hospital were found to be statistically significantly similar to the pulse rate, systolic blood pressure, diastolic blood pressure, and MSI values measured after labor. The shock index after birth was found to be statistically significantly higher in the eclampsia and GHT group compared to the other groups (p<0.05) (Table 4).

It was determined that there was a positive, significant correlation between SI on admission and embolism and arrhythmia while there is a positive, significant correlation between SI during labor and seizures. Moreover, a positive, significant correlation was found between MSI during labor and creatinine levels, IUGR, and seizures (p<0.05) (Table 5).

Table 1. Demographic data

	Preeclampsia (n=140)	Eclampsia (n=15)	ChHT (n=24)	GHT (n=13)	p
Age (years)	31.36±6.33	27.20±7.28	36.63±4.12	34.92±6.06	0.001*[b]
BMI (kg/m2)	31.22±4.85 (30.38)	31.99±8.21 (30.49)	33.34±5.90 (31.6)	32.25±2.93 (32.8)	0.196[m]
Gestational Age (weeks)	36+3	35±3	33±3	37±2	0.015*[m]
Hospital stay (day)	4.7±2.4(4)	4.4±0.9(5)	6.75±5.83(5)	3.62±1.33(3)	0.205[m]
BUN (mg/dL)	10.86±3.92(10)	11.73±6.06(10)	10.5±40.7(10.5)	9.38±4.81(9)	0.348[m]
ALT (IU)	52.8±120.8(16)	54.8±79.1(20)	16.1±8.1(14)	56±111.2(11)	0.269[m]
AST (IU)	84.24±305.1(22.5)	102.3±174.8(27)	23.3±8.1(21)	79.2±147.1(20)	0.057[m]
Hb (g/dL)	12.42±8.38(11.8)	11.92±1.95(12.5)	11.49±1.34(11.7)	11.91±2.13(11.6)	0.787[m]
Htc (%)	34.56±4.73	36.1±4.96	34.49±3.35	35.69±5.83	0.559[b]
Creatinine (mg/dL)	0.65±0.24(0.6)	0.76±0.23(0.78)	0.63±0.15(0.6)	0.52±0.14(0.49)	0.018[m]
INR	0.97±0.95(0.96)	1.05±0.13(1)	0.98±0.07(0.98)	0.91±0.31(1.02)	0.010*[m]
Albumin (g/dL)	2.82±0.48(2.9)	2.59±0.43(2.6)	2.94±0.39(3.04)	3.05±0.39(3.1)	0.030*[m]
PLT (x10^9/L)	195.69±81.87	165.87±73.38	205.46±53.78	192.77±73.42	0.469[b]

[b]One-Way ANOVA test: values are given as mean±standard deviation; [m]Kruskal-Wallis H test: values are given as mean±standard deviation (median+Iqr); *p<0.05: statistically significant difference. ChHT: chronic hypertension; GHT: gestational hypertension; BMI: body mass index; kg: kilogram; mg: miligram; dL: deciliter. ALT: alanine transaminase; AST: aspartate transaminase; IU: international unit; g: gram; Hb: hemoglobin; Htc: hematocrite; INR: international normalized ratio; PLT: platelet; L: liter.

Table 2. Effects of pregnancy-related hypertensive disorders on the newborn

	Preeclampsia (n=140)	Eclampsia (n=15)	ChHT (n=24)	GHT (n=13)	p
Birth weight (g)	1985±888	1961±879	2116±850	2551±750	0.156[b]
APGAR (1st min;5th min)	8;9	7;9	7.5;9	9;10	0.212[m]

[b]One-Way ANOVA test: values are given as mean±standard deviation; [m]Kruskal-Wallis H test: values are given as mean±standard deviation (median+Iqr); *p<0.05: statistically significant difference; ChHT: chronic hypertension; GHT: gestational hypertension; g: gram; min: minute.

Table 3. Haemodynamic data recorded on admission and during labour

	Admission (n=192)	Labour (n=192)	p
Pulse rate	94.06±14.21(95)	104.59±18.38(102)	0.001*[a]
SBP	167.53±20.19(168)	167.2±22.61(170)	0.878[a]
DBP	100.39±14.87(100)	102.04±16.74(100)	0.276[a]
SI	0.57±0.12(0.6)	0.63±0.14(0.6)	0.001*[a]
MSI	0.78±0.16(0.8)	0.86±0.18(0.8)	0.001*[a]

[a]Mann Whitney U test: values are given as mean±standard deviation (median); *p<0.05: statistically significant difference. n: number; SBP: systolic blood pressure; DBP: diastolic blood pressure; SI: shock index; MSI: modified shock index.

Table 4. Distribution of haemodynamic data at admission and during labour among the different clinical manifestations of the disorder

	Preeclampsia (n=140)	Eclampsia (n=15)	ChHT (n=24)	GHT (n=13)	p
Pulse rate on admission	94.4±13.7(95)	87.3±14.5(92)	95.5±16.3(93.5)	95.5±14.3(98)	0.409[m]
SBP on admission	166.6±19.6(167)	160.9±23.4(160)	177.5±21.7(175)	166.5±14.9(170)	0.061[m]
DBP on admission	100.7±14.9(100)	100.8±17.7(105)	99.1±13.6(100)	98.5±15.4(100)	0.823[m]
SI on admission	0.58±0.12(0.6)	0.56±0.11(0.6)	0.55±0.11(0.5)	0.58±0.12(0.6)	0.527[m]
MSI on admission	0.78±0.16(0.8)	0.75±0.16(0.8)	0.76±0.11(0.75)	0.8±0.16(0.8)	0.885[m]
Pulse rate during birth	103.6±18.2(100)	116.9±21.4(110)	100.8±16.4(100)	107.7±16.6(105)	0.088[m]
SBP during birth	167.6±22.9(170)	161.1±23.8(162)	171.2±22.7(174)	162.6±18.4(165)	0.508[m]
DBP during birth	102.3±16.9(100)	101±17.5(100)	103.7±16(100)	97.5±15.7(100)	0.838[m]
SI during labour	0.62±0.13(0.6)	0.74±0.18(0.7)	0.6±0.09(0.6)	0.68±0.14(0.7)	0.042*[m]
MSI during labour	0.85±0.18(0.8)	0.95±0.21(0.9)	0.81±0.12(0.8)	0.89±0.18(0.9)	0.147[m]

[m]Kruskal-Wallis H test: values are given as mean±standard deviation (median+Iqr). *p<0.05: statistically significant difference. ChHT: chronic hypertension; GHT: gestational hypertension; n: number; SBP: systolic blood pressure; DBP: diastolic blood pressure; SI: shock index; MSI: modified shock index.

Table 5. Correlation of SI and MSI on admission and during labour with patient outcome(s)

	Creatinine	IUGR	Pulmonary embolism	Seizure	Postoperative serious arrhythmia
SI on admission	0.802	0.913	0.010	0.617	0.035
MSI on admission	0.653	0.658	0.066	0.245	0.092
SI during labour	0.395	0.169	0.654	0.002	0.543
MSI during labour	0.049	0.045	0.829	0.007	0.960

P<0.05: statistically significant difference. IUGR: intrauterine growth retardation; SI: shock index; MSI: modified shock index.

Table 6. The correlation between SI, MSI and transfusion of blood products and maternal and fetal outcomes

	RBC	FFP	Platelets	Birth weight	APGAR	Hospital stay
SI on admission	0.771	<0.001	<0.001	0.870	0.676	0.385
MSI on admission	0.982	<0.001	<0.001	0.495	0.579	0.528
SI during labour	0.013	0.005	0.040	0.205	0.406	0.344
MSI during labour	0.004	0.004	0.065	0.691	0.836	0.315

P<0.05: statistically significant difference. RBC: packed red blood cells; FFP: fresh frosen plasma; APGAR: appearance pulse grimace activity respiration; SI: shock index; MSI: modified shock index.

No statistically significant difference was detected between the groups regarding the use of blood products (p>0.05).

There is a positive, significant correlation between SI and MSI on admission and transfusion of fresh frozen plasma (FFP) and platelet suspension. There is a positive, significant correlation between SI and MSI during labor and transfusion of packed red blood cells (RBC), FFP, and platelet suspension. Moreover, MSI during labor was found to have a positive, significant correlation with the transfusion of FFP and platelet suspension (p<0.05). On the other hand, no significant correlation was detected between the SI and MSI scores and hospital stay, APGAR score, and birth weight (Table 6).

No correlation was observed between the use of blood product(s) and systolic and diastolic blood pressures (p>0.05).

As a result of the regression analysis, the model for estimating the RBC, FFP, and platelet values of the shock index result used during the application was 80.2% successful. Similarly, the model for estimating the RBC, FFP, and platelet values of the modified shock index result used during the application was 73.4% successful. It was observed that the model for estimating the RBC, FFP, and platelet values of the shock index result used during delivery was 69.8% successful, and the model for estimating the RBC, FFP, and platelet values of the modified shock index result used during delivery was 71.9% successful.

DISCUSSION

This study aimed to reveal the predictive value of maternal SI and MSI in the prediction of maternal and fetal outcomes and the need for transfusion of blood and blood products after giving birth. When the patients' values at admission were compared with the values at birth, no difference was found in systolic and diastolic blood pressure values, which are routine follow-up parameters, while a significant increase was found in pulse rate, SI, and MSI values. Moreover, there was a significant relation between admission SI and postoperative embolism and arrhythmia, and between MSI during labor and creatinine and IUGR. The increase in admission and labor SI and MSI values were found to be associated with the transfusion of FFP and platelets, and the increase in SI and MSI during labor were associated with the transfusion of FFP, RBC, and platelets, and the increase in labor SI was associated with elevated platelet transfusion.

There are studies in the literature demonstrating that increased SI and MSI values are effective in the prediction of massive blood transfusion in addition to standard hemodynamic monitoring methods for ensuring early prediction of postpartum hemorrhage. Nathan et al.[16] found the increased SI value to be associated with massive blood transfusion after postpartum hemorrhage. Additionally, Le Bas et al.[17] determined that a SI score of >1.1 at the 10th and 30th minutes after giving birth were effective in predicting hemorrhage and blood transfusion. However, Le Bas et al.[17] did not indicate a significantly increased level in patients with preeclampsia. In this study, we found that increased MSI and SI values recorded on admission to the hospital and during labor in the patient group with the pregnancy-related hypertensive disorder were correlated with the increase in FFP and RBC transfusion. On the other hand, it was also demonstrated that SI on admission and during labor was associated with the transfusion of platelet suspension, and thus, SI was superior to MSI in this regard.

Nevertheless, Borovac-Pinheiro et al.[13] found a positive correlation between the elevated SI value measured during and after labor in patients undergoing vaginal delivery and increased need for blood transfusion, but they did not observe a significant correlation in patients with cesarean section. We, on the other hand, observed that besides increased SI during labor, increased SI at admission was also related to greater transfusion need. Additionally, we observed that elevated SI was indicative of elevated need for blood transfusion in cesarean section patients, as well.

There are studies in the literature demonstrating the predictive value of blood pressure on maternal mortality and morbidity in pregnant women with preeclampsia.[18] However, we did not find a difference between the admission and labor SBP and DBP values of the patients, and moreover, the SI, MSI, and pulse rate on admission were statistically significantly higher than those during labor. These results gave rise to thought that the SI and MSI values of the patients at the time of labor may be more valuable in the prediction of the clinical course of the disease in pregnancy-related hypertensive disorders. Again, in the literature, there are studies indicating that postpartum hemorrhage and blood transfusion are associated with systolic blood pressure.[16] However, in our study, neither systolic nor diastolic blood pressure was found to be correlated with postoperative transfusion. Considering these results, we think that blood pressure measurement cannot be a sufficient predictor for postpartum hemorrhage and need for transfusion in patients who already have pregnancy-related hypertensive disorders, and that although a specific cutoff value could not be determined as in our results, SI and MSI may be effective in predicting postoperative transfusion need in the early period.

There are also studies reporting an association between SI and increased ICU admission and need for reoperation.[16] However, we did not identify a difference regarding the length of hospital stay. We are of the opinion that it may be due to the fact that our sample group was composed of patients with pregnancy-related hypertensive disorders who were followed up at our clinic and underwent caesarean section. Although there was not a statistically significant difference between the groups, the hospital stay in the GHT group was shorter compared to the other groups. This may be due to the fact that the clinical course of GHT is milder compared to other forms of pregnancy-related hypertensive disorder.

There is an increased risk for preterm labor in pregnancy-related hypertensive disorders.[19] It was observed in our study that preterm delivery was statistically significantly higher only in the gestational hypertension group. As in our study, Barton et al.[20] also observed that the risk of preterm labor increased in women with gestational hypertension. There was not a statistically significant difference between the groups regarding birth weight and APGAR scores. However, the majority of studies in the literature reported that the higher the severity of a hypertensive disease is, the higher the risk for preterm birth and small for gestational age (SGA) become.[21] This was associated with the small sample group in our study. However, Sheen et al.[22] examined women with pregnancy-related hypertensive disorders in 2019 and found that eclampsia was seen in the younger patient group. These results are similar to our results and suggest that our sample selection is correct independent of the number of patients included. Also, the fact that the groups did not differ significantly in terms of BMI shows that the patients included in the study may represent a homogeneous group.

Gouda et al.[23] found that increased MSI and SI were positively correlated with fatal arrhythmias in patients with STEMI. We also demonstrated that an admission SI >0.9 was positively correlated with postoperative arrhythmia. As the majority of previous studies reported the MSI >1.3 as a critical level, we accepted 1.3 as the critical MSI value in our study while investigating maternal and fetal complications.[14] However, we did not observe a similar correla-

tion when admission MSI was over 1.3. We thought that it might be due to the differences between patient groups in our study and other studies. We, therefore, believe that there is a need for further studies investigating the correlation with arrhythmia in patient groups with pregnancy-related hypertensive disorders.

Keller et al.[24] found in their study that an SI >0.89 was strongly associated with mortality in cases with pulmonary embolism. In the present study, we observed that the rate of pulmonary embolism was higher among the patients with pregnancy-related hypertensive disorders who had increased SI at admission. Although it has not been indicated in previous studies, we thought that during labor, an SI value >0.7, the upper limit in patients with eclampsia, may have a predictive value regarding seizure development.

The major limitation of our study is that it was designed as a retrospective analysis. Also, the failure to perform a more detailed outcome analysis due to insufficient follow-up data in the postoperative period is another important limitation. It is another important point to note that there are studies showing that there is an increased risk of postpartum hemorrhage and maternal mortality when the SI is above 0.9 in pregnant women, and the normal range of the SI has not been determined in the pregnant patient group, yet.[5,12,13] The SI levels were found to be lower in cases of preeclampsia, eclampsia, and GHT. However, there is a need for further studies addressing this issue.[1]

In several studies, MSI and SI were evaluated together as a part of hemodynamic monitoring. There are also studies indicating that the SI value is higher in healthy individuals presenting to the emergency department compared to hypertensive individuals. However, there are not any studies in the literature investigating SI and MSI in pregnant patients with hypertensive disorders. This is the unique characteristic of our study. It is clear that more studies are needed in this area to reduce maternal and fetal mortality by optimizing patient safety.

Conclusions

We concluded that MSI and SI have a significant predictive value not only in the prediction of maternal and fetal complications but also in predicting the need for postpartum blood transfusion for pregnancy-related hypertensive disorders.

Ethics Committee Approval

This study approved by the Marmara University Faculty of Medicine Ethics Committee (Date: 02.02.2018, Decision No: 09.2018.163).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Conflict of Interest

None declared.

REFERENCES

1. Chaudhary M, Maitra N, Sheth T, Vaishnav P. Shock Index in the prediction of adverse maternal outcome. J Obstet Gynaecol India 2020;70:355–9. [CrossRef]
2. von Schmidt auf Altenstadt JF, Hukkelhoven CWPM, van Roosmalen J, Bloemenkamp KWM. Pre-eclampsia increases the risk of postpartum haemorrhage: A nationwide cohort study in the Netherlands. PLoS ONE 2013;8:e81959. [CrossRef]
3. Chappell LC, Enye S, Seed P, Briley AL, Poston L, Shennan AH. Adverse perinatal outcomes and risk factors for preeclampsia in women with chronic hypertension: A prospective study. Hypertension 2008;51:1002–9. [CrossRef]
4. Roberts JM, Gammill HS. Preeclampsia: Recent insights. Hypertension 2005;46:1243–9. [CrossRef]
5. Nathan HL, Seed PT, Hezelgrave NL, De Greeff A, Lawley E, Anthony J, et al. Shock index thresholds to predict adverse outcomes in maternal hemorrhage and sepsis: A prospective cohort study. Acta Obstet Gynecol Scand 2019;98:1178–86. [CrossRef]
6. Suthar R, Abdelfattah S, Goldman H, Garcia G, Romero-Fischmann D, Escobar M, et al. Pre-eclampsia and acute pulmonary embolism-the importance of making a differential diagnosis: A case report. J Anesth 2017;31:903–6. [CrossRef]
7. Maneschi F, Perrone S, Di Lucia A, Ianiri P. Shock parameters and shock index during severe post-partum haemorrhage and implications for management: A clinical study. J Obstet Gynaecol 2020;40:40–5. [CrossRef]
8. Kohn JR, Dildy GA, Eppes CS. Shock index and delta-shock index are superior to existing maternal early warning criteria to identify postpartum hemorrhage and need for intervention. J Matern Fetal Neonatal Med 2019;32:1238–44. [CrossRef]
9. Birkhahn RH, Gaeta TJ, Terry D, Bove JJ, Tloczkowski J. Shock index in diagnosing early acute hypovolemia. Am J Emerg Med 2005;23:323–6. [CrossRef]
10. Kristensen AK, Holler JG, Hallas J, Lassen A, Shapiro NI. Is shock index a valid predictor of mortality in emergency department patients with hypertension, diabetes, high age, or receipt of β- or calcium channel blockers? Ann Emerg Med 2016;67:106–13. [CrossRef]
11. Mutschler M, Nienaber U, Münzberg M, Wölfl C, Schoechl H, Paffrath T, et al. The Shock Index revisited - a fast guide to transfusion requirement? A retrospective analysis on 21,853 patients derived from the TraumaRegister DGU. Critical Care 2013;17:R172. [CrossRef]
12. Nwafor JI, Obi VO, Onwe BI, Ugoji DPC, Onuchukwu VU, Obi CN, et al. Comparison of performance of shock index and conventional vital sign parameters for prediction of adverse maternal outcomes following major postpartum hemorrhage in Abakaliki, Southeast Nigeria. Tropical J Obstet Gynaecol 2019;36:431–6. [CrossRef]
13. Borovac-Pinheiro A, Ribeiro FM, Morais SS, Pacagnella RC. Shock index and heart rate standard reference values in the immediate postpartum period: A cohort study. PLoS ONE 2019;14:e0217907. [CrossRef]
14. Liu Y, Liu J, Fang A, Shan G, Qi Z, Zhu H, et al. Modified shock index and mortality rate of emergency patients. World J Emerg Med 2012;3:114–7. [CrossRef]
15. Rau CS, Wu SC, Kuo SC, Pao-Jen K, Shiun-Yuan H, Chen YC, et al. Prediction of massive transfusion in trauma patients with shock index, modified shock index, and age shock index. Int J Environ Res Public Health 2016;13:683. [CrossRef]
16. Nathan HL, El Ayadi A, Hezelgrave NL, Seed P, Butrick E, Miller S, et al. Shock index: an effective predictor of outcome in postpartum haemorrhage? BJOG 2015;122:268–75. [CrossRef]

17. Le Bas A, Chandraharan E, Addei A, Arulkumaran S. Use of the "obstetric shock index" as an adjunct in identifying significant blood loss in patients with massive postpartum hemorrhage. Int J Gynaecol Obstet 2014;124:253–5. [CrossRef]
18. Nathan HL, Seed PT, Hezelgrave NL, De Greeff A, Lawley E, Anthony J, et al. Early warning system hypertension thresholds to predict adverse outcomes in pre-eclampsia: A prospective cohort study. Pregnancy Hypertens 2018;12:183–8. [CrossRef]
19. Sibai BM. Management of late preterm and early-term pregnancies complicated by mild gestational hypertension/pre-eclampsia. Semin Perinatol 2011;35:292–6. [CrossRef]
20. Barton JR, Barton LA, Istwan NB, Desch CN, Rhea DJ, Stanziano GJ, et al. Elective delivery at $34^{0}(/)^{7}$ to $36^{6}(/)^{7}$ weeks' gestation and its impact on neonatal outcomes in women with stable mild gestational hypertension. Am J Obstet Gynecol 2011;204:44.e1-5. [CrossRef]
21. Premkumar A, Baer RJ, Jelliffe-Pawlowski LL, Norton ME. Hypertensive disorders of pregnancy and preterm birth rates among black women. Am J Perinatol 2019;36:148–54. [CrossRef]
22. Sheen JJ, Huang Y, Andrikopoulou M, Wright JD, Goffman D, D'Alton ME, et al. Maternal age and preeclampsia outcomes during delivery hospitalizations. Am J Perinatol 2020;37:44–52. [CrossRef]
23. Gouda M, Saad AM, Al-Daydamony MM. Modified Shock Index as a predictor of in-hospital outcome in cases of st-segment elevation myocardial infarction treated with primary percutaneous coronary intervention. J Cardiol Curr Res 2016;7:00255. [CrossRef]
24. Keller K, Coldewey M, Geyer M, Beule J, Balzer JO, Dippold W. Shock index for outcome and risk stratification in acute pulmonary embolism. Artery Res 2016;15:30–5. [CrossRef]

Şok İndeks ve Modifiye Şok İndeksi, Gebeliğe Bağlı Hipertansif Bozukluklarda Morbiditeyi Tahmin Etmede Güvenilir Olabilir

Amaç: Maternal erken uyarı kriterleri sistolik – diyastolik kan basıncı (SKB/DKB), periferik oksijen satürasyonu ile idrar çıkışını içeren ve postoperatif komplikasyonların öngörülmesinde yararlı bir belirteçtir. Şok indeks (SI) ve Modifiye Şok indeks (MSI) ise hipovolemide sıvı ve transfüzyon ihtiyacının belirlenmesinde kullanılmaktadır. Bu çalışmada, gebeliğe bağlı gelişen hipertansif hastalıklarda postpartum kan transfüzyonu ihtiyacı, anne ve fetüste gelişebilecek komplikasyonların ve mortalitenin ön görüsü için erken uyarı sisteminin bir parametresi olarak SI ve / veya MSI kullanımı etkinliğinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Çalışmaya yerel Etik Kurul onayı alındıktan sonra, 2012-2017 tarih aralığında preeklampsi, eklampsi, kronik hipertansiyon ve gebelik hipertansiyonu nedeniyle sezaryen operasyonu geçiren 13-47 yaş aralığında 192 hasta çalışmaya dahil edildi.

Bulgular: Hastaların SI ile başvuru sırasındaki emboli ve aritmi arasında ve doğum sırasında MSI ile İntrauterin Büyüme Geriliği arasında pozitif korelasyon vardı ($p<0.05$). Başvuru sırasındaki SI ve MSI ile taze donmuş plazma ve Trombosit süspansiyonu transfüzyonu arasında anlamlı pozitif korelasyon bulunmaktadır. Doğum sırasındaki SI ile paketlenmiş kırmızı kan hücreleri, taze dondurulmuş plazma ve trombosit süspansiyonu transfüzyonu arasında anlamlı bir pozitif korelasyon vardır. Taze donmuş plazma teslimi ile paketlenmiş kırmızı kan hücresi transfüzyonları sırasındaki MSI arasında anlamlı pozitif korelasyon vardır ($p<0.05$).

Sonuç: Modifiye şok indeksi ve şok indeksinin gebelik ve postpartum kan transfüzyonuna bağlı hipertansif hastalıklarda maternal ve fetal komplikasyonları öngörmede önemli belirteçler olabileceği sonucuna varılmıştır.

Anahtar Sözcükler: Modifiye şok indeks; mortalite; preeklampsi; şok indeks.

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Original Article

A Rare Cause of Pulmonary Hypertension in Patients With Renal Transplant: High-Flow Arteriovenous Fistula

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Keywords: High-flow arteriovenosus fistula; pulmonery hypertension; renal transplantation.

ABSTRACT

Objective: Renal transplant is the most effective form of renal replacement therapy. Most of the patients with renal transplant have a history of hemodialysis before transplantation. Therefore, most have arterıovenous fistulas (AVF). Persistent, high flow AVF, which is a rare cause of pulmonary hypertension, should not be overlooked in patients who develop pulmonary hypertension after transplantation.

Methods: In our study, we retrospectively presented our renal transplant patients who newly developed pulmonary hypertension and followed up in our center. We performed fistula closure in our patients with high-flow AVF, which is one of the rare causes of pulmonary hypertension. We recorded our renal (creatinine, glomerular filtration rate, albuminuria, proteinuria), cardiac (ejection fraction) and pulmonary function (pulmonary pressure) data in the 1st and 3rd month follow-ups after the AVF closure procedure.

Results: We observed improvement in cardiac, renal and pulmonary functions of our patients. While creatinine, proteinuria, albuminuria, and pulmonary artery pressure values decreased after AVF closure; GFR and ejection fraction increased. Changes were statistically significant (p values <0.001)

Conclusion: Pulmonary hypertension may develop in renal transplant patients. High-flow fistula is a rare cause of pulmonary hypertension. The presence of high-flow fistula should be kept in mind among the causes of pulmonary hypertension in patients with renal transplantation. Nephrologists should keep in mind the presence of high-flow AVF in patients with newly developing symptoms of pulmonary hypertension.

INTRODUCTION

Kidney transplantation (KT) is the preferred treatment option and provides a significant survival advantage in patients with end-stage kidney disease (ESKD).[1] A large proportion of patients are being treated with hemodialysis (HD) until transplantation. Arteriovenous fistulas (AVF) are the most preferred access in hemodialysis.[1] For most patients, the AV access is maintained after KT in view of the potential risk of losing allograft function and the future need to restart HD. In current clinical practice, the AV access is ligated in the vast minority of transplant recipients as reported in a study about a cohort of 167,000 patients in which only 4.6% of patients underwent AV access ligation after KT.[1] The presence of persistent arteriovenous fistula in patients with KT has effects on the pulmonary and cardiovascular systems. The hemodynamic effects after AVF creation include decreased peripheral resistance and thus increased cardiac output. Because of this continuous hyperdynamic circulation, both left ventricular mass and pulmonary artery pressure increase. In some patients, the effective cardiac output decreases, leading to insufficient systemic perfusion.[2]

Most of the studies in hemodialysis and kidney transplant patients are concerned with the development of fistula-associated pulmonary hypertension (PAH), often caused by high pulmonary blood flow and/or increased pulmonary vascular resistance.[2-4] PAH is generally more frequent in patients on hemodialysis (31.6%) compared with patients on peritoneal dialysis (8.3%) or after kidney transplantation (5%). Remodeling of the pulmonary vascular system seems to be reversible after renal transplantation. This remodeling may be blocked or PAH may even deteriorate in patients with high-flow fistulas.[1] It is controversial whether fistula ligation or reconstruction should be performed in transplant recipients with pulmonary hypertension. There is no consensus on this issue. Clarkson et al.[5] and Kabitz et al.[6] showed that elevated systolic pulmonary artery

pressure can be corrected immediately after fistula ligation. Vanderweckene et al.[7] showed that persistent functional AVF was associated with decreased renal clearance and increased risk of graft loss in renal recipients. On the other hand, some researchers have discussed that prolonged persistent AVF is not at risk for cardiac function in renal transplant recipients.[8-10] Reviewing this controversial issue, Einollahi et al.[11] reported that more prospective data are needed on the long-term effects of fistula ligation on morbidity and mortality in kidney transplant patients.

The aim of our study is to examine the effects of post-transplant AV fistula ligation in our patients with pulmonary hypertension on the symptoms, kidney functions, pulmonary artery pressures, and ejection fractions of our patients.

MATERIALS AND METHODS

We retrospectively reviewed the files of our renal transplant recipients between December 2008 and December 2022. We evaluated 15 patients with pulmonary hypertension of unknown etiology who had dyspnea in their post-transplant follow-up. Our patients were in the hemodialysis program before renal transplantation and had persistent AVF. They were admitted to our outpatient clinics with dyspnea, increased creatinine levels, and unexplained pulmonary edema at different times after transplantation. All kidney transplant patients had no previous pulmonary hypertension and heart failure, and all of them had a fistula with a brachial arterial flow rate of at least 1,200 mL/min. We recorded clinical demographic data [age, gender, body weight, height, body mass index (BMI)], presence of hypertension and diabetes mellitus, RRT characteristics (type, duration), the flow rates and diameters of the fistulas. We also recorded serum creatinine, estimated glomerular filtration rate (eGFR) values, albuminuria, proteinuria, the left ventricle ejection fraction (LVEF), and systolic pulmonary artery pressure (sPAP) values before AVF surgical closure (T0), one month (M1), and 3 months (M3) after surgery. Ethics committee approval of our study was obtained from the ethics committee of Dr. Lütfi Kırdar City Hospital with the number 2023/514/247/7. Written informed consent was obtained from all patients. Statistical Analysis Descriptive statistics were presented as mean ± standard deviation for normally distributed variables or median with interquartile range (IQR) for non-normally distributed continuous variables. Categorical variables were expressed with frequency and percentages (%). Normal distribution of data was assessed by using the Shapiro-Wilk test. The Friedman test was performed to examine statistical differences between baseline, first, and last measurement for serum creatinine, eGFR, albuminuria, proteinuria, PAP, and ejection fraction. The differences between repeated measurements during follow-up were illustrated with a box plot by using the boxplot function in RStudio (v.4.0.2). All statistical analysis was two-tailed, and p values <0.05 were considered statistically significant. All statistical analyses were performed by SPSS software version 21 (Chicago, IL).

Table 1. Patients characteristics

	Patients (n=15)
Age	45.93±15.36
Sex, Male	10 (66.7)
Hypertension	15 (100)
Diabetes	4 (26.7)
Type of kidney transplantatıon (live/deceased)	11(73.3)/4(26.7)
Time after fistula craetıon, mo	109.33±60.99
Time after transplantatıon, mo	76,3±49.15
Fistula flow, ml/dak	2632±1436.51
Fistula diameter, mm	5.1 (4.6–6.2)
Body mass index	26.46±3.20
Hemoglobin, gr/dl	11.99±0.84
Systolic blood pressure	136 (126–140)
Diastolic blood pressure	82.6±10.29
Heart rate, beats/min	80.5±6.5

RESULTS

Clinical demographic and laboratory characteristics of our patients are presented in Table 1. Five of our patients were female and ten were male. The median age was 45.9±15.36 years. AVFs were in all patients located on the forearm. Eleven patients had living-donor kidney transplantations, four patients had deceased-donor kidney transplantations. Fifteen patients had hypertension and four patients had diabetes. The complaints of our patients were swelling of

Table 2. Comparıson of values before and after of AVF closure procedure

	Before AVF closure valeus	After AVF closure valeus (first month)	After AVF closure valeus (third month)	P values
Serum kreatinin, mg/dl	1.4 (1.2-1.9)	1.2 (0.9-1.3)	1.1 (0.9-1.2)	<0.0011,2
Proteinuria, mg/day	284 (159-934)	154 (81-650)	180 (68-350)	<0.0011,2
Albuminuria, mg/day	110 (62-299)	61 (14-130)	68 (18-102)	<0.0011,2
eGFR ml/dk	66 (51-88)	72 (56-96)	70 (62-96)	<0.0011,2
PAB mmHg	35 (30-40)	20 (18-22)	18 (16-20)	<0.0011,2
Ejection fractions, %	35 (30-40)	60 (55-60)	65 (60-66)	<0.0011,2

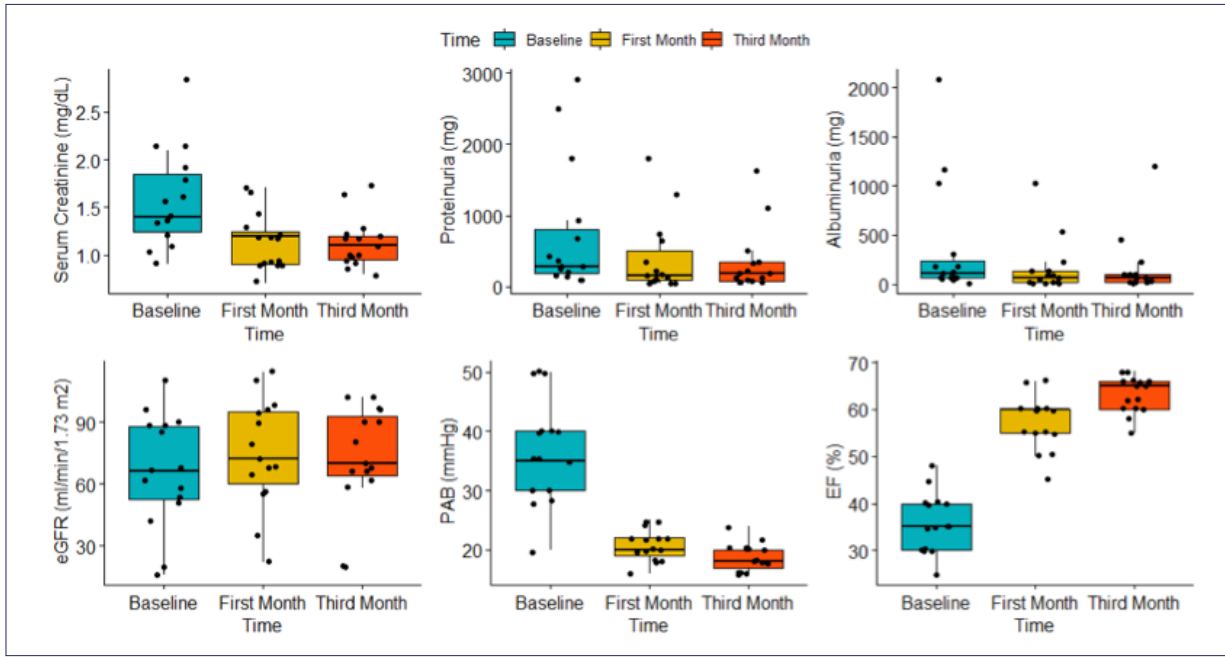

Figure 1. Serum creatinine, proteinüri, albuminuri, pulmonary arter pressure values decreased after closing AVF fistulas. Ejection fraction and EGFR values increaed after closing AVF fistulas.

the legs, shortness of breath, and decreased effort capacity. No signs of rejection were detected. Transthoracic echocardiography showed signs of heart failure, and a significant increase in pulmonary artery pressures. Flow velocity was found to be high in the fistula in Doppler ultrasonography. The median fistula flow rate was 2632 mL/min. After the AVF fistulas were closed, the complaints of our patients decreased. Comparison of data before and after the AVF (arterio-venous fistula) closure procedure are presented in Table 2. After the AVF closure procedure, the serum creatinine, albuminuria, proteinuria, ejection fraction, and PAP values significantly decreased compared to the values obtained before the AVF closure procedure ($p<0.001$). The values between the 1st month and the 3rd month are not statistically significant. Changes in serum creatinine, eGFR, proteinuria, albuminuria, sPAP, LVEF values of our patients are shown in Figure 1. The differences between repeated measurements during follow-up were illustrated with a box plot.

DISCUSSION

In our study, we presented the findings obtained before and after AVF surgical closure in our renal transplant patients. Our 1st and 3rd-month results were statistically significant compared to results obtained before AVF surgical closure. While there was an increase in eGFR and ejection fractions, we found a decrease in creatinine, proteinuria, albuminuria, and pulmonary artery pressures.

Persistent AVF is one of the rare causes that can cause pulmonary hypertension and can cause steal syndrome, edema, cosmetic defects, and heart failure. There is no clear consensus on the management of persistent fistulas after successful kidney transplantation. Although the general opinion is that persistent fistulas that are symptomatic should be closed, there is great variation in routine clinical management.[7] There are retrospective data showing that the closure of previously performed fistulas prevents the formation of high-output heart failure up to 25%. In a study by Abedini et al.[3] in 2013, systolic PAP was found to be higher in hemodialysis patients compared to previous peritoneal dialysis or kidney transplant patients, and it was shown to decrease after kidney transplantation. Based on these retrospective data, in 2020 Hetz et al.[12] conducted a prospective, randomized, controlled trial evaluating the potential benefit of ligature for high-flow AV fistulas. In this study, it was shown that the load on the right and left heart systems is reduced after fistula ligation. Several studies have shown a decrease in the left ventricle (LV) volume after AVF closure procedure. Patients referred for fistula closure are generally those who develop symptomatic heart failure.[5] Most studies in renal transplant patients have shown that AVF closure regresses LV hypertrophy, especially in symptomatic patients.[13-19]

In a randomized controlled study planned by Hertz et al.[20] in 2020 with 28 renal transplant patients with AVF, it was commented that prophylactic fistula closure might prevent heart failure.

Our study has some limitations. The small number of patients is the main limitation of the study. Secondly, asymptomatic patients were not included in the study.

Conclusion

AVF closure in symptomatic renal transplant recipients is associated with improved renal and cardiac functions. AVF flow should be evaluated in renal transplant patients who

develop symptoms of pulmonary hypertension. Further studies with larger samples, including both symptomatic and asymptomatic kidney transplant patients, are needed to assess the long-term clinical outcomes of AVF surgical closure.

Ethics Committee Approval

This study approved by the Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee (Date: 12.04.2023, Decision No: 2023/514/247/7).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: S.Y.; Design: S.Y.; Supervision: S.Y.; Fundings: S.Y.; Materials: S.Y.; Data: S.Y.; Analysis: S.Y.; Literature search: S.Y.; Writing: S.Y.; Critical revision: S.Y.

Conflict of Interest

None declared.

REFERENCES

1. National Kidney Foundation - Dialysis Outcomes Quality Initiative. NKF-DOQI clinical practice guidelines for vascular access. Am J Kidney Dis 1997;30:S150–91. [CrossRef]
2. Yigla M, Abassi Z, Reisner SA, Nakhoul F. Pulmonary hypertension in hemodialysis patients: An unrecognized threat. Semin Dial 2006;19:353–7. [CrossRef]
3. Abedini M, Sadeghi M, Naini AE, Atapour A, Golshahi J. Pulmonary hypertension among patients on dialysis and kidney transplant recipients. Ren Fail 2013;35:560–5. [CrossRef]
4. Agarwal AK. Systemic effects of hemodialysis access. Adv Chronic Kidney Dis 2015;22:459–65. [CrossRef]
5. Clarkson MR, Giblin L, Brown A, Little D, Donohoe J. Reversal of pulmonary hypertension after ligation of a brachiocephalic arteriovenous fistula. Am J Kidney Dis 2002;40:e8.1–4. [CrossRef]
6. Kabitz HJ, Walterspacher S, Geyer M, Fischer KG, Huber TB, Muendlein E, et al. Reversible pulmonary hypertension in a kidney transplant with patent A-V fistula. Clin Kidney J 2012;5:347–9. [CrossRef]
7. Vanderweckene P, Weekers L, Lancellotti P, Jouret F. Controversies in the management of the haemodialysis-related arteriovenous fistula following kidney transplantation. Clin Kidney J 2018;11:406–12. [CrossRef]
8. Soleimani MJ, Shahrokh H, Shadpour P, Shirani M, Arasteh S. Impact of dialysis access fistula on cardiac function after kidney transplantation. Iran J Kidney Dis 2012;6:198–202.
9. Głowiński J, Małyszko J, Głowińska I, Myśliwiec M. To close or not to close: Fistula ligation and cardiac function in kidney allograft recipients. Pol Arch Med Wewn 2012;122:348–52. [CrossRef]
10. De Lima JJ, Vieira ML, Molnar LJ, Medeiros CJ, Ianhez LE, Krieger EM. Cardiac effects of persistent hemodialysis arteriovenous access in recipients of renal allograft. Cardiology 1999;92:236–9. [CrossRef]
11. Einollahi B, Sadeghi Ghahrodi M. Hemodialysis arteriovenous fistula after transplant: To keep or not to keep? Iran J Kidney Dis 2012;6:159–61.
12. Hetz P, Pirklbauer M, Müller S, Posch L, Gummerer M, Tiefenthaler M. Prophylactic ligature of AV fistula prevents high output heart failure after kidney transplantation. Am J Nephrol 2020;51:511–9. [CrossRef]
13. Unger P, Xhaët O, Wissing KM, Najem B, Dehon P, van de Borne P. Arteriovenous fistula closure after renal transplantation: A prospective study with 24-hour ambulatory blood pressure monitoring. Transplantation 2008;85:482–5. [CrossRef]
14. van Duijnhoven EC, Cheriex EC, Tordoir JH, Kooman JP, van Hooff JP. Effect of closure of the arteriovenous fistula on left ventricular dimensions in renal transplant patients. Nephrol Dial Transplant 2001;16:368–72. [CrossRef]
15. Unger P, Wissing KM, de Pauw L, Neubauer J, van de Borne P. Reduction of left ventricular diameter and mass after surgical arteriovenous fistula closure in renal transplant recipients. Transplantation 2002;74:73–9. [CrossRef]
16. Sumida K, Molnar MZ, Potukuchi PK, Thomas F, Lu JL, Ravel VA, et al. Association between vascular access creation and deceleration of estimated glomerular filtration rate decline in late-stage chronic kidney disease patients transitioning to end-stage renal disease. Nephrol Dial Transplant 2017;32:1330–7. [CrossRef]
17. Golper TA, Hartle PM, Bian A. Arteriovenous fistula creation may slow estimated glomerular filtration rate trajectory. Nephrol Dial Transplant 2015;30:2014–8. [CrossRef]
18. Korsheed S, Eldehni MT, John SG, Fluck RJ, McIntyre CW. Effects of arteriovenous fistula formation on arterial stiffness and cardiovascular performance and function. Nephrol Dial Transplant 2011;26:3296–302. [CrossRef]
19. Schier T, Göbel G, Bösmüller C, Gruber I, Tiefenthaler M. Incidence of arteriovenous fistula closure due to high-output cardiac failure in kidney-transplanted patients. Clin Transplant 2013;27:858–65. [CrossRef]
20. Hetz P, Pirklbauer M, Müller S, Posch L, Gummerer M, Tiefenthaler M. Prophylactic ligature of AV fistula prevents high output heart failure after kidney transplantation. Am J Nephrol. 2020;51:511–9. [CrossRef]

Böbrek Nakilli Hastalarda Pulmoner Hipertansiyonun Nadir Bir Sebebi: Yüksek Akımlı Arteriyovenöz Fistül

Amaç: Renal transplantasyon, günümüzde renal replasman tedavisinin en etkili şeklidir. Böbrek nakli olan hastaların çoğunda nakil öncesi hemodiyaliz öyküsü vardır. Bu nedenle hastaların çoğunda hemodiyaliz giriş yolu olan arteriyovenöz fistül (AVF) mevcuttur. Pulmoner hipertansiyonun nadir bir nedeni olan persistan yüksek akımlı AVF, transplantasyon sonrasında pulmoner hipertansiyon gelişen hastalarda göz ardı edilmemelidir.

Gereç ve Yöntem: Çalışmamızda merkezimizde takip edilen ve nakil sonrası yeni pulmoner hipertansiyon gelişen renal transplant hastalarımızı retrospektif olarak sunduk. Pulmoner hipertansiyonun nadir nedenlerinden biri olan yüksek akımlı AVF'li hastalarımıza fistül kapatma işlemi gerçekleştirdik. İşlem sonrası 1. ay ve 3. ay takiplerde renal (kreatinin, glomeruler filtrasyon hızı (GFR), albumünüri, proteinüri), kardiyak (ejeksiyon fraksiyonu) ve pulmoner fonksiyon (pulmoner basınç) verilerimizi kaydettik. Takiplerde hastalarımızın renal kardıyoloji k ve pulmoner fonksiyonlarında iyileşme gözlemledik.

Bulgular: Takiplerde hastalarımızın renal kardıyoloji ve pulmoner fonksiyonlarında iyileşme gözlemledik.

İşlem sonrası 1. ay ve 3. ay takiplerde renal (kreatinin, glomeruler filtrasyon hızı, albumünüri, peroteinüri), kardiyak (ejeksiyon fraksiyonu) ve pulmoner fonksiyon (pulmoner basınç) verilerimiz: AVF Kapatma işleminden sonra kreatin, proteinüri, albüminüri ve pulmoner arter basınç değerleri azalırken; GFR ve ejeksiyon fraksiyonu arttı. Değişiklikler istatistiksel olarak anlamlıydı (p değerleri <0.001)

Sonuç: Renal transplantlı hastalarda pulmoner hipertansiyon gelişebilir. Yüksek akımlı fistül pulmoner hipertansiyonun nadir nedenlerindendir. Renal nakilli hastalarda hastalarda pulmoner hipertansiyon sespleri arasında yüksek akımlı fistül varlığı akılda tutulmalıdır. Nefrologlar, yeni gelişen pulmoner hipertansiyon semptomları olan hastalarda yüksek akımlı AVF'nin varlığını akılda tutmalıdırlar.

Anahtar Sözcükler: Pulmoner hipertansiyon; renal transplant; yüksek akımlı arteriyovenöz fistül.

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Original Article

Factors Effecting Readmission of Acute Heart Failure Patients to Emergency Department

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Keywords: Acute heart failure; emergency department; hospital readmission.

ABSTRACT

Objective: The clear reasons for the re-presentation of acute heart failure patients to the emergency department have not been definitively established in the literature, yet it is anticipated that this patient group will utilize emergency services more frequently in the future. In our study, we aimed to determine the impact of demographic, biochemical, imaging, and outcome variables on the re-presentation to the emergency department within 90 days in patients revisiting due to acute heart failure.

Methods: Patients revisiting the emergency department within 90 days due to acute decompensated heart failure between January 1, 2019, and January 1, 2021, were included in our study. A retrospective analysis of patients' demographic and clinical characteristics was conducted, and factors influencing re-presentation were evaluated.

Results: Our study included 250 patients who revisited the emergency department on average after 34±12.5 days. A significant relationship was observed between patients requiring intensive care unit or hospital admission and their re-presentation within 90 days ($p<0.005$). Furthermore, patients who received non-invasive mechanical ventilation in the emergency department re-presented earlier compared to those who did not ($p<0.005$). Patients' ejection fraction values were also found to be associated with early re-presentation ($p<0.005$). Pearson's R correlation analysis revealed a significant relationship between the use of furosemide within 90 days and re-admission ($r=0.2015$, $p=0.0014$).

Conclusion: Our research demonstrated that re-presentation is influenced by the use of NIMV, furosemide, low ejection fraction, and hospitalization. Consequently, exercising caution while discharging patients receiving NIMV and high-dose furosemide in the emergency department, as well as formulating a follow-up strategy for patients with low ejection fraction in acute heart failure, holds paramount importance.

INTRODUCTION

Heart failure is a disease characterized by multiple acute decompensations, progressive deterioration of heart function, and, eventually, death of the patient. Heart failure has been reported as one of the most important causes of unplanned hospitalizations, along with polypharmacy, urinary incontinence, and dementia.[1,2] It is known that heart failure patients use every aspect of the healthcare system, and the applications of this patient group to primary healthcare services have decreased in recent years,[3] which might eventually lead to more acute decompensations and eventually more utilization of emergency department resources.

Acute heart failure is a global public health problem, and the overall clinical prognosis of patients with acute heart failure is grim.[4] According to U.S. data, acute heart failure results in over one million annual hospitalizations and is one of the leading causes of rehospitalization within 30 days.[5] Patients with acute heart failure are primarily treated in emergency departments, regardless of the severity of their symptoms. Although various studies have been conducted with the aim of reducing hospitalizations for heart failure, the literature lacks detailed information from emergency departments. While some risk factors predicting readmission of heart failure patients have been identified in the literature, there are contradictory views about which parameters are most valuable.[6]

Because heart failure is one of the most common reasons for hospital admission of adults older than 65 years, it is vital to find ways to predict readmission in order to re-

duce costs, morbidity, and mortality.[7] The decision to discharge a patient from the emergency department is generally based on an evaluation of the patient's clinical status, response to treatment, and the presence of acute coronary syndrome.[8] Previous studies have shown that rehospitalization of up to 50% of patients can be prevented with a short follow-up and treatment, suggesting that emergency department discharge criteria need to be revised.[9] Identifying the clinical parameters of heart failure patients that can be easily measured in the emergency department may help clinicians predict hospital readmission and aid in discharge planning.[10] Determining the risk factors for a patient's return to the emergency department may contribute to planning the patient's ongoing treatment.[11]

Our study aimed to determine the effects of demographic, biochemical, imaging, and outcome parameters on readmission rate within 90 days in patients admitted to the emergency department with acute heart failure.

MATERIALS AND METHODS

This study included patients with acute decompensated heart failure who applied to a tertiary research hospital emergency department between January 1, 2019 and January 1, 2021, and who reapplied within 90 days. Based on the results of the HAPPY study, the country-wide population prediction was calculated as 6.9%. Based on this study, the required number of patients was determined as 100 in the sample size calculation made with a 95% confidence interval and 5% margin of error; our study's final sample size included 250 patients. If a patient had more than one application within 90 days, only the data obtained from the first application were included. In this retrospective study, the following information was collected from the hospital information management system (HIMS): sociodemographic information (age, gender); biochemical results, including hemogram, urea, creatinine, CRP, sodium, potassium, calcium, AST, ALT, BNP, pH, lactate; imaging data (echocardiography [ECHO]); noninvasive mechanical ventilation [NIMV] treatment , and patient outcome data (discharge, regular ward admission, or intensive care admission) and hospital length of stay. The normal values of the investigated parameters were as follows: urea 16.6–48.5 mg/dL, creatinine 0.7–1.2 mg/dL, CRP 0–5 mg/dL, sodium 136–145 mEq/L, potassium 3.5–5.5 mEq/L, calcium 8.4–102 mg/dL, pH 7.35–7.45, lactate 0–0.9 mmol/L , and BNP 0–100 pg/mL. Hemogram values were analyzed according to the recommendations of the World Health Organization.[12] In line with the 2021 European Society of Cardiology acute heart failure guidelines, the patients were categorized as having heart failure with a mild/low ejection fraction, heart failure with a preserved ejection fraction, or heart failure with a low ejection fraction.[13] Posteroanterior chest X-rays were analyzed to detect pleural effusion. We also used a scoring system developed by Kobayashi et al.[14] in 2019, which aims to determine the prognosis of heart failure (HF) patients. The reapplication rate of the patients within 90 days was determined using the HIMS and recorded.

Statistical Analyses

The data were analyzed using the SPSS V.19.0 statistical analysis program, and the findings were analyzed at a 95% confidence interval and a 5% significance level.[15] Number and percentage were used to describe categorical data; mean and standard deviation were used for numerical data. Kolmogorov–Smirnov or Shapiro–Wilk test was used to determine whether the groups were normally distributed. Student's t-test and Mann–Whitney U test were selected to evaluate numerical data, and Chi-square test was used to evaluate categorical data. Correlation analysis was performed between the continuous data with a nominal distribution. Linear regression analysis was performed to evaluate the relationship between the data. A value of $p \leq 0.05$ was considered statistically significant.

RESULTS

Our study included 250 patients who were readmitted to the emergency department after an average of 34±12.5 days. The relationships between age, gender, biochemical parameters, diagnostic parameters, the use of NIMV, and the readmission of patients are presented on Table 1. Table 2 shows the relationship between the patients' comorbidities and their readmission. There was a significant difference between the readmission times of discharged patients (n=124) and patients who were hospitalized in the intensive care unit (n=76) ($p<0.005$). There was also a significant difference between the readmission times of patients discharged from the hospital and those admitted to the cardiology ward ($p<0.005$). Table 3 shows the analysis of the parameters affecting readmission using multiple regression analysis; it was determined that hospitalized patients showed a high readmission rate ($p<0.005$). The comorbidities in our patient population included hypertension (n=190), diabetes mellitus (n=96), coronary artery disease (n=121), chronic renal failure (n=71), chronic obstructive pulmonary disease (n=71), atrial fibrillation (n=41), malignancy (n=24), and neurological disease (n=8). The average readmission times of patients with these diseases were 34.94±23.12, 34.83±22.55, 36.35±23.19 35.19±21.79, 30.87±21.57, 38.07±23.91, and 36.8±18 days, respectively.

The potassium values of the patients were categorized as below 3.5 mEq/L, between 3.5 and 5.5 mEq/L, or above 5.5 mEq/L, and were included in the additional analysis. Ten patients had potassium levels below 3.5 mEg/L; 226 patients had potassium levels between 3.5 and 5.5 mEq/L; and 14 patients had potassium levels above 5.5 mEq/L. While hospital readmission and low/average potassium values were correlated ($p=0.0033$), there was no relationship between hospital readmission and average/high potassium values ($p=0.553$).

The mean BNP level was 3463 pg/mL. The effect of BNP value on readmission was not statistically significant ($p=0.648$) A significant relationship was found between furosemide use and readmission time ($r=0.2015$, $p=0.0014$). There was no significant difference between

Table 1. Characteristics of patients and relationship with readmission times

		n	Mean readmission duration in days (Mean+SD)	p	r	CI
Gender						
Male		119	32.25±22.19	0.23	0.48	-2.27 to 9.23
Female		131	35.73±23.84	0.25	0.59	-3.87 to 7.65
Na		250	34.5±5.25	0.39	0.002	-0.07 to 0.17
≤135 meq/L		109	32.46±6.58			
>135 meq/L		143	35.29±4.63			
K		250	44.49±0.63	0.05	0.01	-0.003 to 0.24
≤3.5 meq/L		14	11.22±4.96			
3.5-5.5 meq/L		219	35.41±5.49			
>5.5 meq/L		17	28.93±3.54			
Lactate		250	33.5±1.07	0.89	6.54	-0.13 to 0.11
≤0.9 mmol/L		60	32.7±1.56			
>0.9 mmol/L		190	34.51±4.65			
Hemogram		250	41.18±2.06	0.63	0.008	-0.15 to 0.09
Male	Female					
≤8 g/dl	≤8 g/dl	15	46.56±6.53			
11-8 g/dl	11-8 g/dl	102	49.75±4.98			
13-11 g/dl	12-11 g/dl	65	44.66±3.67			
>13 g/dl	>12 g/dl	68	45.85±2.5			
Blood urea nitrogen		250	40.89±7.98	0.63	0.0009	-0.25 to 0.18
≤48 mg/dl		90	34.39±24.6			
>48 mg/dl		160	34.6±22.42			
Creatinine		250	38.96±3.65	0.92	0.0009	-2.65 to 4.96
≤1.2 mg/dl		118	45.5±9.86			
>1.2 mg/dl		132	45.5±8.75			
C-reactive protein		250	46.97±3.46	0.43	0.08	-3.47 to 1.69
≤100 mg/dl		238	47.45±9.56			
>100 mg/dl		12	45.98±6.63			
Aspartate aminotransferase		250	43.56±9.46	0.11	0.04	-1.98 to 0.62
≤40 mg/dl		221	44.96 ±8.63			
>40 mg/dl		29	42.36±4.36			
Alanin aminotransferase		250	39.78±5.22	0.108	0.025	-2.62 to 0.96
≤40 mg/dl		226	39.75±4.69			
>40 mg/dl		24	39.98±7.32			
ph		250	39.32±4.66	0.156	0.0235	-0.78 to 3.45
≤7.35		68	37.35±5.78			
7.35-7.45		139	40.21±7.65			
>7.45		43	39.86±4.69			
Ejection fraction		250	46.68±12.91			
<41%		98	34.29±23.03	0.02	0.04	-1.10 to 1.12
41%-49%		17	45±0	<0.001	0.009	-0.10 to 0.15
>49%		135	56.78±6.12	0.007	0.01	-2.26 to 0.38
Congestion scores						
1		82	42.6±5.69	0.68	0.12	-2.50 to 7.61
2		146	38.86±7.56	0.15	0.27	-0.004 to 2.15
3		22	37±9.56	0.31	0.96	-1.35 to 3.64
Noninvasive mechanical ventilation						
Yes		28	32.92±22.65	0.02	0.006	-0.57 to 0.98
No		222	43.25±24.91	0.09	0.07	-3.54 to 7.85
Outcome						
Hospitalisation		124	28.22±21.19	0.03	0.06	-0.13 to 0.11
Discharge		50	37.58±22.87	0.000	0.004	-0.25 to 0.89
Intensive care		76	41.33±24.05	0.62	0.15	-1.98 to 1.78
Furosemide dosage						
<140mg		110	28.75±23.10	0.01	0.02	-1.10 to 1.12
>140mg		140	38.59±23.19			

Table 2. Relationship between readmission times and chronic diseases

											t	P	Estimate	STD	95% confidence interval
Readmission time in days	1										8.03	<0.0	33.4	4.16	25.2 to 41.6
Hypertension	-0.58	1									0.12	0.89	0.438	3.45	-6.37 to 7.24
Diabetes mellitus	-0.22	-0.15	1								0.47	0.63	-1.4	3.13	-7.65 to 4.70
Coronary artery disease	-0.52	0.05	0.00	1							1.13	0.25	3.57	3.15	-2.64 to 9.78
Valve disease	-0.16	0.03	0.04	0.06	1						1.65	0.09	-11.4	6.94	-25.1 to 2.19
Chronic pulmonary disease	-0.31	0.03	0.02	0.07	0.03	1					1.20	0.22	-4.01	3.32	-10.5 to 2.53
Chronic renal disease	-0.21	-0.05	-0.11	-0.003	0.08	0.12	1				0.30	0.75	-1.05	3.43	-7.81 to 5.70
Neurological disease	-0.26	-0.05	0.15	0.17	0.04	0.00	0.11	1			0.29	0.77	-1.39	4.75	-10.7 to 7.98
Atrial fibrillation	-0.32	-0.03	0.09	0.30	-0.06	0.00	0.07	0.07	1		1.59	0.11	6.78	4.24	-1.57 to 15.1
Malignancy	-0.21	-0.01	0.03	0.09	0.01	0.06	0.04	0.06	0.13	1	0.01	0.989	0.067	4.95	-9.69 to 9.82

Table 3. Multiple regression analysis showing the relationship between parameters affecting readmission time

Variable	Estimate	SE	95% CI	t	P
Outcome	5.78	1.54	2.74 to 8.81	3.75	0.0002
Potassium	4.39	2.25	-0.03 to 8.83	1.95	0.05
Congestion score	2.55	2.56	-2.50 to 7.61	0.99	0.32
Ejection fraction	0.12	0.11	-0.09 to 0.34	1.08	0.27
Non-invasive mechanical ventilation	0.14	0.13	0.01- 0.26	1.24	0.02

lactate values (n=190) (p=0.597).

Correlations were found between EF, congestion score, and BNP, and the status of NIMV use. The mean EF value of the patients treated with NIMV was significantly lower (p=0.0144), while the mean congestion score of the patients treated with NIMV was significantly higher (p<0.0001). No significant correlation was found between the BNP values and NIMV need (p=0.9121). An analysis revealed a significant relationship between furosemide use and the 90-day readmission rate (r=0.2015, p=0.0014).

In the study, 124 of the patients were admitted during their first visit. The average duration of hospitalization was determined as 7.48 days with a median of 3.8. While an association was found between the length of hospital stay and hemoglobin levels (p=0.038), no relationship was observed between the length of stay and EF (ejection fraction), the utilization of NIMV in the emergency department, or the dosage of Lasix administered in the emergency department (with respective p-values of 0.952, 0.097, and 0.852).

DISCUSSION

The reasons for hospital readmission within 90 days of a visit to an emergency department with acute heart failure are unclear. In previous studies, the time before hospital readmission of patients presenting with acute heart failure is unclear, the clinical characteristics of patients are ignored, and the treatments provided to patients are varied and not standard. For this reason, standardization is necessary in evaluating the parameters that lead to readmission.

A study of 116 heart failure patients who were hospitalized for any reason found that many comorbidities, in particular depression and chronic lung disease, predicted readmission within 30 days.[16] Another study reported that parameters such as low health literacy, a history of cerebrovascular disease, and not using beta blockers affected readmission within 30 days, mostly in patients with heart failure.[17] Contrary to the literature, our study found that no other disease predicted readmission to the emergency department. Since our study was retrospective, we could not measure the severity of the diseases that might cause early return to the emergency department.

Previous studies have examined the effects of biochemical parameters and the clinical characteristics of patients at the time of admission on out-of-hospital outcomes. For example, in a study evaluating readmission to the emergency department for heart failure, patients' hemoglobin levels were classified according to the criteria of the World Health Organization, and it was observed that anemia increased both hospitalization and emergency department visits.[18] A study of 1.033 patients showed that approximately 10% of patients with BNP, troponin elevation, clinical tachypnea, and dialysis experienced adverse events.[19] In a study examining the readmission of patients discharged from the emergency department, previous percutaneous intervention or bypass, the use of antiarrhythmics, heart rate above 80/min, systolic blood pressure below 140 mmHg, oxygen saturation above 96%, high troponin level, and pleural effusion were shown to be effective.

[20] In a study of patients discharged from the emergency department, 30-day adverse effects were examined, and heart valve disease, COPD, malignancy, New York Class 3, and low serum sodium were found to be predictive for readmission. In that study, the precipitating factors were anemia, acute kidney injury, and a lack of detailed and precise recommendations for discharge.[21] Another analysis stated that a significant portion of the patients reapplied to the emergency department after 16–30 days, and the most influential parameters during the 30-day readmission period were disability, more than one emergency service admission, hospitalization for more than five days at the first admission, and a high BUN value.[22] Another study examining the relationship between discharge from the emergency department and readmission found no relationship between readmission and patients' age, gender, blood pressure, EF, or coronary artery disease, while a relationship was found between readmission and high creatinine levels and previous hospitalization due to HF.[23]

In our study, EF and potassium levels lower than accepted clinical values were predictive of readmission, while no effects on readmission were demonstrated for other parameters, including BNP and anemia. Anemia is a clinical condition that has been shown to affect mortality and morbidity in heart failure patients, and clinicians provide effective treatment for heart failure patients with anemia. [23] Therefore, anemia evaluated in the emergency department may not have affected readmission, as the condition is likely to be treated after hospitalization at outpatient clinics. As ejection fraction is one of the main determinants of the severity of heart failure and a worse prognosis,[24] a relationship between low ejection fraction and early return to the emergency department is expected.

Indices such as HOSPITAL, which are based on data that can be easily obtained retrospectively, such as hospitalization, hemoglobin level, and emergency service admissions, have been put forward in evaluating readmissions to hospitals due to various diseases. However, the relationship between these scores and the readmission of acute heart failure patients to emergency services has not been demonstrated.[25] In a study performed on 704 patients with previously mentioned scores,[25] the hospitalization of heart failure patients was found to be a predictor of unplanned visits to the emergency department within 30 days, which is in line with the results of our study.

As can be seen, most of the studies in the literature are retrospective studies conducted with a small sample in a single center. Even though emergency departments are the first place to treat patients with acute heart failure, large population and intervention studies may overlook emergency department data[26] and only a small number of studies have investigated treatments given in emergency departments, ejection fraction parameters, and standard pleural effusion scores. In our study, hospital readmission increased with low EF, hospitalization, and NIMV and furosemide treatment. Among these, hospitalization mainly determines readmission. NIMV is used more frequently in patients with high congestion scores and low EF, and patients who receive NIMV and have a low EF are more frequently hospitalized from the emergency department. Our study revealed the importance of predicting future readmissions of patients based on the performance of ECHO by emergency physicians. In a study of over 10.000 patients discharged home after hospitalization for heart failure, follow-up with a cardiologist or general medical provider within seven days of discharge was found to reduce 30-day hospital readmission.[27] According to our results, patients who received NIMV or high-dose furosemide treatment in the emergency department or who had a low EF were re-admitted to the emergency department. Careful post-discharge plans for this patient group, follow-up with a cardiology consultation, and necessary medication adjustments may reduce readmission.[28]

The most important limitation of our study is that it was a single-center study with a relatively small number of patients and, in particular, a small number of young heart failure patients. Also, only the applications to our hospital were evaluated, although applications to private or other hospitals may have occurred during the study period. In addition, echocardiograms were not performed by a single physician, but by a physician who was scheduled to perform the examination that day. For this reason, there may not have been standardization in evaluating the echocardiograms. The fact that some of the chest radiographs used in the evaluation of the congestion score of the patients were conducted at the bedside may have resulted in a suboptimal imaging evaluation.

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Ethics Committee Approval

This study approved by the Medeniyet University Faculty of Medicine Ethics Committee (Date: 30.03.2022, Decision No: 2013-KAEK-64).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: Ö.F.G., G.A.S.; Design: Ö.F.G., G.A.S., Ş.Ş.; Supervision: G.A.S., F.A.; Fundings: Ö.F.G., F.A.; Materials: Ö.F.G., Ş.Ş.; Data: Ö.F.G., G.A.S.; Analysis: Ö.F.G., G.A.S; Literature search: Ö.F.G., G.A.S., F.A, Ç.N.; Writing: Ö.F.G., F.A, Ç.N.; Critical revision: G.A.S., C.N.

Conflict of Interest

None declared.

REFERENCES

1. Rönneikkö JK, Jämsen ER, Mäkelä M, Finne-Soveri H, Valvanne JN. Reasons for home care clients' unplanned hospital admissions and

their associations with patient characteristics. Arch Gerontol Geriatr 2018;78:114–26. [CrossRef]
2. Oliveira J. e Silva L, Jeffery MM, Campbell RL, Mullan AF, Takahashi PY, Bellolio F. Predictors of return visits to the emergency department among different age groups of older adults. Am J Emerg Med 2021;46:241–6. [CrossRef]
3. Kim D, Hayhoe B, Aylin P, Cowie MR, Bottle A. Health service use by patients with heart failure living in a community setting: A cross-sectional analysis in North West London. Br J Gen Pract 2020;70:e563–72. [CrossRef]
4. Wang GG, Wang SJ, Qin J, Li CS, Yu XZ, Shen H, et al. Characteristics, management, and outcomes of acute heart failure in the emergency department: A multicenter registry study with 1-year follow-up in a Chinese cohort in Beijing. Chin Med J Engl 2017;130:8. [CrossRef]
5. Jencks SF, Williams MV, Coleman EA. Rehospitalizations among patients in the Medicare fee-for-service program. N Engl J Med 2009;360:1418–28. [CrossRef]
6. Au AG. Predicting the risk of unplanned readmission or death within 30 days of discharge after a heart failure hospitalization. Am Heart J 2012;164:8. [CrossRef]
7. Platz E, Jhund PS, Claggett BL, Pfeffer MA, Swedberg K, Granger CB, et al. Prevalence and prognostic importance of precipitating factors leading to heart failure hospitalization: Recurrent hospitalizations and mortality. Eur J Heart Fail 2018;20:295–303. [CrossRef]
8. Maw AM, Lucas BP, Sirovich BE, Soni NJ. Discharge-ready volume status in acute decompensated heart failure: A survey of hospitalists. J Community Hosp Intern Med Perspect 2020;10:199–203. [CrossRef]
9. Horton CF, Collins SP. The role of the emergency department in the patient with acute heart failure. 2013;15:365. [CrossRef]
10. Blecker S, Ladapo JA, Doran KM, Goldfeld KS, Katz S. Emergency department visits for heart failure and subsequent hospitalization or observation unit admission. Am Heart J 2014;168:901–8. [CrossRef]
11. Tantarattanapong S, Keeratipongpun K. Predictive factors of 30-day adverse events in acute heart failure after discharge from emergency department; A historical cohort study. Arch Acad Emerg Med 2021;9:e58.
12. WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Available at: https://iris.who.int/bitstream/handle/10665/85839/WHO_NMH_NHD_MNM_11.1_eng.pdf?sequence=22. Accessed Feb 20, 2024.
13. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. Corrigendum to: 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 2021;42:4901.
14. Kobayashi KJ, Knuesel SJ, White BA, Bravard MA, Chang Y, Metlay JP, et al. Impact on length of stay of a hospital medicine emergency department boarder service. J Hosp Med 2020;15:147–53. [CrossRef]
15. Değertekin M, Erol C, Ergene O, Tokgözoğlu L, Aksoy M, Erol MK, et al. Heart failure prevalence and predictors in Türkiye: HAPPY study. Turk Soc Cardiol 2012;40:298–308. [CrossRef]
16. Shammas NW, Kelly R, Lemke J, Niwas R, Castro S, Beuthin C, et al. Assessment of time to hospital encounter after an initial hospitalization for heart failure: Results from a tertiary medical center. Cardiol Res Pract 2018;2018:1–4. [CrossRef]
17. Cox SR, Liebl MG, McComb MN, Chau JQ, Wilson AA, Achi M, et al. Association between health literacy and 30-day healthcare use after hospital discharge in the heart failure population. Res Soc Adm Pharm 2017;13:754–8. [CrossRef]
18. Son YJ, Kim BH. Prevalence of anemia and its influence on hospital readmissions and emergency department visits in outpatients with heart failure. Eur J Cardiovasc Nurs 2017;16:687–95. [CrossRef]
19. Collins SP, Jenkins CA, Jr FEH, Liu D, Miller KF, Lindsell CJ, et al. Identification of emergency department patients with acute heart failure at low risk for 30-day adverse events. JACC Heart Fail 2015;3:737–47. [CrossRef]
20. Claret PG, Calder LA, Stiell IG, Yan JW, Clement CM, Borgundvaag B, et al. Rates and predictive factors of return to the emergency department following an initial release by the emergency department for acute heart failure. CJEM 2018;20:222–9. [CrossRef]
21. Bradford C. Patient and clinical characteristics that heighten risk for heart failure readmission. Res Social Adm Pharm 2017;13:1070–81. [CrossRef]
22. Shah A, Mentz RJ, Sun JL, Rao VN, Alhanti B, Blumer V, et al. Emergency department visits versus hospital readmissions among patients hospitalized for heart failure. J Card Fail 2022;28:916–23. [CrossRef]
23. Sîrbu O, Floria M, Dascalita P, Stoica A, Adascalitei P, Sorodoc V, et al. Anemia in heart failure - from guidelines to controversies and challenges. Anatol J Cardiol 2018;20:52–9. [CrossRef]
24. Solomon SD, Anavekar N, Skali H, McMurray JJV, Swedberg K, Yusuf S, et al. Influence of ejection fraction on cardiovascular outcomes in a broad spectrum of heart failure patients. Circulation 2005;112:3738–44. [CrossRef]
25. Ibrahim AM, Koester C, Al-Akchar M, Tandan N, Regmi M, Bhattarai M, et al. HOSPITAL Score, LACE Index and LACE+ Index as predictors of 30-day readmission in patients with heart failure. BMJ Evid-Based Med 2020;25:166–7. [CrossRef]
26. Wadhera RK, Joynt Maddox KE, Desai NR, Landon BE, Md MV, Gilstrap LG, et al. Evaluation of hospital performance using the excess days in acute care measure in the hospital readmissions reduction program. Ann Intern Med 2021;174:86–92. [CrossRef]
27. Lee KK, Yang J, Hernandez AF, Steimle AE, Go AS. Post-discharge follow-up characteristics associated with 30-day readmission after heart failure hospitalization. Med Care 2016;54:365–72. [CrossRef]
28. Tabit CE, Coplan MJ, Spencer KT, Alcain CF, Spiegel T, Vohra AS, et al. Cardiology consultation in the emergency department reduces re-hospitalizations for low-socioeconomic patients with acute decompensated heart failure. Am J Med 2017;130:1112.e17–1112.e31. [CrossRef]

Akut Kalp Yetmezliği Hastalarının Acil Servis Tekrar Başvurularını Etkileyen Faktörler

Amaç: Akut kalp yetmezliği hastalarının acil servise tekrar başvurusunu nedenleri literatürde net olarak ortaya konmamıştır ve gelecekte bu hasta grubunun acil servisi daha sık kullanacağı öngörülmektedir. Çalışmamızda, acil servise akut kalp yetmezliği nedeni 90 gün içinde tekrar başvuran hastaların demografik, biyokimyasal, görüntüleme ve sonlanım değişkenlerinin tekrar başvuruya etkisini belirlemeye çalıştık

Gereç ve Yöntem: Çalışmamıza 1 Ocak 2019-1 Ocak 2021 tarihleri arasında 90 gün içinde akut dekompanse kalp yetmezliği nedeni ile acile servise tekrar başvuran olan hastalar dahil edildi. Hastaların demografik ve klinik özelliklerinin retrospektif analizi ve yeniden başvuruyu etkileyen faktörlerin değerlendirilmesi yapıldı.

Bulgular: Çalışmamıza ortalama 34±12.5 gün sonra tekrar acil servise başvuran 250 hasta dahil edildi.Hastaların yoğun bakım veya servise yatırılmaları ile 90 gün içinde tekrar başvurmaları arasında anlamlı ilişki saptanmıştır. ($p<0,005$). Ek olarak acil serviste non-invazif mekanik ventilasyon alan hastaların acil servise tekrar almayanlara göre daha erken başvurmaktadır ($p<0,005$). Hastaların EF değerleri de erken tekrar başvuru ile ilişkili bulundu. ($p<0,005$). Pearson'ın R korelasyon analizi, 90 gün içinde furosemid kullanımı ile yeniden kabul arasında anlamlı bir ilişki olduğunu ortaya kondu ($r=0.2015$, $p=0.0014$).

Sonuç: Araştırmamız, yeniden başvurunun NIMV kullanımı, furosemid kullanımı, hastanın ejeksiyon fraksiyonunun düşük olması ve hastaneye yatıştan etkilendiğini göstermiştir. Sonuç olarak, acil serviste NIMV ve yüksek doz furosemid uygulanan hastaların ve düşük ejeksiyon fraksiyonu olan akut kalp yetmezliği hastalarını taburcu ederken titiz davranmak ve hastalar için takip stratejisi oluşturmak önem arz etmektedir.

Anahtar Sözcükler: Acil servis; hastane; hastanın yeniden başvurusu; kalp yetersizliği.

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Original Article

Correlations of Different Objective and Patient Related Outcome Measures for Patellar Instability Patients

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Keywords: Functional outcome; patellar subluxation; patellofemoral instability; recurrent patellar dislocation.

ABSTRACT

Objective: We aimed to evaluate the effectiveness of modified Aberdeen Weight-Bearing Test (Knee) (AWT-K) and KSS (Knee Society Score) comparing their correlations with the Tegner Lysholm (TL) score in patellar instability patients.

Methods: Patients treated for patellar dislocation were divided into two groups. The first group consisted of patients operated on for patellar instability and the second group patients followed by conservative means. Duration of follow-up, age, gender, Caton-Deschamps index, and type of surgical interventions were recorded. Since the TL scoring system was previously validated in the follow-up of patellar instability treatment, the compatibility of KSS and modified AWT-K scoring systems with the TL scoring system was evaluated and their effectiveness in the follow-up of patellar instability was examined.

Results: A moderate correlation was found between TL and total KSS scores.However, when the relationship between KSS subgroups ES, SS, OKS, FAS and TL is examined; a weak and moderate correlation was found between the TL scoring system and OKS, SS, and FAS. When weak and non-correlated ES and SS were excluded, there was a strong correlation between TL score and mtKSS.There was a low correlation between TL scores and AWT-K 60-second average load difference and there was a low correlation between FA and AWT-K 60-second mean load difference and ratios.

Conclusion: The weak correlation of the AWT-K test for weight-bearing on the knee with findings of KSS and the TL scoring system reveals that may not be an adequate follow-up instrument for patients with patellar instability in short-term follow ups.

INTRODUCTION

There are several anatomical structures and biomechanical forces that affect the stable position of the patellofemoral joint. The impairment between these structures can lead to patellar dislocation, instability, and disability.[1] Recurrent patellar instability is a common phenomenon after patellar dislocation, and the literature suggests that between 40% and 60% of patients experience recurrent patellar dislocation and subluxation after the first dislocation.[2] Several treatment procedures have been presented in the literature to prevent instability; nevertheless, there is no common consensus about the current treatment of patellar instability yet. Traditionally, patients are followed non-operatively following a first-time dislocation, and surgery is generally reserved for cases of recurrent instability following initial conservative management.[1,3] Patellofemoral degenerative changes causing anterior knee discomfort is a common complication that can be seen after both conservative and surgical treatment. Studies comparing clinical results of different treatment procedures for patellar dislocation have used subjective patient-reported outcome measures (PROMs) rather than objective outcomes. International Knee Documentation Committee (IKDC),[4] Tegner Lysholm (TL), and Kujala scores are widely used similar PROMs for the evaluation of patellar instability. Of these, the TL score is the most used tool even though it has been developed to evaluate knee ligament injuries rather than patellar instability. PROMs reflect a patient's subjective opinion on the burden of the disease, which is very important in clinical practice.[5,7] However, PROMs can also give mixed messages and can be negatively influenced

by psychosocial factors, measuring the patient's perception of an outcome, rather than the true outcome.[8] To appropriately evaluate the impact of the treatment on knee pain for patellar instability, it is necessary to use objective outcome measures in addition to PROMs.[9] Objective outcomes can be performed by a detailed evaluation of joint motion and muscle activity, with types of equipment and objective performance-based functional outcome tools in which the patient is observed performing tasks such as walking, getting up from a chair, or climbing stairs, and their performance quantified in a timeline.[9,10] On the other hand, objective scoring systems are only physician-derived and must be correlated with PROMs because the patient perspective on satisfaction and activity levels is more critical than the physician's perspective.[11] The Knee Society Score (KSS) is a validated system that combines an objective physician-derived component with a subjective patient-derived component that evaluates pain relief, functional abilities, satisfaction, and fulfillment of expectations.[12] Although this system has been developed to evaluate knee arthroplasty patients, it is currently being used after several knee surgeries also because this tool evaluates the knee globally and can be used in conjunction with other outcome measures.[12] The Aberdeen Weight-Bearing Test (Knee) (AWT-K) is an objective test specific for anterior knee discomfort assessed via direct load bearing.[9] However, both tests have not been correlated for their effectiveness in the treatment of patellar instability. In this study, we aimed to evaluate the effectiveness of modified AWT-K and KSS scores comparing their correlations with the TL score in patellar instability patients.

MATERIALS AND METHODS

After obtaining institutional ethics committee approval (ID:B10.1.TKH.4.34.H.GP.0.01/46), medical records of patients who were treated for patellar dislocation and instability in a single center between September 2015 and September 2020 were reviewed retrospectively. This study was conducted in accordance with principles for human experimentation as defined in the Declaration of Helsinki. Informed consent was obtained from all individuals prior to treatment.

Patients treated for patellar dislocation were divided into two groups. The first group consisted of patients operated on for patellar instability, and the second group consisted of patients followed by conservative means. Inclusion criteria for the surgery group were as follows: being operated on for patellar instability (indications for surgery; at least 2 verified dislocations, failed conservative treatment, ± tibial tuberosity-trochlear groove (TT-TG) distance ≥20mm, positive apprehension test), undergoing patellar realignment surgery (MPFL reconstruction with or without tuberosity tibia osteotomy), having the necessary medical records, at least 12 months of follow-up. The conservative group consisted of patients treated successfully by conservative means who did not sustain redislocation or any instability complaints. Patients undergoing an arthroscopic extraction of chondral fragments without medial reefing or MPFL repair after the first dislocation were also included in the second group as this was a symptomatic intervention rather than therapeutic. Patients undergoing an intra-articular fragment fixation after the first dislocation were not included in either of the groups.

Duration of follow-up, age, gender, injured site, TT-TG distance, Caton-Deschamps index, and type of surgical interventions were recorded for all patients. Functional and clinical outcomes were measured using three different scoring systems. Since the TL scoring system was previously validated in the follow-up of patellar instability treatment, the compatibility of KSS and modified AWT-K scoring systems with the TL scoring system was evaluated, and their effectiveness in the follow-up of patellar instability was examined. TL scoring is a PROM system evaluating daily activity and pain level with questions about eight aspects (limp, support, locking, instability, pain, swelling, stair-climbing, and swelling) at the final follow-up. With this tool, patient-derived results are scored from 0 to 100 points.

AWT-K was modified and used to assess anterior knee discomfort. Originally, this test evaluates the mean difference and weight-bearing ratio on a scale of 0, 15, 30, 45, and 60 seconds. However, we used weight distributions only at 60 seconds to ease the analyses of the data. The difference in the amount of weight between injured and uninjured extremities is defined as the mean difference in weight distribution at 60s (injured – uninjured), and the ratio of the amount of weight between injured and uninjured knees is defined as the mean ratio of weight distribution at 60s (injured:uninjured).

KSS combines objective physician-derived knee indicators (alignment, instability, ROM, symptoms; max; 100 points) with subjective patient-derived components that evaluate pain relief and function using functional activity (max; 100 points), satisfaction (max; 40 points), and expectation scores (15 points). The KSS system can be evaluated separately for every subgroup. However, we also evaluated the total KSS (max; 260) under these 5 subheadings.

Statistical Analyses Data were analyzed using SPSS software (ver. 22.0; IBM Corp., Armonk, NY, USA). The normality of the data distribution was evaluated by the Shapiro-Wilk test. Student's T-test and One-way ANOVA tests were used to compare quantitative data between independent groups. Categorical variables were compared using the Pearson chi-squared test and Monte Carlo simulations with Fisher's exact test. The Pearson correlation coefficient (rho) was calculated as a measure of the associations between categorical variables, and Spearman's correlation coefficient (r) was used to evaluate the association between non-parametric variables. (1=perfect positive correlation and -1=perfect negative correlation. r/rho <0.3 indicates none, r/rho 0.3-0.5 indicates weak, 0.5-0.7 indicates moderate, and r/rho >0.7 indicates strong correlation). Quantitative variables are expressed as mean ± standard deviation and minimum and maximum values.

Table 1. Demographic features of both groups 1

	Mean	Standart deviation	p
Age			
surgery	20,05	10,4650,092	
conservative	21,14	6,807	
Follow-up (months)			
surgery	25,1500	12,07989	1,000
conservative	25,5517	16,88318	
Deschamps İndex			
surgery	0,9950	0,26325	0,023
conservative	1,0841	0,18362	
TT-TG distance			
surgery	18,7650	5,27180	0,176
conservative	16,6448	5,03109	
Instability severity score			
surgery	4,5000	1,19208	0,0001
conservative	2,2707	1,59662	

TT-TG; Tibial Tuberosity-Trochlear Groove, Mann-Whitney U test.

Qualitative variables are expressed as frequencies or ratios. P-values <0.05 were considered to indicate statistical significance.

RESULTS

After initial review, 76 patients were identified to be followed for patellar dislocation. Of these, 32 had undergone patellar realignment surgery. Ten patients who were lost to follow-ups and two patients who had short follow-up durations were excluded from the study. Finally, the remaining 20 patients were included in the surgery group. Ten patients treated by conservative means were lost to follow-ups, and five who had undergone an articular fragment fixation after the initial dislocation were excluded as well. Nine patients who had undergone an arthroscopic extraction of chondral fragments without medial reefing, fragment fixation, or MPFL repair or reconstruction after initial referral, and 20 patients treated successfully by conservative means with a follow-up duration ≥12 months were included in the conservative group.

At the last follow-up, none of the patients in either the surgery group or the conservative group had sustained a redislocation. The mean follow-up time was 25.1 months in the surgery group and 25.2 months in the conservative group (p=1.0). While there was no significant difference between the mean age of the two groups and TT-TG distance (p=0.092 and 0.17), the Caton-Deschamps index was significantly lower in the surgery group, as expected (p=0.023). However, a TT osteotomy was performed for only 2 (10%) patients (Table 1, 2).

When the PROMs and objective knee findings of the two groups were compared, no significant difference was found between AWT-K mean difference and ratio weight distribution at 60s (p=0.46 and 0.343, respectively), total KSS score (p=0.427), satisfaction score (SS) (p=0.305), functional outcome score (FAS) (p=0.261), and TL scores (p=0.077). However, a significant difference was found between the expectation score (ES) (p=0.041) and objective knee scores (OKS) (p<0.005) of patients who underwent patellar knee surgery and those who were followed up conservatively. The mean OKS score was 92.7±3.29 in patients who underwent alignment surgery and 96.3±3.09 in

Table 2. Demographic features of both groups 2

Gender	**Female**	**Male**	**p**
Surgery	12 (60,0%)	8 (40,0%)	0,109
Conservative	11 (37,9%)	18 (62,1%)	
Dominant/injured side	**Right**	**Left**	**p**
Surgery	19 (95,0%)/9 (45,0%)	1 (5,0%)/11 (55,0%)	0,609/0,079
Conservative	22 (75,9%)/13 (44,8%)	7 (24,1%)/16 (55,2%)	

Pearson Chi-Square test.

Table 3. Comparison of mean values of scores between surgery and conservative groups

Group	Mean	Std. Deviation	P
OKS			
Surgery	92,7000	3,29433	0,000
Conservative	96,3793	3,09855	
SS			
Surgery	35,0000	6,30789	0,305
Conservative	34,3448	4,34475	
FAS			
Surgery	83,8000	17,38905	0,261
Conservative	91,0690	10,13809	
ES			
Surgery	13,6500	2,13431	0,041
Conservative	12,3793	2,33626	
KSS total			
Surgery	225,1500	26,13382	0,427
Conservative	234,4483	15,29142	
mtKSS Total(OKS +FAS)			
Surgery	176,5000	19,00277	0,026
Conservative	187,4483	11,58073	
Tagner-Lysholm Score			
Surgery	84,3000	17,35117	0,077
Conservative	90,7241	12,48398	
AWT-K mean difference			
Surgery	-5,8000	13,04486	0,461
Conservative	-1,8621	3,14784	
AWT-K mean ratio			
Surgery	0,8615	0,30947	0,343
Conservative	0,9366	0,09279	

KSS: Knee society scores; OKS: objective knee scores; SS; satisfaction scores; ES: expectation scores; FAS: functional activity scores; mKSS: modified total knee society score AWT-K: Aberdeen Weight-Bearing Test (Knee). Mann-Whitney U test.

patients who were followed conservatively. On the other hand, while the mean ES was 13.65±2.13 in patients who underwent alignment surgery, it was 12.3±2.3 in patients who were followed up conservatively (Table 3).

When the relationship between the 3 different scoring systems was examined, a moderate correlation was found between TL scores and total KSS scores ($p<0.001$, $r=0.618$). However, when the relationship between KSS subgroups ES, SS, OKS, and FAS and TL is examined in detail, a weak and moderate correlation was found between the TL scoring system and OKS, SS, and FAS ($p<0.001$, $r=0.423$, $r=0.307$, $r=0.546$, respectively), with no correlation found between patient expectation (ES) and TL scoring ($r=0.258$). When weak and non-correlated ES and SS were excluded and a modified total KSS (mtKSS) (consisting of FAS and OKS) was calculated and correlated, it was found that there was a strong correlation between TL score and mtKSS ($p<0.001$, $r=0.707$). In addition, the mtKSS was significantly different between surgically and conservatively treated groups ($p=0.026$). There was a low correlation between TL scores and AWT-K 60-second average load difference and ratios ($p<0.05$, $r=0.315$, $r=0.350$), and there was a weak correlation ($p<0.05$, $r=0.300$, $r=0.310$) between FAS scores and AWT-K. It was noted that there was no correlation between AWT-K, total KSS, mtKSS, ES, SS, and OKS subgroups (Table 4).

DISCUSSION

Patellofemoral pain is one of the most common symptoms encountered in the field of sports medicine and knee trauma. Considering the lack of a reliable objective assessment tool for patellofemoral pain after patellofemoral instability, we investigated the effectiveness of modified AWT-K and KSS scores by comparing their correlations with the TL score. We had hypothesized that patellar dislocation or subluxation, which disrupts patellofemoral anatomy, must result in a certain level of patellofemoral pain, causing the loss of functions. However, our results revealed that there was no notable correlation between objectively measured (AWT-K) pain and TL score and a very weak correlation between pain and KSS subgroups during short-term follow-ups. Our results showed that impairment in functional outcomes, which represents the daily activity

Table 4. Results of correlation evaluation of scoring system in association with treatment method

Spearman's rho	Tagner-Lysholm Score	KSS total	OKS	ES	SS	FAS mean	AWT-K mean difference	AWT-K method ratio	Treatment
Tagner-Lysholm									
CC	1,000	0,618**	0,423**	0,258	0,307*	0,546**	0,315*	0,350*	0,255
KSS total									
CC	0,618**	1,000	0,358*	0,505**	0,721**	0,877**	0,291*	0,272	0,115
mtKSS total (OKS +FAS)									
CC	0,707**	0,843**	0,601**	0,268	0,416**	0,926**	0,302*	0,327*	0,128
OKS									
CC	0,423**	0,358*	1,000	0,011	-0,089	0,328*	0,042	0,097	0,511**
ES									
CC	0,258	0,505**	0,011	1,000	0,513**	0,312*	0,155	0,087	-0,295*
SS									
CC	0,307*	0,721**	-0,089	0,513**	1,000	0,544**	-0,005	-0,080	-0,148
FAS									
CC	0,546**	0,877**	0,328*	0,312*	0,544**	1,000	0,300*	0,310*	0,162
AWT-K mean difference									
CC	0,315*	0,291*	0,042	0,155	-0,005	0,300*	1,000	0,981**	0,107
AWT-K mean ratio									
CC	0,350*	0,272	0,097	0,087	-0,080	0,310*	0,981**	1,000	0,137
Treatment method									
CC	0,255	0,115	0,511**	-0,295*	-0,148	0,162	0,107	0,137	1,000

**Correlation is significant at the 0.01 level (2-tailed). *Correlation is significant at the 0.05 level (2-tailed). KSS: Knee society scores; OKS: objective knee indicators; SS: satisfaction scores; ES: expectation scores; FAS: functional activity scores; mKSS: modified total knee society score; AWT-K: Aberdeen Weight-Bearing Test (Knee); CC: correlation coefficient.

levels of the patients, tends to occur due to malfunction of the patellofemoral joint rather than pain. Presumably, patellar instability or dislocation, causing weakness of surrounding muscle structures in conjunction with loss of proprioception, is the first to affect the functions prior to pain.[13] These are regained after proper rehabilitation and tend to improve during follow-ups.[13] Inversely, cartilage degeneration, which is the most likely mechanism to cause pain and disability in the patellofemoral joint, rarely causes pain before the third decade, and as revealed by this study, measuring the pain with AWT-K does not provide a practical benefit, at least for short-term follow-ups.[14]

Traditionally, patients are followed non-operatively following a first-time dislocation, and surgery is generally reserved for cases of recurrent instability following initial conservative management. The exception to this algorithm is that arthroscopic or open removal or fixation of intra-articular chondral fragments can be performed after the first dislocation.[15] In the case of patellar instability, underlying reasons for instability, including alignment pathologies of the patellofemoral joint, must be addressed surgically. These can be done with trochleoplasty, distal bony realignment of the tibial tuberosity, femoral and/or tibial derotational osteotomies, and medial soft tissue reconstruction procedures. However, the cause of recurrent dislocation is often multifactorial. Thus, a combination of procedures is often necessary to fully correct the alignment of the patellofemoral joint.[16] We operated on our patients following the algorithm mentioned above; thus, although outcomes were better for the conservatively treated group as expected, statistically significant differences could not be detected among conservatively and surgically treated patients by the means of AWT-K mean difference and ratio weight distribution, total KSS score, SS score, FAS score, and TL score. Our TL score outcomes were comparable with the current literature for the same treatment algorithm.[17] We believe that similar results of both groups represent the appropriate application of the algorithm to the practice, which results in good outcomes for the surgery group. However, the insignificant difference may have resulted from the ineffectiveness of the evaluation tools. Previously published studies have reported increased TL scores postoperatively, but perfect healing after surgery is not expected when compared with control groups or the contralateral extremity.[18,19]

As mentioned above, patellofemoral instability is a result of an alignment disorder in most cases, and the difference in OKS in both groups supports this claim.[20] Although

a combination of procedures is often necessary to fully correct the alignment of the patellofemoral joint, we did not perform femoral or tibial derotational osteotomies or trochleoplasty to fully correct the alignment as these osteotomies do not prevent the development of osteoarthritis in long-term follow-ups.[14] Thus, the OKS in the surgery group was worse as a result of alignment impairments despite the fact that the patella had centered over the femoral groove. Also, the ES was higher in the surgery group as expected because these patients suffer from patellar instability until surgery and mostly experience dislocations more than two or three times. Therefore, a postoperative stable patellofemoral joint seems to satisfy these patients, and they were better than they thought after surgery. However, the conservatively treated group mostly consisted of anatomically well-aligned patients with no functional impairment and good outcomes after rehabilitation without redislocation are expected. Thus, these patients seem to have met their expectations after the rehabilitation protocol.

The moderate correlation between TL score and total KSS score shows the KSS score to be useful for the evaluation of patellofemoral instability. But the weak correlation of ES, SS, and TL scores makes SS and ES scores ineffective. From this point of view, when we exclude weak and non-correlated ES and SS and calculated a mtKSS (consisting of FAS and OKS), we found that there was a strong correlation between TL score and mtKSS ($p<0.001$, $r=0.707$). In addition, the mtKSS was significantly different between surgically and conservatively treated groups ($p=0.026$). Although TL scores showed a near significant (0.077) difference (but not significant), a mtKSS showed a significant difference between groups and also a strong correlation with TL score. This finding showed that a combination of objective tools (OKS) and PROMs (FAS) were as effective as TL scores in the evaluation of patellofemoral instability. Because the TL score, which is a PROM, when used alone lacks objective evaluation tools, possesses the risk of measuring only the patient's perception of the outcome, rather than the true outcome.[8]

One of the major drawbacks of PROMs is the preoperative "floor" and postoperative "ceiling" effects.[21] However, Cronbach's alpha, floor/ceiling effects, and test-retest reliabilities were not evaluated in this study, as all three scoring systems were evaluated and validated for knee pathologies previously.[7,12,22] The Kujala Anterior Knee Pain Scale is another validated scoring system that is designed particularly for patients with patellofemoral pain, used after a patellar dislocation or subluxation.[6] The Kujala scoring system evaluates patient daily activity and pain level similarly to the TL scoring system, with questioning 13 items (running, jumping, atrophy of the thigh, flexion deficiency, squatting, and the 8 items of the TL scoring system). Previous studies have used the Kujala score to assess anterior knee pain and the TL score to evaluate daily activity levels, even though both are PROMs.[17] As mentioned previously, to appropriately evaluate the impact of the treatment on knee pain for patellar instability, it is necessary to use objective outcome measures in addition to PROMs.[9] Thus, rather than using two PROMs to evaluate patellofemoral instability outcomes, as revealed in this study, using a PROM in conjunction with an objective tool could be more useful. We preferred to use the TL score in this study because it was easier to use and analyze. However, the Kujala tool could also be used, as both are questioning similar items and are valid PROMs for patellofemoral instability.

There were some limitations in this study. First, the number of patients included was relatively low. Second, we evaluated the effectiveness of modified AWT-K and KSS scores by comparing their correlations with the TL score. However, modified AWT-K and KSS scores must also be compared with other commonly used scoring systems for the evaluation of the knee after patellofemoral instability (such as the International Knee Documentation Committee, Kujala scores, etc.) in larger cohorts to draw exact conclusions.

Conclusion

The TL scoring system, which is a frequently used PROM in the follow-up of patellar instability, may be assessed together with the mtKSS scoring system and its subgroups, objective knee scores, and functional activity scores safely. However, the weak correlation of the AWT-K test for weight-bearing on the knee with both the objective findings of KSS and the Tegner-Lysholm scoring system reveals that it is not an adequate instrument for follow-up in patients with patellar instability, at least in short-term follow-ups. We believe this study may create a base for further studies to advance a better scoring system for patellofemoral instability patients.

Ethics Committee Approval

This study approved by the Umraniye Training and Research Hospital Ethics Committee (Date: 10.02.2022, Decision No: B.10.1.TKH.4.34.H.GP.0.01/46).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: M.S.S.; Design: G.A.; Supervision: M.E.K.; Fundings: M.E.K.; Materials: M.M.O.; Data: M.M.O.; Analysis: M.S.S.; Literature search: M.E.K.; Writing: M.E.K.; Critical revision: G.A.

Conflict of Interest

None declared.

REFERENCES

1. O'Sullivan ST, Harty JA. Patellar stabilization surgeries in cases of recurrent patellar instability: A retrospective clinical and radiological audit. Ir J Med Sci 2021;190:647–52. [CrossRef]

2. Mäenpää H, Lehto MU. Patellar dislocation. The long-term results of nonoperative management in 100 patients. Am J Sports Med 1997;25:213–7. [CrossRef]
3. Petri M, Liodakis E, Hofmeister M, Despang FJ, Maier M, Balcarek P, et al. Operative vs conservative treatment of traumatic patellar dislocation: Results of a prospective randomized controlled clinical trial. Arch Orthop Trauma Surg. 2013;133:209–13. [CrossRef]
4. Irrgang JJ, Anderson AF, Boland AL, Harner CD, Kurosaka M, Neyret P, et al. Development and validation of the international knee documentation committee subjective knee form. Am J Sports Med 2001;29:600–13. [CrossRef]
5. Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. Clin Orthop Relat Res 1985;198:43–9. [CrossRef]
6. Kujala UM, Jaakkola LH, Koskinen SK, Taimela S, Hurme M,Nelimarkka O. Scoring of patellofemoral disorders. Arthrosc 1993;9:159–63. [CrossRef]
7. Collins NJ, Misra D, Felson DT, Crossley KM, Roos EM. Measures of knee function: International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form, Knee Injury and Osteoarthritis Outcome Score (KOOS), Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS), Knee Outcome Survey Activities of Daily Living Scale (KOS-ADL), Lysholm Knee Scoring Scale, Oxford Knee Score (OKS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Activity Rating Scale (ARS), and Tegner Activity Score (TAS). Arthritis Care Res Hoboken 2011;63(Suppl 11):S208–28. [CrossRef]
8. Rosenberger PH, Jokl P, Ickovics J. Psychosocial factors and surgical outcomes: An evidence-based literature review. J Am Acad Orthop Surg 2006;14:397–405. [CrossRef]
9. MacDonald DRW, Rehman H, Carnegie CA, Tomas-Hernandez J, Johnstone AJ. The Aberdeen Weight-Bearing Test (Knee): A new objective test for anterior knee discomfort. Eur J Trauma Emerg Surg 2020;46:93–8. [CrossRef]
10. Podsiadlo D, Richardson S. The timed "Up & Go": A test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 1991;39:142–8. [CrossRef]
11. Scuderi GR, Bourne RB, Noble PC, Benjamin JB, Lonner JH, Scott WN. The new Knee Society Knee Scoring System. Clin Orthop Relat Res 2012;470:3–19. [CrossRef]
12. Noble PC, Scuderi GR, Brekke AC, Sikorskii A, Benjamin JB, Lonner JH, et al. Development of a new Knee Society scoring system. Clin Orthop Relat Res 2012;470:20–32. [CrossRef]
13. Małecki K, Fabiś J, Flont P, Fabiś-Strobin A, Niedzielski K. Assessment of knee flexor muscles strength in patients with patellar instability and its clinical implications for the non-surgical treatment of patients after first patellar dislocation - pilot study. BMC Musculoskelet Disord 2021;22:740. [CrossRef]
14. Rouanet T, Gougeon F, Fayard JM, Rémy F, Migaud H, Pasquier G. Sulcus deepening trochleoplasty for patellofemoral instability: A series of 34 cases after 15 years postoperative follow-up. Orthop Traumatol Surg Res 2015;101:443–7. [CrossRef]
15. Paša L, Veselý R, Kočiš J, Kužma J, Herůfek R. Treatment of Extensive Chondral Defects of the Patella after Patellar Dislocation. Acta Chir Orthop Traumatol Cech [Article in Czech] 2017;84:441–7. [CrossRef]
16. Cerciello S, Lustig S, Costanzo G, Neyret P. Medial retinaculum reefing for the treatment for patellar instability. Knee Surg Sports Traumatol Arthrosc 2014;22:2505–12. [CrossRef]
17. Pautasso A, Sabatini L, Capella M, Saccia F, Rissolio L, Boasso G, et al. Anatomic medial patellofemoral ligament (MPFL) reconstruction with and without tibial tuberosity osteotomy for objective patellar instability. Musculoskelet Surg 2022;106:441–8. [CrossRef]
18. Su P, Liu X, Jian N, Li J, Fu W. Clinical outcomes and predictive factors for failure with MPFL reconstruction combined with tibial tubercle osteotomy and lateral retinacular release for recurrent patellar instability. BMC Musculoskelet Disord 2021;22:632. [CrossRef]
19. Sappey-Marinier E, Sonnery-Cottet B, O'Loughlin P, Ouanezar H, Reina Fernandes L, Kouevidjin B, et al. Clinical outcomes and predictive factors for failure with ısolated MPFL reconstruction for recurrent patellar ınstability: A series of 211 reconstructions with a minimum follow-up of 3 years. Am J Sports Med 2019;47:1323–30. [CrossRef]
20. Smith TO, Donell S, Song F, Hing CB. Surgical versus non-surgical interventions for treating patellar dislocation. Cochrane Database Syst Rev 2015;26;CD008106. [CrossRef]
21. Wamper KE, Sierevelt IN, Poolman RW, Bhandari M, Haverkamp D. The Harris hip score: Do ceiling effects limit its usefulness in orthopedics? Acta Orthop 2010;81:703–7. [CrossRef]
22. Crossley KM, Bennell KL, Cowan SM, Green S. Analysis of outcome measures for persons with patellofemoral pain: Which are reliable and valid? Arch Phys Med Rehabil 2004;85:815–22. [CrossRef]

Patellar İnstabilitesi olan Hastalarda Farklı Skorlamalar ve Hasta Bağımlı Sonuçların Korelasyonu

Amaç: Patellar instabilite hastalarında modifiye Aberdeen Weight-Bearing Testi (Diz) (AWT-K) ve KSS (Knee Society Score) ile Tegner Lysholm (TL) skoru arasındaki korelasyonun etkinliğini değerlendirmeyi amaçladık.

Gereç ve Yöntem: Patella çıkığı nedeniyle tedavi edilen hastalar iki gruba ayrıldı. Birinci grup patellar instabilite nedeni ile opere edilen hastalardan, ikinci grup ise konservatif yöntemlerle takip edilen hastalardan oluşturdu. İzlem süresi, yaş, cinsiyet, Caton-Deschamps indeksi ve uygulanan cerrahi girişimlerin tipi kaydedildi. TL skorlama sistemi daha önce patellar instabilite tedavisi takibinde valide edildiğinden, KSS ve modifiye AWT-K skorlama sistemlerinin TL skorlama sistemi ile uyumu değerlendirilerek patellar instabilite takibindeki etkinliği incelenmiştir.

Bulgular: TL ile toplam KSS puanları arasında orta düzeyde bir korelasyon bulundu. Ancak KSS alt grupları ES, SS, OKS, FAS ve TL arasındaki ilişki incelendiğinde; TL puanlama sistemi ile OKS, SS ve FAS arasında zayıf ve orta düzeyde bir korelasyon bulundu. Zayıf ve korelasyonsuz ES ve SS hariç tutulduğunda, TL puanı ile mtKSS arasında güçlü bir korelasyon vardı. TL puanları ile AWT-K 60 saniye ortalama yük farkı arasında düşük bir korelasyon vardı ve FA ile AWT-K 60 saniye ortalama yük farkı ve oranları arasında düşük bir korelasyon vardı.

Sonuç: AWT-K testinin diz üzerine yük bindirme ile KSS bulguları ve TL skorlama sistemi arasındaki zayıf korelasyonu, patella instabilitesi olan hastalarda kısa dönem takiplerde yeterli bir takip aracı olmayabileceğini ortaya koymaktadır.

Anahtar Sözcükler: Fonksiyonel sonuç; patellofemoral instabilite; patellar subluksasyon; tekrarlayan patella çıkığı.

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Original Article

The Impact of the COVID-19 Pandemic in Schizophrenia Patients Registered with the Community Mental Health Center

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Keywords: Community Mental Health Center; Covid-19 pandemic; schizophrenia.

ABSTRACT

Objective: The aim was to examine the effect of the COVID-19 pandemic on schizophrenia patients registered at the Community Mental Health Center (CMHC) in terms of depression, suicide risk, and tendency to violence.

Methods: The study was conducted on patients registered at the CMHC who were regularly followed up. It was carried out on one hundred and eight individuals who met the diagnosis of schizophrenia according to the DSM-V and the inclusion criteria. Individuals were respectively classified as hospitalized patient group during the Covid-19 pandemic period (n=39), non-admitted patients with an emergency plan without hospitalization (n=37), and stable patient group (n=32). In the study, the Socio-Demographic Questionnaire, the Calgary Depression Scale for Schizophrenia (CDSS), the Buss-Perry Aggression Questionnaire (BPAQ), and the Suicide Probability Scale (SPS) were used.

Results: While there was a significant difference between the groups in CDSS and BPAQ scores ($p<0.05$), there was no significant difference between the groups in the total score of SPS ($p>0.05$). There was no significant difference between the groups in terms of physical, verbal aggression, and anger in the BPAQ sub-dimensions ($p>0.05$), but a significant difference was found in the hostility subgroup ($p<0.05$). While there was no significant difference between the groups in the sub-dimensions of negative self and exhaustion, hostility in the SPS ($p>0.05$), a difference was found between the groups in the sub-dimension of disconnection from life ($p<0.05$). Also, a significant negative correlation was found between education level and CDSS values (r: 0.451; p: 0.025).

Conclusion: In our study, the significant difference found in CDSS and BPAQ total scores of the three groups showed that schizophrenia patients with CMHC follow-up who tend to depression or violence were significantly affected by the pandemic period, and their treatment follow-up was more severe.

INTRODUCTION

The Covid-19 epidemic, which has become a source of concern worldwide and was announced as a "pandemic",[1,2] makes all health services more difficult to provide, strains their capacity, and keeps people with mental illnesses from getting the psychosocial care they require.[3] In addition, studies have stated that the pandemic process may deprive individuals with mental disorders of regular face-to-face rehabilitation, routine psychiatric controls, and even treatment.[4,5]

Schizophrenia is a chronic mental health disease characterized by significant deterioration in thought, behavior, adjustment, and functionality.[6] It requires lifelong psychosocial support (family, community mental health centers, and foundations). Although the incidence of Schizophrenia in adults varies between 0.3-1.5%, the lifetime rate of contracting this disease is around 1%.[6-8]

Twenty to fifty percent of patients with schizophrenia (PwS) attempt suicide, and it is strongly linked to depression, aggression, and suicide risk.[7,8] According to the literature, these suicide instances are explained by severe anxiety at the outset, persistent anxiety along with auditory hallucinations, or severe depression symptoms after a psychotic exacerbation.[9] Suicide risk increases and the disease's progression is adversely affected by persistent depression in PwS.[10,11] Research indicates that PwS have a higher propensity for aggression than those with other mental illnesses, and there is a regular correlation between violence and suicide in these individuals.[12,13]

Rehabilitation treatments are acknowledged to be highly necessary for PwS because of their poor physical health, socioeconomic difficulties, and social disintegration.[14] Community Mental Health Centers (CMHC) are designed to assist local residents who suffer from severe mental diseases and comprise a multidisciplinary team of specialists that includes social workers, counselors, psychologists, psychiatrists, and others.[14-16] Due to the stress of the COVID-19 pandemic and the limitations in face-to-face rehabilitation services, both the participation in rehabilitation programs at CMHC and the content of the programs had to be restricted.[17,18]

Regarding depression, aggression, or suicide risk, no research has been done in the literature on PwS in CMHC during the COVID-19 pandemic. Consequently, the aim of our study was to investigate the effects of the COVID-19 pandemic on depression, suicidal ideation, and violent tendencies in PwS who were registered with the CMHC.

MATERIALS AND METHODS

This study was carried out on PwS registered at the CMHC and followed up regularly. The study included 108 individuals who were diagnosed with schizophrenia by a psychiatrist and met the inclusion criteria in view of the DSM-V (American Psychiatric Association, 2013). Participants in the study who gave written consent were divided into three groups: those hospitalized during the COVID-19 pandemic (n=39), those not admitted but had an emergency action plan (n=37), and those who were stable and had no emergency action plan (n=32). The inclusion criteria for the study were as follows: being 18-65 years old, receiving CMHC services, having had a schizophrenia diagnosis for at least two years, not experiencing symptoms of the disease, not having an organic mental disorder, not having another psychiatric illness, and being literate to be considered for the study. Individuals with cognitive and physical dysfunction, mental retardation, and a variety of psychiatric diseases were excluded from the study, as were those who refused to participate.

Ethical committee approval for the study was acquired from the Ethics Committee Presidency with decision number 514/194/41 on 27/01/2021.

Measurement and Evaluation Tools

The clinical and sociodemographic information of the patients was collected by an experienced psychiatrist who conducted the study before the psychiatric interview. Clinical assessments were made using the Calgary Depression Scale for Schizophrenia (CDSS), the Buss-Perry Aggression Questionnaire (BPAQ), and the Suicide Probability Scale (SPS). The scales are explained in detail below.

Calgary Depression Scale for Schizophrenia (CDSS): Addington et al.[19] (1994) created it to assess the depression situation and the severity of depressive symptoms in schizophrenia patients. The depression scale involves nine items that are responded to on a four-point Likert scale. Oksay et al.[20] (2000) investigated the scale's validity and reliability among Turkish schizophrenia patients. Cronbach's alpha coefficient was 0.88 in the reliability study. As a result, the scale's cutoff point was set at 11.

Buss-Perry Aggression Questionnaire (BPAQ): The scale, adapted from Buss and Perry's (1992) Buss-Durkee Hostility Inventory, includes 29 items and five-point Likert types.[21] This scale involves questions of physical and verbal aggression, hostility, and anger. On the scale, questions 9 and 16 are scored in reverse order. The scale's score value varies in direct proportion to the level of aggression. That is, the higher the score, the more aggressive the person is. The physical aggression subscale has a Cronbach Alpha internal consistency coefficient of 0.89, the verbal aggression subscale has a Cronbach Alpha internal consistency coefficient of 0.72, the hostility subscale has a Cronbach Alpha internal consistency coefficient of 0.77, and the anger subscale has a Cronbach Alpha internal consistency coefficient of 0.83.[22]

Suicide Probability Scale (SPS): Cull & Gill (1989)[23] developed the SPS to assess the risk of suicide in adolescents and adults. Atlı et al.[24] investigated the scale's Turkish validity and reliability (2009). The 36-item scale is graded on a four-point Likert scale of "never or rarely," "sometimes," "often," and "often or always".

Statistical Analysis

SPSS 25.0 package program was used for data analysis. Sociodemographic and clinical characteristics of individuals were calculated as frequencies and percentages for categorical data using descriptive statistical methods. Numerical data are expressed as mean ± standard deviation or median (minimum-maximum) values. To find out whether there was a difference between groups in categorical variables, the Chi-square or Fisher Exact Test was used. The normality distribution of numerical data was assessed using the Shapiro-Wilk test. In triplet groups, the One-Way ANOVA test was used to analyze normally distributed data, and the Levene test determined the homogeneity of variances. In Post-hoc comparisons, Tukey and Fisher's Least Significant Difference tests were used after the variances were found to show homogeneous distribution. Finally, the Kruskal-Wallis test compared three groups of variables that did not show normal distribution. The relationship between the data was evaluated at the Spearman statistical significance $p<0.05$ level.

RESULTS

Sociodemographic Characteristics

The mean age of the 108 individuals comprised in the study was 44.36±7.92. 41.7% were female, and 58.3% were male. 61.1% were single, 22.2% were married, and 16.7% were divorced. Demographic information belonging to the sample groups is given in Table 1. No significant difference was found between all groups in terms of age, gender, duration of education, the total number of hospitalizations,

Table 1. Characteristics of the demographic variables of the participants

	Hospitalized Patients		Non-Admitted Patients with an Emergency Plan		Stable Patients		p
	n	%	n	%	n	%	
Gender							
Female	16	%41.00	13	%35.10	18	%56.30	0.480
Male	23	%59.00	24	%64.90	14	%43.80	
Marital Status							
Single	24	%66.70	21	%62.20	21	%62.50	0.000*
Married	9	%17.90	9	%21.60	6	%18.80	
Divorced	6	%15.40	6	%16.20	6	%18.80	
Income status							
Lower level	9	%23.10	9	%16.20	3	%9.40	0.000*
Intermediate level	30	%76.90	27	%83.80	30	%90.60	
Family structure							
Core	10	%38.50	6	%16.20	3	%9.40	0.000*
Extended	24	%61.50	21	%59.50	27	%81.30	
Broken	0	%0	9	%24.30	3	%9.40	
Social support							
Available	18	%46.20	24	%66.60	12	%37.50	0.000*
None	13	%33.30	6	%18.90	18	%53.10	
Insufficient	8	%20.50	6	%13.50	3	%9.40	
Substance use status							
None	11	%28.20	24	%64.90	9	%28.10	0.000*
Smoking	23	%59.00	9	%24.30	18	%56.30	
Alcohol and smoking	2	%5.10	4	%10.80	2	%9.40	
Psychoactive substance and alcohol	3	%7.70	0	%0	3	%9.40	
Forensic history							
Available	6	%15.40	13	%35.10	6	%18.80	0.000*
None	33	%84.60	24	%64.90	26	%81.30	
Family history of mental illness							
Available	24	%61.50	14	%37.80	20	%62.50	0.441
None	15	%38.50	23	%62.20	12	%37.50	
Involuntary Hospitalization							
Available	20	%51.30	14	%37.80	9	%28.10	0.034*
None	19	%48.70	23	%62.20	24	%71.90	
Suicide status							
Available	9	%23.10	6	%16.20	6	%18.80	0.000*
None	30	%76.90	31	%83.80	26	%81.30	

*p<0.05

mean length of hospitalization, several suicides, and age at the final diagnosis and first treatment (p>0.05) (Table 2).

Comparison of Depression, Buss-Perry Aggression Questionnaire, and Suicide Probability Scale Scores

In the CDSS and BPAQ, there was a statistically significant difference between the groups (p<0.05). It was determined that the significance in CDSS scores was due to stable patients. However, when the BPAQ total score between the groups was examined with the Mann-Whitney U test, it was concluded that this difference was due to hospitalized patients. In contrast, no significant difference was found between the groups in the total score on the SPS (p>0.05) (Table 3).

While there was a significant difference between the groups in the physical, verbal aggression, and anger in the BPAQ sub-dimensions (p>0.05), in the hostility subgroup, there was also found a statistically significant difference (p<0.05) (Table 4). At the same time, while a statistically significant difference was not found between the groups in the Negative Self and Exhaustion and Hostility sub-dimensions in the Suicide Probability Scale (p>0.05), a significant difference was found between the groups in the

Table 2. Comparison of clinical characteristics of hospitalized and non-admitted patients with an emergency action plan and stable patients

	Hospitalized Patients	Non-Admitted Patients with an Emergency Plan	Stable Patients	p
	X±SD	X±SD	X±SD	
Age	43.33±7.52	48.54±8.44	40.90±6.45	0.108
Education duration	8.51±4.47	9.41±5.50	7.54±5.53	0.684
Substance use duration	11.92±10.84	7.16±11.20	16.78±11.15	0.003*
Total number of hospitalizations	3.61±3.67	2.64±3.66	1.90±1.27	0.106
Average length of stay (days)	17.25±13.52	18.51±23.54	25.40±33.29	0.379
Number of Suicides	0.61±1.16	0.37±0.89	0.46±1.01	0.380
Age at first treatment with final diagnosis	29.35±10.01	32.40±12.73	25.28±4.19	0.452

Mean and standard deviations were expressed as X±SD; *p<0.05.

Table 3. Comparison of the total scores of CDSS, BPAQ, SPS between the groups of hospitalized and non-admitted patients with an emergency action plan and stable patients

	Hospitalized Patients		Non-Admitted Patients with an Emergency Plan		Stable Patients		p
	X±SD	Median (Min-Max)	X±SD	Median (Min-Max)	X±SD	Median (Min-Max)	
CDSS Total	13.94±7.83	9 (6-27)	12.43±6.61	10 (1-23)	8.90±5.12	9 (1-19)	0.011*
BPAQ Total	64.64±15.89	61 (49-109)	69.94±16.87	66 (42-98)	75.25±15.77	69 (53-99)	0.003*
SPS Total	78.87±18.74	75 (52-114)	76.94±18.27	711 (32-110)	78.18±16.23	77 (52-108)	0.777

Mean and standard deviations were expressed as X±SD, *p<0.05; CDSS: Calgary Depression Scale in Schizophrenia; BPAQ: Buss-Perry Aggression Questionnaire; SPS: Suicide Probability Scale.

Table 4. Comparison of the BPAQ sub-dimensions of hospitalized and non-admitted patients with an emergency action plan and stable patients between groups

		Hospitalized Patients		Non-Admitted Patients with an Emergency Plan		Stable Patients		p
		X±SD	Median (Min-Max)	X±SD	Median (Min-Max)	X±SD	Median (Min-Max)	
BPAQ	Physical Aggression	19.28±9.21	15 (10-45)	17.91±6.31	19 (10-34)	20.25±6.48	18 (13-33)	0.141
	Verbal Aggression	12.56±3.03	18 (13-31)	14.35±2.25	25 (10-33)	13.15±3.16	23 (15-36)	0.318
	Hostility	19.10±4.78	14 (7-24)	22.33±7.65	17 (8-25)	23.45±6.29	16 (10-34)	0.02*
	Anger	15.02±4.57	12 (10-23)	17.50±5.45	14 (11-19)	17.90±7.17	13 (8-19)	0.137

Mean and standard deviations were expressed as X±SD, *p<0.05, BPAQ: Buss-Perry Aggression Questionnaire.

disconnection from life sub-dimension (p<0.05) (Table 5). Besides, there was found a statistically significant negative correlation between education level and CDSS values (r=0.451, p=0.025).

While a statistically significant and high level of positive correlation was found between CDSS and BPAQ scores

Table 5. Comparison of the SPS sub-dimension results of hospitalized and non-admitted patients with an emergency action plan and stable patients between groups

		Hospitalized Patients		Non-Admitted Patients with an Emergency Plan		Stable Patients		p
		X±SD	Median (Min-Max)	X±SD	Median (Min-Max)	X±SD	Median (Min-Max)	
SPS	Negative self and exhaustion	28.30±9.24	27 (16-45)	28.56±7.43	25 (14-45)	27.87±4.27	28 (20-34)	0.750
	Detachment from life	20.51±3.98	19 (14-30)	20.43±3.75	19 (11-29)	17.78±4.43	17 (11-24)	0.015*
	Hostility	15.02±4.57	13 (8-26)	15.00±4.53	14 (9-25)	14.62±4.17	14 (10-25)	0.143

Mean and standard deviations were expressed as X ± SD, *p<0.05.

Table 6. The relationship between SPS sub-dimension scores and CDSS scores

	SPS					
	Negative self and exhaustion		Detachment from life		Hostility	
	r	p	r	p	r	p
CDSS	0,488**	0,00***	0,244*	0,11***	0,550**	0,00***

* The correlation is significant at the 0.05 level,** The correlation is significant at the 0.01 level, ***p<0.05.

(r=0.403, p=0.00), the same result was found between sub-dimensions of BPAQ negative self and exhaustion, fear of commitment to life and hostility, and CDSS scores (respectively r=0.488, p=0.00; r=0.244, p=0.00; r=0.550, p=0.00) (Table 6).

DISCUSSION

The current study found a statistically significant difference in terms of the CDSS and BPAQ scores between groups. While stable patients caused this significant difference in the CDSS score, hospitalized patients had higher CDSS scores. In terms of BPAQ hostility sub-dimension and SPS sub-dimension of disengagement from life, a statistically significant difference was found.

It is known that suicidal behavior is a common clinical situation in PwS.[25,26] In the literature, in a study conducted by Deveci et al.[27] (2008), it was determined that depression with schizophrenia comorbidity increases the risk of suicide. In another study conducted by Atmaca (2016), a positive correlation was found between hostility and disconnection from life, the sub-dimensions of SARS and CDSS. A negative correlation was found between negative self and exhaustion and CDSS. In our study, on the other hand, there was a high level of positive correlation between the hostility, disconnection from life, negative self, and exhaustion sub-dimensions of SARS and CDSS scores. [28] Furthermore, current literature proposed that aggressive behaviors increase the risk of suicide and depression in PwS. A high positive correlation was found between BPAQ and CDSS, and SPS in this study.[29]

Recent literature implies the frequency of exposure to depression decreases when the education level of patients with schizophrenia increases.[30-32] However, the present study found a negative correlation between PwS with a high level of education and CDSS scores. This may be because educated individuals have better access to written and visual communication tools and accurate information than individuals with low education levels.

As a result, it is known that PwS have to continue their lives in a more isolated way, especially due to the restriction and disruption of CMHC functioning and rehabilitation during the COVID-19 pandemic period. In our study, the CDSS and BPAQ total scores of the patient groups who were hospitalized or not hospitalized during the COVID-19 pandemic period but required emergency intervention were statistically significant compared to the stable follow-up patients. This shows that PwS who are prone to depression or violence with CMHC follow-up are significantly affected by the pandemic period, and that treatment follow-up is more important.

The application of the evaluations used in the study only to PwS during the COVID-19 pandemic is seen as a limitation of the study. Since this study was cross-sectional during the COVID-19 pandemic period, in order to determine whether the schizophrenia patients' susceptibility to violence and depression, as stated in the literature, is entirely due to the COVID-19 pandemic period, evaluating

and comparing them in the same patient group after the pandemic period is over. Rehabilitations have returned to their former state, and functioning may increase the reliability of the study. We suppose that our study will guide other studies on this subject.

Conclusion

As far as we know, this is the first study to see how the COVID-19 pandemic affected PwS at the CMHC in terms of depression, suicide risk, and violent tendencies. Our study may guide the literature on this topic.

Ethics Committee Approval

This study approved by the Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee (Date: 27.01.2021, Decision No: 514/194/41).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: İ.K.; Design: İ.K., E.A.K.; Supervision: İ.K., E.A.K.; Materials: İ.K.; Data: İ.K.; Analysis: İ.K., E.A.K.; Literature search: İ.K., E.A.K.; Writing: İ.K., E.A.K.; Critical revision: İ.K., E.A.K.

Conflict of Interest

None declared.

REFERENCES

1. WHO. Mental health and psychosocial considerations during the COVID-19 outbreak. Available at: https://www.who.int/docs/default-source/coronaviruse/mental-health-considerations.pdf. Accessed Feb 20, 2024.
2. Brown E, Gray R, Lo Monaco S, O'Donoghue B, Nelson B, Thompson A, et al. The potential impact of COVID-19 on psychosis: A rapid review of contemporary epidemic and pandemic research. Schizophr Res 2020;222:79-87.
3. Khosoravi M. COVID–19 pandemic: What are the risks and challenges for schizophrenia? Clin Schizophr Relat Psychoses 2020;14:58–9.
4. Hamada K, Fan X. The impact of COVID-19 on individuals living with serious mental illness. Schizophrenia Res 2020;222:3
5. Adhanom GT. Addressing mental health needs: An integral part of COVID-19 response. World Psychiatr 2020;19:129-30.
6. Kırlı U, Binbay T, Elbi H, Alptekin K. COVID 19 pandemic and psychotic symptoms. Turkish J Clin Psych [Article in Turkish] 2020;23:81-5.
7. Karaakuş G, Kocal Y, Damla S. Schizophrenia: Etiology, clinical features and treatment. Arch Med Rev J [Article in Turkish] 2017;26:251-67.
8. Tiryaki A, Özkorumak E, Ak İ. Psychiatric comorbidities in schizophrenic outpatients. B Clin Psychopharmacol 2007;17:174-80.
9. Ikeshita K, Shimoda S, Norimoto K, Arita K, Shimamoto T, Murata K, et al. Profiling psychiatric inpatient suicide attempts in Japan. Int J Emerg Ment Health 2014;16:217-21.
10. Zisook S, Nyer M, Kasckow J, Golshan S, Lehman D, Montross L. Depressive symptom patterns in patients with chronic schizophrenia and subsyndromal depression. Schizophr Res 2006;86:226-33.
11. Karlıdere T, Uzun Ö, Balıkcı A. Depressive symptoms in first episode schizophrenia patients under treatment: One-year follow-up comparison of classical and atypical antipsychotics. Alpha Psychol [Article in Turkish] 2015;16:7-13.
12. Ishii T, Hashimoto E, Ukai W, Kakutani Y, Sasaki R, Saito T. Characteristics of attempted suicide by patients with schizophrenia compared with those with mood disorders: A case- controlled study in Northern Japan. Plos One. 2014;9:e96272.
13. Lyu J, Zhang J. Characteristics of schizophrenia suicides compared with suicides by other diagnosed psychiatric disorders and those without a psychiatric disorder. Schizophr Res. 2014;155:59-65.
14. Özdemir I, Şafak Y, Örsel S, Kahiloğulları AK, Karadağ H. Investigation of the efficacy of a psychiatric-social rehabilitation performed İn patients with schizophrenia in a community mental health center: Controlled study. Alpha Psychol [Article in Turkish]. 2017;18:419-27.
15. Esen G, Devrim C, Şahin E, Şahin Ş, Şimşek E. The evaluation of the schizophrenia patiens in Kirikkale Community Mental Health Center. KÜ Tıp Fak Derg [Article in Turkish] 2014;16:15-9.
16. Ensari H, Gültekin BK, Karaman D, Koç A, Beşkardeş AF. The effects of the service of community mental health center on the schizophrenia patients - evaluation of quality of life, disabilities, general and social functioning - a summary of one year follow-up. Anatol J Psychiatry 2013;14:2.
17. Kozloff N, Mulsant BH, Stergiopoulos V, Voineskos AN. The COVID-19 global pandemic: Implications for people with schizophrenia and related disorders. Schizophr Bull 2020;46(4):752-7.
18. Tozoğlu E, Alkan EÖ, Özpolat E. The relationship between the service type change of community mental health centers and the anxiety levels in schizophrenia patients in the Covid-19 pandemic. Cukurova Med J [Article in Turkish] 2021;46:966-74.
19. Addington D, Addington J, Maticka-Tyndale E. Specificity of the Calgary Depression Scale for schizophrenics. Schizophr Res 1994;11:239-44.
20. Oksay E, Aksaray G, Kaptanoğlu G et al. Validity and reliability of the Turkish version of Calgary Depression Scale in schizophrenic patients. Turk J Psychiatry 2000;11:278-84.
21. Buss AH, Perry M. The aggression questionnaire. J Pers Soc Psych 1992;63:452-9.
22. Madran HAD. The reliability and validity of the Buss-Perry aggression questionnaire. Turk J Psychiatry [Article in Turkish] 2012;24:1-6.
23. Cull JG, Gill WS. Suicide probability scale (SPS). Los Angeles: Western Psychological Services; 1989.
24. Atlı Z, Eskin M, Dereboy Ç. The validity and the reliability of Suicide Probability Scale (SPS) in clinical sample. J Clin Psychiatry 2009;12:111-24.
25. Heilä H, Isometsä ET, Henriksson MM, Heikkinen ME, Marttunen MJ, Lönnqvist JK. Suicide and schizophrenia: A nationwide psychological autopsy study on age- and sex-specific clinical characteristics of 92 suicide victims with schizophrenia. Am J Psychiatry 1997;154:1235-42.
26. Heilä H, Isometsä ET, Henriksson MM, Heikkinen ME, Marttunen MJ, Lönnqvist JK. Antecedents of suicide in people with schizophrenia. Br J Psychiatry 1998;173:330-3.
27. Deveci A, Esen-Danaci A, Yurtsever F, Deniz F, Gürlek YE. The effects of psychosocial skills training on symptomatology, insight, quality of life, and suicide probability in schizophrenia. Turk Psychiatry J [Article in Turkish] 2008;19:266-73.
28. Atmaca GD. Şizofreni hastalarında intihar olasılığının, depresyon ve

içgörüyle ilişkisi. [master thesis]. Sakarya: Sakarya Üniversitesi; 2016.
29. Gürkan Ş, Yaylacı ET, Özdemir Ç, Çatlı B, Şahiner ŞY, Gürkan D, et al. Comparison of sociodemographic features, psychopathy and aggression levels of criminal and non-criminal schizophrenia patients. Anatol J Psychiatry [Article in Turkish] 2019;20:261-8.
30. Cullen W, Gulati G, Kelly BD. Mental health in the COVID-19 pandemic. QJM Int J Med 2020;113:311-2.
31. Fazel S, Wolf A, Palm C, Lichtenstein P. Violent crime, suicide, and premature mortality in patients with schizophrenia and related disorders: A 38-year total population study in Sweden. Lancet Psychiatry 2014;1:44-54.
32. Bjelland I, Krokstad S, Mykletun A. Does a higher educational level protect against anxiety and depression? The HUNT Study. Soc Sci Med 2008;66:1334-45.

COVID-19 Pandemisinin Toplum Ruh Sağlığı Merkezi'ne Kayıtlı Şizofreni Hastaları Üzerindeki Etkisi

Amaç: COVID-19 pandemisinin Toplum Ruh Sağlığı Merkezi'ne kayıtlı şizofreni hastaları üzerindeki etkisinin depresyon, intihar riski ve şiddete meyil açısından incelenmesi amaçlanmıştır.

Gereç ve Yöntem: Çalışma Toplum Ruh Sağlığı Merkezi'ne (TRSM) kayıtlı ve düzenli olarak takibi yapılan hastalar üzerinde yapılmıştır. Çalışmaya DSM-V (American Psychiatric Association 2013)'e göre şizofreni tanısını karşılayan ve dahil edilme kriterlerine uyan yüz sekiz birey üzerinde gerçekleştirilmiştir. Çalışmaya katılmaya yazılı olarak onam veren bireyler sırasıyla Covid-19 pandemi döneminde hastane yatışı gerçekleşen (n=39), hastane yatışı olmayan ancak acil eylem planı yapılan (n=37) ve yatış veya acil eylem planı yapılmayan stabil hasta (n=32) şeklinde üç gruba ayrılmıştır. 18-65 yaş arasında olan, TRSM'den hizmet alıyor olan, en az iki yıldır şizofreni tanısı almış olan, hastalığın aktif döneminde olmayan, organik mental bozukluğu olmayan, ek psikiyatrik hastalığın olmayan, okur-yazar olan bireyler çalışmaya dahil edilmiştir. Çalışmada hastaların klinik ve sosyodemografik bilgilerini içeren anket, Calgary Şizofrenide Depresyon Ölçeği (CŞDÖ), Buss-perry Saldırganlık Ölçeği (BPSÖ) ve İntihar Olasılığı Ölçeği (İOÖ) kullanılmıştır.

Bulgular: CŞDÖ ve BPSÖ skorlarında gruplar arasında istatistiksel açıdan anlamlı fark bulunurken ($p<0.05$), İOÖ toplam skorunda ise gruplar arasında anlamlı bir fark olmadığı saptanmıştır ($p>0.05$). BPSÖ alt boyutlarda fiziksel, sözel saldırganlık ve öfke açısından gruplar arasında anlamlı bir farklılık bulunmazken ($p>0.05$), düşmanlık alt grubunda ise istatistiksel açıdan anlamlı bir farklılık saptanmıştır ($p<0.05$). İOÖ'nde Olumsuz benlik ve tükenme, düşmanlık alt boyutlarında gruplar arasında istatistiksel açıdan anlamlı bir fark bulunmaz iken ($p>0.05$), hayata bağlılıktan kopma alt boyutunda ise gruplar arasında anlamlı bir farklılık bulunmuştur ($p<0.05$). Eğitim düzeyi ve CŞDÖ değerleri arasında istatistiksel açıdan anlamlı negatif yönde korelasyon saptanmıştır. ($r: 0,451$ $p: 0.025$).

Sonuç: Çalışmamızda Covid-19 pandemi döneminde yatış yapan veya yatış yapmayan ama acil müdahale gerektiren hasta gruplarının stabil takipli hastalara göre CŞDÖ ve BPSÖ toplam skorlarının istatistiksel açıdan anlamlı bulunmasının TRSM takipli depresyona veya şiddete meyilli olan şizofreni hastalarının pandemi döneminden önemli derecede etkilendiklerini ve tedavi takiplerinin daha önem arz ettiği sonucunu göstermektedir.

Anahtar Sözcükler: COVID-19 pandemisi; toplum ruh sağlığı merkezi; şizofreni hastalığı.

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Original Article

Impact of Lowering the Screening Age for Colorectal Cancer on Early Diagnosis and Treatment: A Retrospective Study in a Turkish Cohort

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Keywords: Colorectal cancer; screening age; polyps; malignancies; Türkiye

ABSTRACT

Objective: This study was planned in line with the American Cancer Society's recommendation to lower the colorectal cancer (CRC) screening age from 50 to 45. The study aims to evaluate the results of colonoscopic polypectomy in patients aged 45-49 in Türkiye, examining the prevalence and characteristics of colorectal polyps and malignancies, with the goal of establishing a database for Türkiye.

Methods: Colonoscopies in the endoscopy unit of our hospital between September 2020 and September 2023 were retrospectively examined. Patients aged 45-49 diagnosed with polyps or malignancies were included. Exclusions were made for patients who were unreachable, unable to complete a full colonoscopy, underwent the procedure for screening purposes, had a history of malignancy, suffered from polyp syndromes, or were under surveillance following a prior colonoscopy. We analyzed demographic information, indications for colonoscopy, and pathological findings. Statistical analyses were carried out using SPSS version 25.0, with a p-value of <0.05 considered statistically significant.

Results: From 748 patients, 106 with detected polyps or malignancy were included. Most patients were male (56.6%), with an average age of 47.07±1.52. Key colonoscopy indications were benign perianal diseases (34%), changes in bowel habits (27.4%), and anemia (12.3%). The majority of polyps were located in the left colon and rectum, predominantly low-grade dysplasia adenomas (68.9%) and high-grade dysplasia adenomas (9.4%). The polyp detection rate was 14.2%, and the malignancy rate was 2.8%.

Conclusion: According to the literature, the rate of polyp and malignancy detection in colonoscopies performed as part of the screening program for people aged 50 and over is similar to the rates found in our study. Based on this similarity, it may be appropriate to consider including patients in the 45-50 age group in the screening scope.

INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer in men and the second in women worldwide. According to data reported by the International Agency for Research on Cancer (IARC) in 2018, there are annually 1.8 million new cases of CRC and 0.8 million deaths globally.[1,2] In the United States, CRC is the fourth most commonly diagnosed cancer and is second in cancer-related deaths.[3] In Türkiye, CRC is the third most common cancer type in both sexes and ranks fourth in cancer-related mortality.[4] The most common pathway in the development of CRC is known as the adenoma-carcinoma sequence, first described by Fearon and Vogelstein in 1990.[5] This pathway progresses from the development of an adenoma in normal colon mucosa, through dysplastic changes, to carcinoma.[6] Colonoscopy plays a crucial role in interrupting this process and has advantages such as direct assessment of the colon mucosa, biopsy during the procedure, and excision of polyps and local tumors.[7] Colonoscopy is considered the gold standard in the diagnosis and screening of CRC.[8] In recent years, there have been significant changes in colon and rectum cancer screening guidelines. The American Cancer Society (ACS) recommended lowering the CRC screening start age from 50 to 45, marking a significant shift in this domain.[3] Studies have shown that from 1994 to 2014, there

was a 51% increase in CRC incidence in individuals under 55, and from 2005 to 2015, there was an 11% increase in mortality.[9,10] This change indicates that screening for CRC at a younger age is a critical step for early diagnosis and intervention. Despite the widespread adoption of CRC screening in Western countries, participation in Türkiye remains low. Our study aims to examine the indications and outcomes of colonoscopic polypectomy procedures performed in patients aged 45-49. With this approach, by evaluating the group between the screening age recommended by the ACS and the starting screening age in Türkiye, we aim to establish a foundation for changes in the screening age in our country and for future research.

MATERIALS AND METHODS

We retrospectively analyzed colonoscopies performed by general surgeons in the endoscopy unit of a tertiary reference hospital between September 2020 and September 2023. Patients aged between 45 and 50 were included in the study. Approval for this study was obtained from the local ethics committee (No: 2023/233; Date: November 10, 2023). It was conducted in accordance with the Declaration of Helsinki.

Patients diagnosed with polyps or malignancy were included in the study. Data from patients who were unreachable, those who could not undergo a total colonoscopy, those who underwent colonoscopy for screening purposes, those with a history of malignancy, those with polyp syndromes such as FAP-Attenuated FAP, and patients previously monitored following a colonoscopy were excluded from the study.

In patients undergoing colonoscopy, bowel preparation was achieved with two oral laxatives taken one day before the procedure and two rectal enemas administered on the morning of the procedure. A standard colonoscopy device (Fujifilm, EC-600WM, Tokyo, Japan) was used. During the procedure, patients were administered 1 mg/kg of midazolam and 0.5 mg/kg of meperidine. Patients who could proceed to the cecum during colonoscopy and whose lumen could be evaluated completely were included in the study.

Patients in whom lumen evaluation was not complete and in whom passage from one area to a more proximal area could not be achieved due to solid stool or angulation were considered as having an insufficient colonoscopic examination and were not included in the study. The evaluation parameters for patients were categorized into seven distinct domains: gender, age, indication for colonoscopy, polyp size, number of polyps excised, localization of polyps within the colonic tract, and the histopathological findings.

The colonic anatomy was divided into three regions for the purpose of this study: the right colon, spanning from the cecum to two-thirds of the way along the transverse colon; the left colon, from the last third of the transverse colon to the rectosigmoid junction (up to 15 cm from the anal verge); and the rectum, defined as the section within 15 cm of the anal canal.

Moreover, patients who were undergoing colonoscopy for conditions associated with benign perianal diseases, such as hemorrhoids, anal fissures, or perianal fistulas, were carefully documented and included under the category of benign perianal diseases.

Statistical Analyses

All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences) for Windows version 25.0 (SPSS Inc., Chicago, IL, USA). Normality was tested using the Kolmogorov-Smirnov and Shapiro-Wilk tests, along with graphical methods. If the data were normally distributed, the mean and standard deviation (±) were used; if not, the median and minimum (min)-maximum (max) values were used. Additionally, the data were expressed numerically (n) and as a percentage (%).

RESULTS

Data from 748 patients who met the study criteria within the last three years were examined. Of these, 106 patients with detected polyps and malignancy were included in the study. 56.6% (n=60) of the patients were male, and 43.4% (n=46) were female. Age was found to be normally distributed with an average of 47.07±1.52 (Table 1). Of the 106 patients, 34% (n=36) underwent colonoscopy due to benign perianal diseases, 27.4% (n=29) due to changes in bowel habits, 12.3% (n=13) due to anemia, 8.5% (n=9) due to macroscopic bleeding, 7.5% (n=8) due to nonspecific symptoms, 7.5% (n=8) due to a positive fecal occult blood test (FOBT), and 2.8% (n=3) due to weight loss (Table 2). The size and number of polyps were not normally distrib-

Table 1. The age and gender distribution of patients

	All patients	
	n	%
Sex		
Male	60	56.6%
Female	46	43.4%
Age	47.07±1.52	

Table 2. Indications for Colonoscopy

	Number	n %
Indication		
Bleeding	9	8.5%
Change in bowel habits	29	27.4%
Non- specific	8	7.5%
Fecal occult blood test (FOBT)	8	7.5%
Perianal benign diseases	36	34.0%
Anemia	13	12.3%
Weight loss	3	2.8%

FOBT: Fecal Occult Blood Test

Table 3. Polyp Locations

	Number	n %
Localization		
Rectum	15	14.2%
Left	48	45.3%
Right	23	21.7%
Multiple	20	18.9%

Table 4. Polyp Histopathologies

	Number	n %
Patoloji		
Hyperplastic	20	18.9%
Low Grade Dysplasia	73	68.9%
High Grade Dysplasia	10	9.4%
Malignant	3	2.8%

uted. The average polyp size was found to be 5 mm (min: 1-max: 30). The average number of detected polyps was 1 (min:1 - max:6). 14.2% (n=15) of the polyps were located in the rectum, 45.3% (n=48) in the left colon, 21.7% (n=23) in the right colon, and 18.9% (n=20) had multiple locations (Table 3). In our study, 68.9% (n=73) of the patients had low-grade dysplasia adenomas, 18.9% (n=20) had hyperplastic polyps, 9.4% (n=10) had high-grade dysplasia adenomas, and 2.8% (n=3) had malignancies on pathology (Table 4). During the procedure, endoclips were applied to 3 patients (2.8%) in our study. Two of these were due to bleeding, and one was applied as a precaution against the possibility of perforation due to a very large polyp base. While the rate of malignancy detection was 2.8%, the polyp detection rate was found to be 14.2%.

DISCUSSION

According to World Health Organization data, approximately 1.9 million new cases of CRC and 935,000 deaths from CRC are detected annually.[11] In developing countries, factors such as an aging population, suboptimal dietary habits, consumption of processed foods, obesity, a decrease in physical activity, and smoking are increasing the incidence of CRC.[12] Colonoscopy is considered the gold standard for early diagnosis of CRC. It offers the ability to determine the location of polyps, take biopsies, and perform polypectomies.[13] Given these features, colonoscopy is used as a fundamental tool in cancer screening programs in many countries. In Türkiye, since 2014, it is recommended to perform a colonoscopy every 10 years and a fecal occult blood test every 2 years for screening purposes in individuals over the age of 50.[14]

In our study, we observed that colorectal polyps tend to occur more frequently in males, predominantly located in the left colon and rectum. A significant finding in our study is that many patients between 45-50 years old showed early signs of potentially precancerous adenomatous polyps or even malignancies. The most common reasons for undergoing a colonoscopy in this group were benign perianal diseases, changes in bowel habits, and anemia. This data strongly suggests that lowering the CRC screening age from 50 to 45 in Türkiye could be a significant step towards early detection and intervention in the adenoma-cancer sequence.

In our study, the frequency of polyps in the age range of 45-50 years was determined to be 14.2%. Within the patients with polyps, the rate of malignancy was observed to be 2.8%. Upon examination of the entire patient group, the rate of high-grade dysplasia and malignancy was found to be 1.7%. These rates appear to be consistent with data in the literature. For instance, The National Polyp Study group has reported an adenoma frequency of 13% in patients under the age of 50.[15] We hypothesize that the higher detection rate of polyps in our study may be associated with the inclusion of patients over the age of 45 and a smaller patient count. While Aydemir and Yamak's study [16] found a polyp detection rate of 15% and a malignancy rate of 2%, Kızıltoprak et al.[17] reported these rates as 25.8% and 3.1% respectively. We attribute the higher rates in these studies compared to ours to the increase in CRC incidence with age and the fact that these studies examined patients over the age of 50. In a study conducted by Lieberman et al.,[18] the polyp detection rate was 37.5%, the high-grade dysplasia detection rate was 1.6%, and the malignancy detection rate was 1%; however, in this study, the average age of patients was 62, and 97% of them were male.

Studies on indications for colonoscopy in individuals under the age of 50 are limited in the literature. In the study conducted by Yalçın et al.,[19] indications for colonoscopy were reported as constipation in 35.7% of cases, rectal bleeding in 16.1%, anemia in 12.9%, and fecal occult blood test (FOBT) positivity in 7.5%. In our study, the indications were identified as benign perianal diseases in 34%, changes in bowel habits in 27.4%, anemia in 12.3%, rectal bleeding in 8.5%, and FOBT positivity in 7.5%. Unlike the literature, the lower rate of rectal bleeding indication in our study is attributed to the classification of diseases that can cause bleeding, such as hemorrhoids, anal fissures, and perianal fistulas, as a separate category of benign perianal diseases. For other indications, our study's findings are consistent with those reported in the literature.

In the studies conducted, it has been observed that the frequency of polyp and malignancy localization in the left colon ranges from 66.3% to 69.3%. Moreover, it has been reported that the proportion of male patients varies between 59.3% and 76.4%.[13,20] The results of our study are in line with this trend in the literature; polyps and malignancies were detected in the left colon and rectum in 59.5% of patients, with males constituting 56.6% of this patient group.

In the study conducted by Coşkun et al.,[13] the rate of adenomatous polyps was established at 82.5%. Similarly, Yalçın et al.[19] reported an adenomatous polyp rate of 77.2% in their research. In these studies, adenomatous polyps were classified as tubular, tubulovillous, and villous adenomas. In our study, the adenomatous polyp rate was found to be

78.3%. Taking into consideration the risk of malignancy, we examined adenomatous polyps in two categories: those with low-grade dysplasia and those with high-grade dysplasia. Low-grade dysplasia was detected in 68.9% of patients, while high-grade dysplasia was observed in 9.4%.

However, our study is not without limitations. The primary one is the lack of colonoscopies performed mainly for screening purposes, which is likely due to the initiation of CRC screening programs at the age of 50 in our country. Another limitation is the small patient sample and the absence of follow-up data. Since we do not have a control group to compare with, our study contains epidemiological information and a comparison had to be made with literature data.

Conclusion

In conclusion, considering the studies mentioned above, the rate of polyp and malignancy detection in colonoscopy performed according to the screening program for people aged 50 and over is similar to the rates found in our study. Based on this similarity, it may be appropriate to include patients in the 45-50 age group within the scope of screening. However, it is obvious that randomized controlled studies with a large patient population are needed to decide this.

Ethics Committee Approval

This study approved by the Sehit Prof. Dr. İlhan Varank Training And Research Hospital Ethics Committee (Date: 08.11.2023, Decision No: 2023/233).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: C.B.O., F.M., A.Ç., M.M.A.; Design: C.B.O., F.M., M.M.A., A.Ç.; Supervision: C.B.O., F.M., M.M.A., A.Ç.; Materials: F.M., C.B.O.; Data: C.B.O.; Analysis: F.M.; Literature search: A.Ç.; Writing: C.B.O.; Critical revision: M.M.A.

Conflict of Interest

None declared.

REFERENCES

1. El Kinany K, Huybrechts I, Kampman E, Boudouaya HA, Hatime Z, Mint Sidi Deoula M, et al. Concordance with the World Cancer Research Fund/American Institute for Cancer Research recommendations for cancer prevention and colorectal cancer risk in Morocco: A large, population-based case-control study. Int J Cancer 2019;145:1829–37. [CrossRef]
2. World Cancer Research Fund. Colorectal cancer statistics. Available at: https://www.wcrf.org/dietandcancer/cancer-trends/colorectal-cancer-statistics. Accessed Feb 21, 2024.
3. Wolf AMD, Fontham ETH, Church TR, Flowers CR, Guerra CE, LaMonte SJ, et al. Colorectal cancer screening for average-risk adults: 2018 Guideline update from the American Cancer Society. CA Cancer J Clin 2018;68:250–81. [CrossRef]
4. Türkiye Cumhuriyeti Sağlık Bakanlığı Türkiye Halk Sağlığı Kurumu. Türkiye Cancer Statistics. Available at: https://hsgm.saglik.gov.tr/depo/birimler/kanser-db/Dokumanlar/Istatistikler/ANA_rapor_2012sooonn.pdf. Accessed Feb 21, 2024.
5. Vogelstein B, Fearon ER, Hamilton SR, Kern SE, Preisinger AC, Leppert M, et al. Genetic alterations during colorectal-tumor development. N Engl J Med 1988;319:525–32. [CrossRef]
6. Burgart LJ. Colorectal polyps and other precursor lesions: Need for an expanded view. Gastroenterol Clin North Am 2002;31:959–70. [CrossRef]
7. Rex DK, Johnson DA, Anderson JC, Schoenfeld PS, Burke CA, Inadomi JM; American College of Gastroenterology. American College of Gastroenterology guidelines for colorectal cancer screening 2009 [corrected]. Am J Gastroenterol 2009;104:739–50. [CrossRef]
8. Sonnenberg A, Delcò F, Inadomi JM. Cost-effectiveness of colonoscopy in screening for colorectal cancer. Ann Intern Med 2000;133:573–84. [CrossRef]
9. Surveillance Epidemiology and End Results (SEER) Program. SEER*Stat Database: Incidence - SEER 9 Regs Research Data with Delay-Adjustment, Malignant Only, Nov 2016 Sub (1975-2014) <Katrina/Rita Population Adjustment> - Linked To County Attributes - Total US, 1969-2015 Counties. Bethesda (MD): National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program; 2017. Available at: https://seer.cancer.gov/data-software/documentation/seerstat/nov2016/#:~:text=Delay%20Adjustment%20Databases%3A%20Rate%20Session%20Only. Accessed Feb 21, 2024.
10. Surveillance Epidemiology and End Results (SEER) Program. SEER*Stat Database: Mortality-All COD, Aggregated With State, Total US (1969-2014) <Katrina/Rita Population Adjustment>. Bethesda : National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program, Cancer Statistics Branch; 2017.
11. World Health Organization. WHO world cancer fact sheets. Available at: https://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf. Accessed May 8, 2021.
12. Kuipers EJ, Grady WM, Lieberman D, Seufferlein T, Sung JJ, Boelens PG, et al. Colorectal cancer. Nat Rev Dis Primers 2015;1:15065. [CrossRef]
13. Coşkun A, Kandemir A. Analysis of colonoscopic polypectomy results. Endoscopy Gastrointest 2017;25:66–9.
14. Türkiye Cumhuriyeti Sağlık Bakanlığı Sağlık Hizmetleri Genel Müdürlüğü. Colorectal Cancer Clinical Protocol. Available at: https://dosyamerkez.saglik.gov.tr/Eklenti/31682/0/kolorektal-kanser-klinik-proto-kolpdf.pdf. Accessed Feb 21, 2024.
15. Loeve F, Boer R, Zauber AG, Van Ballegooijen M, Van Oortmarssen GJ, Winawer SJ, et al. National Polyp Study data: Evidence for regression of adenomas. Int J Cancer 2004;111:633–9. [CrossRef]
16. Aydemir YG, Yamak M. Results of colonoscopy at a special surgical diagnosis center. Maltepe Med J 2020;1:6–10. [CrossRef]
17. Kızıltoprak N, Karadağ M, Özcan B, Genç MS, Ozkan Ö. Screening colonoscopy results in patients over fifty. J Surg Arts 2023;16:45–8.
18. Lieberman DA, Weiss DG, Bond JH, Ahnen DJ, Garewal H, Chejfec G. Use of colonoscopy to screen asymptomatic adults for colorectal cancer. Veterans Affairs Cooperative Study Group 380. N Engl J Med 2000;343:162–8. [CrossRef]
19. Yalçın MS, Sayın S, Bursalı BA. Analysis of colonoscopic polypectomy results in Aksaray. Middle East Med J 2019;11:219–23. [CrossRef]
20. Solakoğlu T, Atalay R, Köseoğlu H, Özer Sarı S, Demirezer Bolat A, Akın E, et al. Analysis of 2222 colorectal polyps in 896 patients: A tertiary referral hospital study. Turk J Gastroenterol 2014;25:175–9. [CrossRef]

Kolorektal Kanser Tarama Yaşının Düşürülmesinin Erken Tanı ve Tedavi Üzerindeki Etkisi: Türk Kohortunda Retrospektif Bir Çalışma

Amaç: Bu çalışma, Amerikan Kanser Derneği'nin kolorektal kanser (CRC) tarama yaşını 50'den 45'e düşürme önerisi doğrultusunda planlandı. Çalışmamız, 45-49 yaş arası Türkiye'deki hastalarda kolonoskopik polipektomi sonuçlarını değerlendirmeyi amaçlamaktadır. Böylelikle kolorektal poliplerin ve malignitelerin prevalansı ve özellikleri incelenerek Türkiye için bir veri tabanı oluşturulması hedeflenmektedir.

Gereç ve Yöntem: Hastanemiz endoskopi ünitesinde Eylül 2020 ile Eylül 2023 tarihleri arasında gerçekleştirilen kolonoskopiler retrospektif olarak incelendi. Polip veya malignite tanısı almış 45-49 yaş aralığındaki hastalar çalışmaya dahil edildi. Verilerine ulaşılamayan hastalar, tam kolonoskopi yapılamayanlar, tarama amaçlı yapılan kolonoskopiler, malignite öyküsü ve polip sendromu olanlar, polipektomi sonrası takipte olan hastalar çalışma dışı bırakıldı. Çalışmaya alınan hastaların demografik bilgileri, kolonoskopi endikasyonları ve patolojik bulguları analiz edildi. İstatistiksel analizler SPSS sürüm 25.0 kullanılarak yapıldı ve p değeri <0.05 istatistiksel olarak anlamlı kabul edildi.

Bulgular: 748 hastadan polip veya malignite tespit edilen 106'sı çalışmaya dahil edildi. Hastaların çoğunluğu erkek (%56.6), ortalama yaş 47.07±1.52 idi. Önemli kolonoskopi endikasyonları benign perianal hastalıklar (%34), bağırsak alışkanlıklarında değişiklik (%27.4) ve anemi (%12.3) idi. Poliplerin çoğu sol kolon ve rektumda yer alıyor, çoğunlukla düşük dereceli displazi adenomları (%68.9) ve yüksek dereceli displazi adenomları (%9.4) idi. Polip tespit oranı %14.2 ve malignite oranı %2.8 idi.

Sonuç: Literatüre göre, 50 yaş ve üzeri kişiler için tarama programı kapsamında yapılan kolonoskopilerdeki polip ve malignite tespit oranı, çalışmamızda bulunan oranlarla benzerdir. Bu benzerlik temel alındığında, 45-50 yaş grubundaki hastaları tarama kapsamına almayı düşünmek uygun olabilir.

Anahtar Sözcükler: Kolorektal kanser; malignite; polip; tarama yaşı; Türkiye.

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Original Article

Motorcycle Accident Cases Presented to the Emergency Department Before and During the COVID-19 Pandemic

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Keywords: COVID-19; EMTRAS; ESI; motorcycle accident; pandemic; trauma.

ABSTRACT

Objective: To examine patients who presented to the emergency department following motorcycle accidents before and during the COVID-19 pandemic period in order to comparatively assess the incidence of these accidents, associated trauma severity, and patient outcomes.

Methods: In this retrospective observational study, we evaluated 1,137 patients who presented to the Adult Emergency Department of Bakırköy Dr. Sadi Konuk Training and Research Hospital with injuries caused by motorcycle accidents. The electronic files of the patients who were determined to have presented to the emergency department after a motorcycle accident were screened, and their age, gender, blood pressure, pulse, oxygen saturation, respiratory rate, body temperature (at presentation), time of the accident, motorcycle speed at the time of the accident as reported by the driver, protective equipment used, time of arrival at the emergency department, length of stay in the emergency department and hospital, the types of treatment applied throughout the patients' stay, and the outcomes of the patients were recorded in the case forms.

Results: Of the 1135 patients included in the study, 129 (11.4%) presented to the emergency department before the pandemic and 1,006 (88.6%) during the pandemic period. There were 1,055 (93%) male patients and 80 (7%) female patients. Of all the patients, 145 (12.9%) were hospitalized, and 990 (87.2%) left the hospital. Of those who left the emergency room, 42 (3.7%) refused treatment, and 35 (3.1%) left without the physician's approval. Of the hospitalized patients, 20 (1.8%) were admitted to the intensive care unit, and four (0.4%) were referred to other hospitals. Upon examination of in-hospital mortality, it was determined that 1,132 (99.7%) patients survived, and three (0.3%) died. When assessing the association between injury locations according to the use of full-body protective equipment, a correlation was found in terms of head and neck, lung, extremity, pelvis, and multi-trauma injuries.

Conclusion: Regardless of traffi density, the use of protective equipment by motorcycle drivers prevents serious injuries in accidents. The EMTRAS and ESI scores are clinical prediction tools that can be used to predict mortality and morbidity in motorcycle accidents.

INTRODUCTION

Trauma is one of the leading causes of mortality worldwide.[1] According to the data of the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC), more than nine individuals die every minute in the world as a result of violence and injury.[2] Trauma is the most common cause of death and disability in the population under the age of 35.[3] More than 50 million patients receive some form of trauma-related medical care each year in the USA, and trauma patients constitute 30% of all intensive care patients.[4] Globally, motor vehicle crashes rank as the third most prevalent cause of mortality and are the primary cause of death in young adults, accounting for more than half of road traffi deaths.[5] In Türkiye, deaths due to accidents ranked sixth among all causes of mortality in 2018 and 2019.[6] Therefore, it is crucial to promptly assess injuries resulting from traffi accidents and ensure the use of protective equipment.

The COVID-19 pandemic necessitated that individuals stay at home and opt for home deliveries due to the restrictions implemented. Although this resulted in a decline in general traffic, it also prompted an increased involve-

ment of motor couriers in traffic. In a previous study, Sutherland et al.[7] examined the rates of traffic accidents in different US states during the pandemic, and another study conducted in Peru reported that traffic accidents decreased during the pandemic lockdown period.[8] However, the authors expected an increase in traffic accidents in the post-lockdown period.

In this study, we examined 1,137 cases that presented to the emergency department of a tertiary health center following motorcycle accidents, with the aim of comparing the differences in the incidence of these accidents, associated trauma severity, and patients' outcomes between the pre-pandemic and pandemic periods.

MATERIALS AND METHODS

This retrospective observational study included 1,137 patients aged 18 years and over who presented to the Adult Emergency Department of Bakırköy Dr. Sadi Konuk Training and Research Hospital after incurring injuries in motorcycle accidents from March 11, 2019, through March 10, 2022. The study was conducted in accordance with the ethical standards of the Declaration of Helsinki and approved by the Hospital Clinical Research Ethics Committee (No: 2022-15-04/Date: 01-08-22).

The emergency department where the study was conducted serves a tertiary training and research hospital, to which approximately 300,000 patients are admitted annually. In addition to being a level 3 trauma center, this department is the center for cardiological and neurological emergencies.

The adult emergency department contains two red zones, one of which is allocated for trauma patients, and accepts ambulance referrals from the 112-emergency line. There are six stretchers and monitors in both rooms. In addition to these critical care rooms, there is a resuscitation room where only cardiac arrest patients are managed. There are also yellow and green zones where all outpatients are evaluated. In the red zone, patient admissions can be made through the 112-ambulance service. After the triage evaluation and doctor's examination of outpatients, if necessary, the management of the diagnosis and treatment process of patients is transferred to the red zone. Due to the round-the-clock provision of emergency services, the study was conducted continuously for 24 hours without interruption.

The study included 1,137 patients after sustaining injuries as a result of motorcycle accidents. The electronic files of the patients who were determined to have presented to the emergency department after a motorcycle accident were screened, and their age, gender, blood pressure, pulse, oxygen saturation, respiratory rate, body temperature (at presentation), time of the accident, motorcycle speed at the time of the accident as reported by the driver, protective equipment used, time of arrival at the emergency department, length of stay in the emergency department and hospital, the types of treatment applied throughout the patients' stay, and the outcomes of the patients were recorded in the case forms. In addition, the emergency severity index (ESI) scores of the patients were calculated according to the information obtained at the time of presentation and recorded in the case forms. Lastly, the emergency trauma score (EMTRAS) was calculated based on imaging, examination, and test findings accessed through the electronic system and recorded in the same forms.

Patients were evaluated for all exclusion criteria, and eligible patients with complete data were included in the sample. According to their presentation dates, the patients included in the sample were evaluated in three groups: pre-pandemic (March 11, 2019-March 10, 2020), lockdown period during the pandemic (March 11, 2020-March 10, 2021), and post-lockdown period during the pandemic (March 11, 2021-March 10, 2022). After the study was completed, the data in the study forms were recorded in electronic format for statistical analysis. A data collection form prepared by the researchers was used to collect data in a standard way. Using this form, the following information was recorded regularly throughout the study:

The patient's name, surname, and protocol number; the date and time of the patient's presentation to the emergency department; whether the patient presented during the lockdown or post-lockdown period for those who presented during the pandemic; the patient's age and gender; the time of the accident; the speed at which the accident occurred (according to the anamnesis taken from the driver); protective equipment use; whether the patient was working as a motor courier; vital parameters (pulse, respiratory rate, blood pressure, body temperature, and SpO2) at the time of presentation to the emergency department; physical examination findings; injury areas; types of injuries; fracture area in the presence of a bone fracture; laboratory findings according to the blood samples taken at the time of presentation; EMTRAS and ESI scores; length of stay in the emergency department and hospital; hospitalization and discharge status; inpatient clinic to which the patient was admitted if hospitalization was required; and outcomes (ward admission, intensive care unit admission, and in-hospital mortality).

Inclusion criteria

- Presenting to the emergency department following a motorcycle accident from March 11, 2019, through March 10, 2022, and being assigned the International Classification of Diseases code V29.9

- An age of 18 or over

- Complete data being accessible through the electronic system

- Examination findings being accessible through the electronic system

- Data availability for the calculation of the ESI and EMTRAS scores

Exclusion criteria

- Lack of patient consent to participate in the study

The primary endpoint of the study was the incidence of patient presentations to the emergency department as a result of a motorcycle accident. The secondary endpoint was the relationship between the evaluation scores and outcomes of patients who presented to the emergency department following a motorcycle accident.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation or median (minimum-maximum) according to normal or non-normal data distributions. Categorical variables were presented as absolute values and percentages. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to evaluate the distribution of the data. In correlation analyses, Pearson's rho test was used for parametric data and Spearman's rho test for non-parametric data. The comparison of the groups was undertaken using the Mann-Whitney U and Wilcoxon W tests for continuous variables, while the Pearson $\chi 2$ and Fisher's exact tests were utilized for categorical variables. The Kruskal-Wallis test was conducted to examine the relationship of the ordinal three-group data with other independent groups. The statistical alpha significance level was accepted as $p<0.05$. Statistical analysis of the data was undertaken using IBM SPSS version 25.

RESULTS

A total of 754,961 patients presented to the Adult Emergency Department of Bakırköy Dr. Sadi Konuk Training and Research Hospital between March 11, 2019, and March 10, 2022. Of these patients, 626,066 were excluded because they had reasons other than trauma. In addition, 126,045 of the trauma patients were excluded because they were not motorcycle drivers; 375 were excluded because they were motorcycle drivers under the age of 18; and 836 were excluded due to missing data. Lastly, although 502 patients had available electronic data, they were not included in the study due to a lack of information on whether they used protective equipment. After applying the inclusion and exclusion criteria, the study was conducted with a total of 1,137 motorcycle drivers who had had a traffic accident. Of the patients included in the study, 129 (11.4%) presented to the emergency department before the pandemic, and 1,006 (88.6%) during the pandemic. There were 1,055 (93%) male and 80 (7%) female patients. The mean age of the patients was 25.61±5.74 years.

Table 1 shows the comparison of the demographic characteristics and vital parameters of the patients according to their presentation periods. Upon examining the laboratory values of the patients presenting before and during the pandemic, statistically significant differences were detected in white blood cell count (p=0.000), platelet count (p=0.006), neutrophil count (p=0.000), and activated partial thromboplastin time (p=0.000) (Table 2).

The ESI scores statistically significantly differed between the pre-pandemic and pandemic lockdown groups, with the latter having a higher mean rank than the former (p=0.000). There was also a statistically significant difference in the EMTRAS scores of the pre-pandemic and pan-

Table 1. Comparison of the demographic characteristics and vital parameters of the patients according to the presentation period

	Pre-pandemic (n=129) median (25th- 75th)	**Pandemic (n=1,006) median (25th-75th)**	**p**	**z**	**u**
SBP (mmHg)	120.0 (115.5-124.0)	122.0 (119.0-127.0)	0.002	-3.172	53,860.50
DBP (mmHg)	75.0 (72.5-80.0)	80.0 (74.0-85.0)	0.000	-4.849	48,388.50
Pulse (beats/min)	76.0 (74.0-80.5)	75.0 (75.0-78.0)	0.096	-1.666	59,180.50
Respiratory rate (breaths/min)	15 (13-15)	15 (15-16)	0.000	-4.645	49,706.50
SpO_2 (%)	99 (99-100)	99 (98-99)	0.000	-4.165	51,409.00
Body temperature (°C)	36.2 (36.1-36.4)	36.2 (36.2-36.4)	0.068	-1.822	58,607.00
Speed at the time of accident (km/h)	40 (40-60)	40 (30-40)	0.000	-7.217	40,765.00
Length of stay in emergency department (min)	95.0 (48.5-233.5)	103.0 (54.0-201.0)	0.686	-0.404	63,469.50
Length of hospital stay (min)	97.0 (50.0-258-5)	103.0 (54.0-210.0)	0.894	-0.133	64,420.00
	Pre-pandemic (n=129) mean±SD	**Pandemic (n=1,006) mean±SD**	**P**	**t**	**95% confidence interval Lower bound** **Upper bound**
Age	24.74±5.68	25.72±5.74	0.68	-1.82	-2.033 0.073

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; SpO_2: Oxygen saturation; SD: Standard deviation.

Table 2. Laboratory values of patients admitted before and during the pandemic period

	Pre-pandemic (n=129) median (25th- 75th)	Pandemic (n=1,006) median (25th-75th)	P	Z	U
WBC count (10 e³/uL)	9.03 (7.57-10.75)	8.17 (6.69-9.57)	0.000	-4.442	49,318.00
Platelet count (10 e³/uL)	238.0 (197.5-277.0)	228.5 (189.0-264.0)	0.006	-2.756	55,238.50
Neutrophil count	5.60 (4.42-7.35)	4.61 (3.55-6.23)	0.000	-4.710	48,379.00
Lymphocyte count	2.49 (1.93-2.82)	2.31 (1.75-2.74)	0.068	-1.828	58,479.00
Neutrophil/lymphocyte ratio	2.15 (1.63-3.80)	2.03(1.49-2.86)	0.056	-1.910	58,192.50
Hematocrit (%)	43.20 (41.55-45.50)	43.80 (41.90-45.80)	0.132	-1.506	59,610.50
ALT (U/L)	19 (15-27)	19 (15-26)	0.355	-0.925	61,651.00
AST (U/L)	26 (20-34)	29 (21-37)	0.208	-1.259	60,483.00
PTT (sec)	14.0 (12.5-15.1)	13.9 (13.1-14.7)	0.947	-0.066	64,656.00
aPTT (sec)	29.40 (27.15-33.50)	28.10 (25.70-29.60)	0.000	-5.142	46,881.00
INR	1.05 (0.97-1.13)	1.04 (0.96-1.11)	0.091	-1.688	58,977.00
Base excess (mmol/L)	1.2 (-0.1-2.1)	1.5 (0.3-2.3)	0.060	-1.883	58,295.50
Lactate (mmol/L)	1.50 (1.10-1.95)	1.60 (1.20-2.00)	0.244	-1.166	60,811.00

	Pre-pandemic (n=129) mean±SD	Pandemic (n=1,006) mean±SD	P	t	95% confidence interval Lower bound	Upper bound
Hemoglobin (gr/dL)	14.36±1.58	14.64±1.17	0.5 1	-1.96	-0.567	0.001

WBC: White blood cell; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; PTT: Prothrombin time; aPTT: Active partial prothrombin time; INR: International normalized ratio.

demic lockdown groups, with the former having a higher mean rank than the latter [318.17 (median: 0 (min: 0-max: 7)) vs. 277.28 (median: 0 (min: 0-max: 4))] (p=0.000). Concerning the GCS scores, a statistically significant difference was found between the pre-pandemic and pandemic post-lockdown groups, with the latter having a higher mean

Table 3. Comparison of fractures between the pre-pandemic and pandemic periods

	Pre-pandemic n (%)	Pandemic n (%)	p
Skull fracture	3 (2.3)	20 (2.0)	0.739*
Maxillofacial fracture	10 (7.8)	54 (%5.4)	0.269
Cervical vertebra fracture	4 (3.1)	13 (1.3)	0.118*
Thoracal vertebral fracture	5 (3.9)	12 (1.2)	0.035*
Lumbar vertebral fracture	4 (3.1)	20 (2.0)	0.341*
Pelvic-sacroiliac bone fracture	8 (6.2)	10 (1.0)	0.000*
Rib fracture	7 (5.4)	47 (4.7)	0.705
Femoral fracture	4 (3.1)	16 (1.6)	0.272*
Patellar fracture	0 (0.0)	9 (0.9)	0.609*
Tibial fracture	7 (5.4)	35 (3.5)	0.316*
Fibular fracture	2 (1.6)	29 (2.9)	0.567*
Foot-ankle fracture	15 (11.6)	53 (5.3)	0.004
Humerus fracture	4 (3.1)	21 (2.1)	0.517*
Radius fracture	3 (2.3)	37 (3.7)	0.613*
Ulnar fracture	3 (2.3)	9 (0.9)	0.147*
Hand-wrist fracture	5 (3.9)	50 (5.0)	0.586
Clavicular fracture	4 (3.1)	19 (1.9)	0.321*
Scapular fracture	3 (2.3)	6 (0.6)	0.072*

rank than the former (351.06 [median: 15 (min: 6-max: 15)] vs. 326.60 [median: 15 (min: 3-max: 15)]) (p=0.000).

Upon examining the use of protective equipment at the time of the accident, statistically significant differences were detected between the pre-pandemic, pandemic lockdown, and pandemic post-lockdown periods in terms of helmet use, glove use, knee pad use, jacket use, and full-body equipment use (p=0.000, 0.019, 0.000, 0.001, and 0.000, respectively). In addition, the rates of thoracic vertebral fractures, pelvic-sacroiliac bone fractures, and foot-ankle fractures statistically significantly differed between the pre-pandemic and pandemic periods (p=0.035, 0.000, and 0.004, respectively) (Table 3).

The evaluation of the injury sites of the patients according to whether they presented to the emergency department before or during the pandemic period revealed cardiac injuries in two (1.6%) cases before the pandemic and no case during the pandemic, extremity injuries in 100 (77%) and

Table 4. Comparison of injury sites between the pre-pandemic and pandemic periods

	Pre-pandemic n (%)	Pandemic n (%)	p
Head and neck injury	24 (18.6)	232 (23.1)	0.254
Thoracic injury	23 (17.8)	177 (17.6)	0.947
Cardiac injury	2 (1.6)	0 (0.0)	0.013*
Abdominal injury	8 (6.2)	89 (8.8)	0.312
Extremity injury	100 (77.5)	967 (96.1)	0.000
Vertebral injury	12 (9.3)	142 (14.1)	0.133
Pelvic injury	9 (7.0)	10 (1.0)	0.000*
Genitourinary injury	3 (2.3)	10 (1.0)	0.176*
Multi-trauma	20 (15.5)	130 (12.9)	0.415

*Fisher's exact test

Table 5. Comparison of injury sites between the pre-pandemic and pandemic periods

	Pre-pandemic n (%)	Pandemic n (%)	p
Outcome			
Discharge	90 (69.8)	823 (81.8)	0.001
Hospitalization	27 (20.9)	111 (11.0)	0.001
Ward admission	19 (14.7)	99 (9.8)	0.087
Intensive care unit admission	8 (6.2)	12 (1.2)	0.001*
Refused treatment	4 (3.1)	38 (3.8)	1.000*
Left hospital without physician's approval	5 (3.9)	30 (3.0)	0.585*
Referred	0 (0.0)	4 (0.4)	1.000*
Death	3 (2.3)	0 (0.0)	0.001*
Inpatient clinic			
Orthopedics	15 (11.6)	82 (8.2)	0.184
General surgery	4 (3.1)	5 (0.5)	0.013*
Anesthesia and reanimation	3 (2.3)	3 (0.3)	0.022*
Neurosurgery	2 (1.6)	13 (1.3)	0.684*
Thoracic surgery	3 (2.3)	7 (0.7)	0.095*
Urology	0 (0.0)	1 (0.1)	1.000*
In-hospital mortality	3 (2,3)	0 (0,0)	0,001*
	Pre-pandemic n=8 median (25th-75th)	**Pandemic n=12 median (25th-75th)**	**P**
Length of hospital stay for those requiring intensive care (min)	19,264 (7,080-33,770)	14,006 (5,131-35,247)	0.396**

*Fisher's exact test; **Mann-Whitney U test.

967 (96.1%) cases, respectively, and pelvic injuries in nine (7.0%) and 10 (1.0%) cases, respectively. In addition, the rates of injury sites between the pre-pandemic and pandemic periods differ from each other (Table 4).

The inpatient clinics to which the patients were admitted were the general surgery clinic for four (3.1%) cases before the pandemic and five (0.5%) cases during the pandemic period, and the anesthesia and reanimation clinic for three (2%) and three (0.3%) cases, respectively. The pre-pandemic and pandemic presentations showed statistically significant differences in relation to the rates of patients admitted to the general surgery and anesthesia and reanimation clinics (p=0.013 and 0.022, respectively). No statistically significant differences were observed in terms of the remaining inpatient clinics to which the patients were admitted (Table 5).

In-hospital mortality occurred in three (2.3%) cases before the pandemic and no case during the pandemic period, indicating a statistically significant difference (p=0.001).

DISCUSSION

Globally, motor vehicle crashes are the third most common cause of death and account for 50% of all road fatalities among young adults. Of the 1,135 cases included in our study, 1,055 (93%) were male and 80 (7%) were female. In a study conducted by Moskal et al.,[9] the rate of male patients was found to be 94.7%. In another study, Santos et al.[10] reported the rate of male cases to be 85.81%. The higher rate of male patients in our study is consistent with the literature.[11,12]

According to WHO, the male gender is an important factor among the reasons that determine the occurrence of traffic accidents.[13]

In this study, the median length of stay in the emergency department was determined to be 101 (min: 53-max: 205) minutes, while the median length of hospital stay was 103 (min: 53-max: 216) minutes. In a study conducted by Qasim et al.,[14] no significant difference was found between patients with/without personal protective equipment in the length of stay of trauma patients in the emergency department. In another study, Güngör et al.[11] evaluated 59 patients who presented to the emergency department due to a motorcycle accident and reported their median stay in the emergency department as 134.50 (min: 15-max: 705) minutes.

In a study conducted with 792 courier accidents in Seoul between 2007 and 2009, it was concluded that although motor accidents constituted only 5% of all accidents, the mortality rate was 12% due to the use of fast engines for fast delivery.[15] In our study, the median speed of the patients at the time of their motorcycle accident was found to be 40 (min: 30-max 40) km/h. Upon examining in-hospital mortality, we determined that 1,132 (99.7%) patients survived, while three (0.3%) patients died.

We consider that the difference is due to the lower speed of motorcycle use in urban areas in our study and the lower vehicle density in traffic resulting from the prevailing pandemic conditions for much of the study period.

Before the pandemic, five (3.9%) of our patients had thoracic vertebral fractures, eight (6.2%) had pelvic-sacroiliac bone fractures, and 15 (11.6%) had foot-ankle fractures, while these fractures were detected in 12 (1.2%), 10 (1.0%), and 53 (5.3%), respectively, during the pandemic period, indicating a statistically significant difference. In a study conducted by Salottolo et al.,[16,17] statistically significant differences were found in the rates of superficial head, lower extremity, and knee injuries between the pre-pandemic and pandemic periods. We consider that the disparity between the two studies may be related to the differences in the rates of injury mechanisms. While Salottolo et al.[16] reported that 42.2% of the pre-pandemic cases were due to a simple fall and 43.8% of the pandemic cases were due to simple fall-related injuries, head trauma cases in our study were lower both before and during the pandemic periods due to the majority of our patients wearing a helmet at the time of the accident (71.3% and 85.8%, respectively).

In a study of 212 patients evaluating motorcycle accidents in Türkiye,[18] it was determined that 50% of the traumas resulting from motorcycle accidents were extremity injuries and 48.6% were head injuries. A study examined 381 motorcycle accident injuries and reported that 75.5% of the fractures were of the lower extremity and 24.5% were of the upper extremity.[19] Similarly, in the current study, the rates of lower extremity fractures were higher both in the pre-pandemic and pandemic periods. In addition, extremity injuries constituted the most frequent injury sites at a rate of 77.5% before the pandemic and 96.1% during the pandemic period, and there was also a statistically significant difference between the two groups.[19]

In this study, there was a negative correlation between the EMTRAS score and working as a motor courier. A negative correlation was also found between working as a motor courier and experiencing multiple traumas. In addition, the ESI score groups statistically significantly differed between the pre-pandemic and pandemic periods. While the rate of patients with ESI scores 1 and 2 was 13.9% before the pandemic, it was 2.1% during the pandemic period. The ESI score groups statistically significantly differed between the pre-pandemic and pandemic periods. ESI is a five-level triage system with four basic decision stages included in its algorithm that identifies patients who require urgent intervention and are at risk of being kept waiting and determines the triage category of the patient based on the probable use of resources.[20,21] An increase in the ESI score indicates a lower possibility of resource use or intervention requirements. Similar to our study, İlhan et al.[22] observed a statistically significant difference in the ESI score of their groups, but since our study was focused on motorcycle accidents, we detected a decrease in the patient group with ESI scores 1 and 2 during the pandemic period, while İlhan et al.[22] reported an increase in these patients during this period since they included all trauma

groups in their evaluation.

In our study, despite the increasing number of motorcycle accidents during the pandemic period, the EMTRAS and ESI scores were found to be better when compared to the pre-pandemic period. The decreased incidence of severe trauma during the pandemic, as indicated by the lower EMTRAS and ESI scores, can be attributed to increased inspections and reduced traffic density during this period, as well as the use of protective gear in accidents involving motor courier drivers. These findings suggest that it would be beneficial to implement company policies supporting protective equipment among motor couriers. Maintaining these policies at the same level in non-pandemic periods will be an important factor in preventing high mortality and morbidity in motorcycle accidents.

Limitations

The first limitation of our study is that it was conducted in a single center in a single province. There is a need for multicenter studies with a larger patient population to confirm the data obtained from our study. In addition, although the study was conducted in a trauma center, our hospital being designated as a pandemic reference center during the pandemic period may have affected the homogeneity of presenting patients, which can be considered another limitation.

Conclusion

In this study, we determined that the use of full-body equipment by motorcycle riders and motor couriers had the potential to prevent serious injuries and trauma. Therefore, it is important for individuals working in this sector and employers to encourage the use of appropriate safety equipment that will protect the head, neck, lungs, extremities, and pelvic area while riding a motorcycle.

Ethics Committee Approval

This study approved by the Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committee (Date: 01.08.2022, Decision No: 2022-15-04).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: E.C., H.D.; Design: E.C., H.D.; Supervision: E.C., H.D.; Fundings: E.C., H.D.; Materials: E.C., H.D.; Data: E.C.; Analysis: E.C.; Literature search: E.C.; Writing: E.C., H.D.; Critical revision: H.D.

Conflict of Interest

None declared.

REFERENCES

1. Murray CJL, Lopez AD. The global burden of disease: Summary; a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020. Geneve: World Health Organization; 1996.
2. World health statistics 2018: monitoring health for the SDGs, sustainable development goals. Available at: https://www.who.int/publications-detail-redirect/9789241565585. Accessed Aug 22, 2023.
3. Alberdi F, Garcia I, Atutxa L, Zabarte M. Epidemiology of severe trauma. Med Intensiva 2014;38:580–8. [CrossRef]
4. MacKenzie EJ, Rivara FP, Jurkovich GJ, Nathens AB, Frey KP, Egleston BL, et al. the national study on costs and outcomes of trauma. J Trauma Acute Care Surg 2007;63:S54. [CrossRef]
5. McNicholas WT. Medico Legal and Economic Aspects of OSA. In Janes SM, editor. Encycl Respir Med (2nd Ed). Oxford: Academic Press; 2022. [CrossRef]
6. TUIK. Life Tables, 2016-2018. Available at: https://data.tuik.gov.tr/Bulten/Index?p=Hayat-Tablolari-2016-2018-30712. Accessed Aug 22, 2023.
7. Sutherland M, McKenney M, Elkbuli A. Vehicle related injury patterns during the COVID-19 pandemic: What has changed? Am J Emerg Med 2020;38:1710–4. [CrossRef]
8. Calderon-Anyosa RJC, Kaufman JS. Impact of COVID-19 lockdown policy on homicide, suicide, and motor vehicle deaths in Peru. Prev Med 2021;143:106331. [CrossRef]
9. Moskal A, Martin JL, Laumon B. Risk factors for injury accidents among moped and motorcycle riders. Accid Anal Prev 2012;49:5–11. [CrossRef]
10. Santos AMRD, Moura MEB, Nunes BMVT, Leal CFDS, Teles JBM. Profile of motorcycle accident victims treated at a public hospital emergency department. Cad Saude Publica [Article in Portuguese] 2008;24:1927–38. [CrossRef]
11. Güngör F, Oktay C, Topaktaş Z, Akçimen M. Characteristics of motorcycle accident cases admitted to the emergency department. Turk J Trauma Emerg Surg [Article in Turkish] 2009;15:390–5.
12. Koçak S, Uçar K, Bayir A, Ertekin B. Characteristics of the cases of bicycle and motorcycle accidents referred to the Emergency Department. Turk J Emerg Med 2010;10:112–8.
13. World Health Organization. WHO global status report on road safety 2013: Supporting a decade of action. Geneva: World Health Organization; 2013.
14. Qasim Z, Sjoholm LO, Volgraf J, Sailes S, Nance ML, Perks DH, et al. Trauma center activity and surge response during the early phase of the COVID-19 pandemic - the Philadelphia story. J Trauma Acute Care Surg 2020;89:821–8. [CrossRef]
15. Chung Y, Song TJ, Yoon BJ. Injury severity in delivery-motorcycle to vehicle crashes in the Seoul metropolitan area. Accid Anal Prev 2014;62:79–86. [CrossRef]
16. Salottolo K, Caiafa R, Mueller J, Tanner A, Carrick MM, Lieser M, et al. Multicenter study of US trauma centers examining the effect of the COVID-19 pandemic on injury causes, diagnoses and procedures. Trauma Surg Acute Care Open 2021;6:e000655. [CrossRef]
17. Hökenek NM, Seyhan AU, Erdoğan MÖ, Tekyol D, Yılmaz E, Korkut S. Evaluation of blood gas analysis as a mortality predictor. South Clin Ist Euras 2019;30:228–231. [CrossRef]
18. Alicioglu B. Injuries associated with motorcycle accidents. Acta Orthop Traumatol Turc 2008;42:106–11. [CrossRef]
19. Tekyol D, Çolak Ş, Tayfur İ, Hökenek NM, Algın A. Evaluation of the effects of airbag and seat belt use on the severity of the injury in traffic accidents. Haydarpaşa Numune Med J. 2020;60:400. [CrossRef]
20. Wuerz RC, Travers D, Gilboy N, Eitel DR, Rosenau A, Yazhari R. Implementation and refinement of the emergency severity index. Acad Emerg Med 2001;8:170–6. [CrossRef]
21. Erdogan MÖ, Hokenek NM. How to score acute pancreatitis in the emergency setting: Five systems against ED-SAS. Signa Vitae 2021;1:8.
22. İlhan B, Bozdereli BG, Aydın H, Arslan Erduhan M, Doğan H. COVID-19 outbreak impact on emergency trauma visits and trauma surgery in a level 3 trauma center. Ir J Med Sci 2022;191:2319–24.

Covid-19 Salgını Öncesinde ve Sırasında Acil Servise Başvuran Motosiklet Kazası Vakalarının Değerlendirilmesi

Amaç: COVİD-19 pandemisi öncesinde ve sırasında motosiklet kazası sonrası acil servise başvuran hastaları inceleyerek, bu kazaların görülme sıklığını, travma şiddetini ve hasta sonuçlarını karşılaştırmalı olarak değerlendirmek.

Gereç ve Yöntem: Bu retrospektif gözlemsel çalışmada, Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi Erişkin Acil Servisi'ne motosiklet kazalarından kaynaklanan yaralanmalarla başvuran 1.137 hastayı değerlendirdik. Motosiklet kazası sonrası acil servise başvurduğu belirlenen hastaların elektronik dosyaları taranarak yaş, cinsiyet, kan basıncı, nabız, oksijen saturasyonu, solunum sayısı, başvuru anındaki vücut ısısı, başvuru zamanı gibi bilgiler incelendi. Kaza, sürücünün bildirdiği kaza anındaki motosiklet hızı, kullanılan koruyucu ekipman, acil servise varış zamanı, acil serviste ve hastanede kalış süresi, hastaların kalış süresi boyunca uygulanan tedavi türleri veri formuna kaydedildi.

Bulgular: Çalışmaya dahil edilen 1135 hastanın 129'u (%11.4) pandemi öncesinde, 1.006'sı (%88.6) pandemi döneminde acil servise başvurdu. 1.055 (%93) erkek hasta ve 80 (%7) kadın hasta vardı. Hastaların 145'i (%12.9) hastaneye yatırıldı, 990'ı (%87.2) hastaneden ayrıldı. Acil servisten ayrılanların 42'si (%3.7) tedaviyi reddetti, 35'i (%3.1) ise doktor onayı olmadan ayrıldı. Yatan hastaların 20'si (%1.8) yoğun bakıma, 4'ü (%0.4) diğer hastanelere sevk edildi. Hastane içi mortalite incelendiğinde 1.132 (%99.7) hastanın hayatta kaldığı, 3 (%0.3) hastanın ise öldüğü belirlendi. Tam vücut koruyucu ekipman kullanımına göre yaralanma yerleri arasındaki ilişki değerlendirilirken, baş ve boyun, akciğer, ekstremite, pelvis ve çoklu travma yaralanmaları açısından bir korelasyon bulundu.

Sonuç: Trafik yoğunluğu ne olursa olsun motosiklet sürücülerinin koruyucu ekipman kullanması kazalarda ciddi yaralanmaların önüne geçimektedir. EMTRAS ve ESI skorları motosiklet kazalarında mortalite ve morbiditeyi tahmin etmek için kullanılabilecek klinik tahmin araçlarıdır.

Anahtar Sözcükler: COVID-19; motosiklet kazası; pandemi; travma; EMTRAS; ESI.

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Original Article

The Relationship Between Hemoglobin A1c and Hemogram-derived Novel Inflammatory Indices

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Keywords: Diabetes mellitus; HbA1c; systemic immune aggregate index; systemic immune inflammation index; systemic immune response index.

ABSTRACT

Objective: An increasing number of studies are investigating the importance of new inflammatory markers derived from hemogram in the clinical management of diabetes, which is a chronic inflammatory condition. In this study, we aimed to assess the relation between HbA1c, Systemic Inflammatory Index (SII), Systemic Inflammation Response Index (SIRI), and Systemic Inflammation Aggregate Index (SIAI).

Methods: A total of 22,183 participants, including the control group (n=9100), prediabetes group (n=7087), and diabetes group (n=5996), were divided into 3 groups according to their HbA1c levels. In these 3 groups, hemogram-derived new inflammatory markers SII, SIRI, and SIAI values, as well as C-reactive protein, sedimentation, and leukocyte values, were evaluated.

Results: The median values of all 3 indices were found to be higher in the diabetes group compared to the other groups [SII=515(380-716), SIRI=0.93(0.66-1.35), SIAI=248(164-374), p<0.001]. In the control group, HbA1c and glucose values were not significantly correlated with inflammation indices (p>0.05). However, in the prediabetes group, significant correlations were detected between SII and SIRI values and glucose (r=0.033, p=0.006; r=0.040, p=0.001) and HbA1c levels (r=0.038, p=0.001; r=0.069, p<0.001).

Conclusion: Hemogram-derived inflammatory indices showed a gradual increase in patient groups based on HbA1c levels, but weak correlations were found between HbA1c levels and inflammatory markers as indicators of glucotoxicity. Hemogram is an easily accessible and widely used test in clinical practice. Therefore, hemogram-derived indices may be an alternative to traditional inflammatory markers in assessing glycotoxicity-induced inflammation. The detection of inflammation, which positively correlated with HbA1c levels through new indices, may help in predicting diabetic complications.

INTRODUCTION

Diabetes Mellitus (DM) is seen at a rate of approximately 10% among adults according to the report published in 2021. In the same report, it was stated that the prevalence of DM in Türkiye is 15% and it affects 7 million adults.[1] In addition to its incidence, diabetes is a disease that requires early diagnosis and treatment due to the microvascular and macrovascular complications it causes. Glycated hemoglobin (HbA1c) is a commonly used test in the diagnosis of diabetes, treatment efficiency, and prediction of complications.[2] HbA1c is a biomarker that increases in direct proportion to non-enzymatically formed blood glucose concentrations and shows the average blood glucose level for the last two to three months.[3] Glucotoxicity caused by chronically high blood glucose levels in patients with elevated HbA1c worsens the prognosis of the disease as it causes inflammation. Glucotoxicity pertains to the damaging effects of high blood sugar levels on tissues and is connected to insulin resistance, which promotes high blood sugar levels. Current studies have shown that chronic hyperglycemia increases the oxidative stress load through the formation of free oxygen radicals, causing inflammation and cell death.[4,5] Therefore, there are several researches in the literature investigating this dynamic relationship between HbA1c and inflammation.[6-8] Inflammation can be demonstrated by many biomarkers, as well as by some formulas obtained from a complete blood count,

which is an easily accessible and inexpensive test in clinical practice.[9] In recent years, systemic inflammatory index (SII), systemic immune response index (SIRI), and systemic immune aggregate index (SIAI) obtained from complete blood count are new inflammatory indices derived from the use of absolute numbers of different cell groups and evaluated in different clinical situations.[10-12] Studies evaluating new hemogram-derived indices with DM, which is a chronic inflammatory process, are scarcely any. Our study aimed to assess the relationship between HbA1c and SII, SIRI, and SIAI.

MATERIALS AND METHODS

In our study, the data of the patients who applied to the Taksim Education and Research Hospital Internal Medicine outpatient clinic between November 2020 and April 2023 were obtained retrospectively from the hospital records. Ethics committee approval was obtained from Gaziosmanpasa Education and Research Hospital Ethics Committee with the date 07.06.2023 and number 73. All procedures were carried out in accordance with the Helsinki Declaration. Patients aged 18-99 years, hemoglobin levels between 12-16g/dL, and C-reactive protein (CRP) levels <5 mg/dL were included in the study. Patients diagnosed with oncological, rheumatic, and autoimmune diseases, advanced liver and heart failure, pregnancy, and who had type 1 diabetes mellitus, incomplete information in their medical records were excluded from the study. Participants were divided into three groups according to HbA1c levels. HbA1c values below 5.7% were in the control group, between 5.7-6.4% were in prediabetes, and above 6.5% were in the diabetes group.[13] HbA1C levels of the patients were measured using ADAMS HV8380V, biochemical tests Roche Cobas c501, complete blood count Mindray BC6800, and erythrocyte sedimentation rate (ESR) Alifax devices.

Formulas of Indices Based on Hemogram:

Systemic inflammatory index (SII) = Neutrophil*Platelet/Lymphocyte,

Systemic inflammation aggregate index (SIAI) = Monocyte*Neutrophil*Platelet/Lymphocyte,

Systemic inflammation response index (SIRI) = Monocyte*Neutrophil/Lymphocyte.

Statistical analysis

Statistical Package for the Social Sciences (SPSS) software, version 20.0 was used for the statistical analysis of the study. Normality analyses of the variables were done with the Kolmogorov-Smirnov test. Variables that were not normally distributed were expressed as median interquartile range (25th-75th percentile), while regularly distributed variables were expressed as mean and standard deviation. Categorical variables were expressed as frequency (%). ANOVA for normally distributed parameters and Kruskal-Wallis test for non-normally distributed parameters were used to assess the differences of groups. The Pearson Chi-square test was performed in terms of categorical parameters. A p-value of <0.05 was considered significant for all analyses.

RESULTS

A total of 22,183 participants, including the control group (n=9100), prediabetes group (n=7087), and diabetes group (n=5996), were categorized into 3 groups according to their HbA1c values. Table 1 summarizes the demographic and laboratory data of the groups. Age distributions were statistically significant in the control, prediabetes, and diabetes groups (41(30-52), 56(47-64), 59(51-67), p<0.001, respectively). 67.6% of participants in the control group, 63.6% in the prediabetes group, and 51.1% in the diabetes group were female, p<0.001. SII, SIRI, and SIAI values, which are inflammatory markers derived from hemogram, were found to be significantly different between the groups. The median values of all 3 indices were found to be higher in the diabetes group compared to other groups [SII=515(380-716), SIRI=0.93(0.66-1.35), SIAI=248(164-374), p<0.001] (Table 1). The correlation of hemogram-derived inflammatory markers with HbA1c and glucose levels is shown in Table 2. While HbA1c and glucose values were not correlated with inflammation indices in the control group (p>0.05), in the prediabetes group, SII and SIRI values were correlated with glucose (r=0.033, p=0.006; r=0.040, p=0.001) and HbA1c levels (r=0.038, p=0.001; r=0.069, p<0.001). Likewise, SIAI values and HbA1c levels (r=0.066, p<0.001) showed a weak positive correlation in prediabetes patients. In the diabetes group, there was a linear relationship between glucose levels, SII, SIRI, and SIAI values (r=0.077, p<0.001; r=0.040, p=0.002; r=0.046, p<0.001, respectively). On the basis of all patients, the highest correlation was found between HbA1c and both SIRI (r=0.112, p<0.001) and SIAI values (r=0.114, p<0.001).

Table 3 summarizes the linear relationship between routine inflammatory markers and HbA1c and glucose levels. In the control group, HbA1c values showed a statistically significant positive correlation with ESR, CRP, and white blood cell (WBC) values (r=0.227, p<0.001; r=0.061, p<0.001; and r=0.046, p<0.001, respectively). In addition, CRP and glucose levels in the control group showed a small correlation but were statistically very significant (r=0.061, p<0.001). In the prediabetes group, correlations were also found between HbA1c levels and inflammatory markers (r=0.135, p<0.001 for CRP, r=0.110, p<0.001 for ESR, and r=0.069, p<0.001 for WBC). Glucose and ESR levels were weakly positively correlated among prediabetes patients (r=0.064, p=0.008). In diabetic patients, glucose and CRP levels were weakly correlated (r=0.079, p<0.001), while HbA1c values were correlated with both CRP (r=0.097, p<0.001) and WBC counts (r=0.070, p<0.001). On the basis of all patients, correlations of glucose values with ESR, CRP, and WBC were found, respectively (r=0.055, p<0.001; r=0.155, p<0.001; and r=0.103, p<0.001). Likewise, linear relationships were observed between HbA1c levels, CRP (r=0.244, p<0.001), ESR (r=0.245, p<0.001),

Table 1. Demographic and laboratory data of the groups

	Control (n=9100)	Prediabetes (n=7087)	Diabetes (n=5996)	p
Age, year	41 (30-52)	56 (47-64)	59 (51-67)	<0.001 *<0.001 **<0.001 ***<0.001
Gender				
Female %	6151 (67.6)	4506 (63.6)	3063 (51.1)	<0.001
Male %	2949 (32.4)	2581 (36.4)	2933 (48.9)	
Glucose, mg/dl	92 (87-98)	101 (93-111)	152 (125-204)	<0.001 *<0.001 **<0.001 ***<0.001
HbA1c, %	5.40 (5.20-5.50)	5.9 (5.8-6.10)	7.70 (6.90-9.20)	<0.001 *<0.001 **<0.001 ***<0.001
Creatinine, mg/dl	0.71 (0.62-0.84)	0.76 (0.65-0.90)	0.80 (0.66-0.96)	<0.001 *<0.001 **<0.001 ***<0.001
AST, U/L	17 (14.06-20.60)	18 (15-21)	17 (14-21.35)	<0.001 *<0.001 **=0.253 ***<0.001
ALT, U/L	15 (11-22)	17 (13-24)	18 (13-26.60)	<0.001 *<0.001 **<0.001 ***<0.001
CRP, mg/dl	1.93 (1.04-3.83)	2.78 (1.43-3.53)	3.74 (1.87-4.07)	<0.001 *<0.001 **<0.001 ***<0.001
ESR mm/h	7 (4-12)	10 (5-18)	11 (6-21)	<0.001 *<0.001 **<0.001 ***=0.021
Hb, g/L	134 (125-145)	133 (124-144)	137 (125-148)	<0.001 *<0.001 **<0.001 ***<0.001
Leukocyte, x10^3/µL	7.02 (5.95-8.29)	7.38 (6.30-8.69)	7.99 (6.78-9.33)	<0.001 *<0.001 **<0.001 ***<0.001
Neutrophil, x10^3/µL	4.09 (3.29-5.10)	4.29 (3.48-5.29)	4.78 (3.88-5.82)	<0.001 *<0.001 **<0.001 ***<0.001
Lymphocyte, x10^3/µL	2.21 (1.84-2.66)	2.33 (1.90-2.84)	2.40 (1.93-2.94)	<0.001 *<0.001 **<0.001 ***<0.001

Monocytes, x10^3/µL	0.43 (0.35-0.52)	0.45 (0.37-0.55)	0.48 (0.39-0.59)	<0.001 *<0.001 **<0.001 ***<0.001
Platelets, x10^3/µL	262 (224-304)	267 (228-311)	265 (222-312)	<0.001 *<0.001 **=0.039 ***=0.001
SII	479 (357-646)	488 (362-655)	515 (380-716)	<0.001 *=0.003 **<0.001 ***<0.001
SIRI	0.78 (0.56-1.09)	0.81 (059-1.16)	0.93 (0.66-1.35)	<0.001 *<0.001 **<0.001 ***<0.001
SIAI	203 (138-304)	218 (149-326)	248 (164-374)	<0.001 *<0.001 **<0.001 ***<0.001

HbA1c: HemoglobinA1c; AST: aspartate aminotransferase; ALT: alanine aminotransferase; CRP: C reactive protein; ESR: erythrocyte sedimentation rate; Hb: hemoglobin; SII: systemic inflammation index; SIRI: systemic inflammation response index; SIAI: Systemic inflammation aggregate index (*: Control vs pre-dm, **: Control vs DM, ***:Pre-dm vs DM).

Table 2. Correlation between hemogram-derived novel inflammatory markers and HbA1c and glucose levels

	SII	SIRI	SIAI
Control			
Glucose	r=0.011	r=0.005	r=-0.011
	p=0.316	p=0.632	p=0.285
HbA1c	r=-0.012	r=0.007	r=0.015
	p=0.252	p=0.520	p=0.149
Prediabetes			
Glucose	r=0.033	r=0.040	r=0.009
	p=0.006	p=0.001	p=0.439
HbA1c	r=0.038	r=0.069	r=0.066
	p=0.001	p<0.001	p<0.001
Diabetes			
Glucose	r=0.077	r=0.040	r=0.046
	p<0.001	p=0.002	p<0.001
HbA1c	r=0.007	r=-0.014	r=-0.009
	p=0.564	p=0.283	p=0.488
All patients			
Glucose	r=0.052	r=0.090	r=0.064
	p<0.001	p<0.001	p<0.001
HbA1c	r=0.058	r=0.112	r=0.114
	p<0.001	p<0.001	p<0.001

HbA1c: Hemoglobin A1c; SII: systemic inflammation index; SIRI: systemic inflammation response index; SIAI: Systemic inflammation aggregate index.

and WBC (r=0.180, p<0.001).

As shown in Table 4, according to the regression analysis, it was seen that uncontrolled diabetes had an effect on hemogram indices.

Table 3. Correlation between routine inflammatory markers and HbA1c and glucose levels

	CRP	ESR	WBC
Control			
Glucose	r=0.061	r=0.026	r=0.018
	p<0.001	p=0.232	p=0.078
HbA1c	r=0.137	r=0.227	r=0.046
	p<0.001	p<0.001	p<0.001
Prediabetes			
Glucose	r=0.032	r=0.064	r=0.009
	p=0.059	p=0.008	p=0.466
HbA1c	r=0.135	r=0.110	r=0.069
	p<0.001	p<0.001	p<0.001
Diabetes			
Glucose	r=0.079	r=0.060	r=0.022
	p<0.001	p=0.088	p=0.086
HbA1c	r=0.097	r=-0.023	r=0.070
	p<0.001	p=0.511	p<0.001
All patients			
Glucose	r=0.155	r=0.055	r=0.103
	p<0.001	p<0.001	p<0.001
HbA1c	r=0.244	r=0.245	r=0.180
	p<0.001	p<0.001	p<0.001

HbA1c: Hemoglobin A1c; CRP: C reactive protein; ESR: erythrocyte sedimentation rate; WBC: white blood cell.

Table 4. Linear regression analysis for hemogram-derived markers and HbA1c levels

	SII			SIRI			SIAI		
	St.B	95 %CI	p	St.B	95% CI	p	St.B	95 %CI	p
Hba1c	0.053	6.32-12.4	<0.001	0.073	0.021-0.034	<0.001	0.059	5.46-9.90	<0.001
	Adjusted R2=0.003; p<0.001			Adjusted R2=0.005; p<0.001			Adjusted R2=0.003; p<0.001		

SII: systemic inflammation index; SIRI: systemic inflammation response index; SIAI: Systemic inflammation aggregate index St. B: Standardized B value; 95% CI: 95% Confidence interval.

DISCUSSION

We analyzed a total of 22,183 patient records and split them into three study groups: control, prediabetes, and diabetes groups. Female participant percentages were higher in all groups. Our results revealed that hemogram-based inflammatory indices including SII, SIRI, and SIAI gradually increase with glycated hemoglobin levels. In parallel with these results, conventional inflammatory markers such as CRP and ESR were elevated in prediabetic and diabetic patients. Additionally, we assessed the directional relationship between the parameters related to glucotoxicity and inflammatory markers. Glucose and glycated hemoglobin levels were poorly correlated with SII, SIRI, and SIAI levels in both prediabetic and diabetic patients, similarly with CRP, ESR, and WBC levels. However, there was no correlation in diabetic patients. That could be caused by the majority of the diabetic patients having similar HbA1c levels between 7-8%.

Blood glucose levels are maintained within the physiological range by the balance between tissue glucose consumption, gluconeogenesis, and insulin production. Hyperglycemia results from a disruption in any one of these three mechanisms. It has been shown in various studies that chronic hyperglycemia also causes inflammation through oxidative stress.[14,15]

Hemogram-derived indices SII, SIRI, and SIAI are markers that are being investigated with increasing interest to determine the systemic inflammation status in various diseases.[16-19] Liu et al.[20] assessed the SII levels in type 2 DM patients and showed that SII was an independent risk factor of diabetes mellitus and the patients who had higher SII levels were more likely to develop type 2 diabetes mellitus.

It is known that there is a relationship between HbA1c level and diabetic complications.[21] The relationship be-

tween hemogram-derived new inflammatory indices and diabetic complications has been shown in various studies. Guo et al.[22] found a positive correlation between high SII values and the development of diabetic nephropathy in a study of 3937 patients. Song et al.[23] reported a retrospective study about the assessment of hemogram-derived indices and diabetic patients with peripheral artery disease. According to their results, SII, SIRI, and SIAI levels were higher in the diabetic patients with peripheral artery disease (PAD) compared to the patients without PAD. Also, they showed a correlation between the severity of disease and the inflammatory indices. Similar to previous studies, in our study, SIRI and SIAI, in addition to SII, were found to be higher in the diabetes group than in other groups. In our study, it was observed that CRP, ESR, and WBC levels, which are acute phase reactants commonly used in clinical practice, were positively correlated with HbA1c levels in all three patient groups. In a retrospective study conducted by Demirkol et al.[24] with 9103 participants, it was shown that CRP values were significantly higher in hyperglycemic conditions. On the other hand, in the study conducted by Elimam et al.,[25] it was observed that the CRP value was significantly higher in the diabetic group than in the control group, but the same result could not be achieved in terms of ESR. Due to the retrospective design of our study, not being able to access the current treatments and complication status of the patients can be considered as our limitations. We could not obtain HbA1c data simultaneously with repeated hemogram measurements of the same patient in a sufficient number of participants. Therefore, the change in HbA1c was not compared with the change in hemogram-derived indices of the same patient. This can be considered as another limitation of the study.

Conclusion

Hemogram-derived inflammatory indices showed a gradual increase in patient groups based on HbA1c levels, but weak correlations were found between HbA1c levels and inflammatory markers as an indicator of glucotoxicity. Hemogram is an easily accessible and widely used test in clinical practice. Therefore, hemogram-derived indices may be an alternative to traditional inflammatory markers in assessing glycotoxicity-induced inflammation. The detection of inflammation, which positively correlated with HbA1c levels through new indices, may help in predicting diabetic complications. Although new hemogram-derived indices have been studied in various clinical situations, to the best of our knowledge, our study is the first to investigate the relationship of all three indices together with HbA1c levels. Further prospective studies will be required to confirm the results of this study.

Ethics Committee Approval

This study approved by the Gaziosmanpasa Education and Research Hospital Ethics Committee (Date: 07.06.2023, Decision No: 73).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: S.Y., O.E.; Design: S.Y., O.E., A.S., E.B.O.; Supervision: S.Y., A.S., O.E.; Fundings: S.Y., A.S., E.B.O., O.E.; Materials: S.Y., O.E., A.S.; Data: S.Y., O.E., A.S., E.B.O.; Analysis: S.Y., A.S., E.B.O.; Literature search: S.Y., O.E., A.S., E.B.O.; Writing: S.Y., O.E., A.S.; Critical revision: S.Y., O.E.

Conflict of Interest

None declared.

REFERENCES

1. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract 2022;183:109–19. [CrossRef]
2. Ceriello A, Monnier L, Owens D. Glycaemic variability in diabetes: Clinical and therapeutic implications. Lancet Diabetes Endocrinol 2019;7:221–30. [CrossRef]
3. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c test in diagnosis and prognosis of diabetic patients. Biomark Insights 2016;11:95–104. [CrossRef]
4. Shoelson SE, Lee J, Goldfine AB. Inflammation and insulin resistance. J Clin Invest 2006;116:1793–801. J Clin Invest 2006;116:2308. [CrossRef]
5. Mota M, Banini BA, Cazanave SC, Sanyal AJ. Molecular mechanisms of lipotoxicity and glucotoxicity in nonalcoholic fatty liver disease. Metabolism 2016;65:1049–61. [CrossRef]
6. Kumar P, Swain MM, Pal A. Hyperglycemia-induced inflammation caused down-regulation of 8-oxoG-DNA glycosylase levels in murine macrophages is mediated by oxidative-nitrosative stress-dependent pathways. Int J Biochem Cell Biol 2016;73:82–98. [CrossRef]
7. Luc K, Schramm-Luc A, Guzik TJ, Mikolajczyk TP. Oxidative stress and inflammatory markers in prediabetes and diabetes. J Physiol Pharmacol 2019;70:809–24
8. Škrha J, Šoupal J, Škrha J Jr, Prázný M. Glucose variability, HbA1c and microvascular complications. Rev Endocr Metab Disord 2016;17:103–10. [CrossRef]
9. Bilgin S, Aktas G, Zahid MK, Atak BM, Kurtkulagi O, Duman TT, et al. Association between novel inflammatory markers derived from hemogram indices and metabolic parameters in type 2 diabetic men. Aging Male 2020;23:923–7. [CrossRef]
10. Ermurat S, Tezcan D. New hematological indices as markers of inflammation and high disease activity in patients with systemic lupus erythematosus. Uludağ Üniv Tıp Fak Derg [Article in Turkish] 2022;48:189–96. [CrossRef]
11. Eissa M, Shaarawy S, Abdellateif MS. The role of different inflammatory indices in the diagnosis of COVID-19. Int J Gen Med 2021;14:7843–53. [CrossRef]
12. Ghobadi H, Mohammadshahi J, Javaheri N, Fouladi N, Mirzazadeh Y, Aslani MR. Role of leukocytes and systemic inflammation indexes (NLR, PLR, MLP, dNLR, NLPR, AISI, SIR-I, and SII) on admission predicts in-hospital mortality in non-elderly and elderly COVID-19 patients. Front Med Lausanne 2022;9:916453. [CrossRef]
13. ElSayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, et al. 2. Classification and diagnosis of diabetes: Standards of care in diabetes-2023. Diabetes Care 2023;46:S19–40. [CrossRef]

14. Kawahito S, Kitahata H, Oshita S. Problems associated with glucose toxicity: Role of hyperglycemia-induced oxidative stress. World J Gastroenterol 2009;15:4137–42.
15. Eguchi N, Vaziri ND, Dafoe DC, Ichii H. The role of oxidative stress in pancreatic β cell dysfunction in diabetes. Int J Mol Sci 2021;22(4):1509. [CrossRef]
16. Uzunoglu H, Kaya S. Does systemic immune inflammation index have predictive value in gastric cancer prognosis? North Clin Istanb 2023;10:24–32.
17. Alagbe AE, Pedroso GA, de Oliveira BB, de Costa E, Maia GAF, Piellusch BF, et al. Hemograms and serial hemogram-derived ratios in survivors and non-survivors of COVID-19 in Campinas, Brazil. Hematol Transfus Cell Ther 2022;28:1–8.
18. Gheita TA, Sakr BR, Rabea RE, Abd ElHamid SM. Value of hematological indices versus VEGF as biomarkers of activity in Behçet's disease. Clin Rheumatol 2019;38:2201–10. [CrossRef]
19. Chen G, Tan C, Liu X, Wang X, Tan Q, Chen Y. Associations between Systemic Immune-Inflammation Index and diabetes mellitus secondary to pancreatic ductal adenocarcinoma. J Clin Med 2023;12:756. [CrossRef]
20. Liu P, Shang J, Luo D, Shi L. The systemic immune-inflammation index is associated with Type 2 diabetes mellitus patients: Evidence from NHANES 2011-2018. Available at: https://assets.researchsquare.com/files/rs-2487403/v1/699147c3-81a0-45c3-a7ce-53bb90eedcc5.pdf?c=1681980282. Accessed Mar 18, 2024.
21. Boye KS, Thieu VT, Lage MJ, Miller H, Paczkowski R. The association between sustained HbA1c control and long-term complications among ındividuals with type 2 diabetes: A retrospective study. Adv Ther 2022;39:2208–21. [CrossRef]
22. Guo W, Song Y, Sun Y, Du H, Cai Y, You Q, et al. Systemic immune-inflammation index is associated with diabetic kidney disease in type 2 diabetes mellitus patients: Evidence from NHANES 2011-2018. Front Endocrinol Lausanne 2022;13:1071465. [CrossRef]
23. Song Y, Zhao Y, Shu Y, Zhang L, Cheng W, Wang L, et al. Combination model of neutrophil to high-density lipoprotein ratio and system inflammation response index is more valuable for predicting peripheral arterial disease in type 2 diabetic patients: A cross-sectional study. Front Endocrinol Lausanne 2023;14:1100453. [CrossRef]
24. Demirkol ME, Alisik M, Yis OM. C-reactive protein to albumin ratio in patients with prediabetes and diabetes mellitus: HbA1c and inflammation. Clin Lab 2022;68(8): 211108. [CrossRef]
25. Elimam H, Abdulla AM, Taha IM. Inflammatory markers and control of type 2 diabetes mellitus. Diabetes Metab Syndr 2019;13:800–4. [CrossRef]

Hemoglobin A1c ile Hemogram Kaynaklı Yeni İnflamatuvar İndeksler Arasındaki İlişki

Amaç: Kronik inflamatuvar bir durum olan diyabetin klinik yönetiminde hemogramdan elde edilen yeni inflamatuvar belirteçlerin önemini araştıran çalışmaların sayısı giderek artmaktadır. Bu çalışmada HbA1c ile Sistemik inflamatuvar indeks (Sİİ), Sistemik inflamasyon yanıt indeksi (SİYİ) ve Sistemik inflamasyon agregat indeksi (SİAİ) arasındaki ilişkiyi değerlendirmeyi amaçladık.

Gereç ve Yöntem: Toplam 22183 katılımcı HbA1c düzeylerine göre kontrol grubu (n=9100), prediyabet grubu (n=7087) ve diyabet grubu (n=5996) olmak üzere 3 gruba ayrıldı. Bu 3 grupta hemogramdan elde edilen yeni inflamatuvar belirteçler Sİİ, SİYİ ve SİAİ değerlerinin yanı sıra C reaktif protein, sedimantasyon ve lökosit değerleri değerlendirilmiştir.

Bulgular: Her üç indeksin ortanca değerleri diyabet grubunda diğer gruplara kıyasla daha yüksek bulundu [Sİİ=515 (380-716), SİYİ=0.93 (0.66-1.35), SİAİ=248 164-374), p<0.001]. Kontrol grubunda, HbA1c ve glukoz değerleri inflamasyon indeksleri ile anlamlı bir korelasyon göstermemiştir (p>0.05). Ancak, prediyabet grubunda Sİİ ve SİYİ değerleri ile glukoz (r=0.033, p=0.006; r=0.040, p=0.001) ve HbA1c düzeyleri (r=0.038, p=0.001; r=0.069, p<0.001) arasında anlamlı korelasyonlar tespit edilmiştir.

Sonuç: Hemogramdan elde edilen inflamatuvar indeksler, HbA1c düzeylerine bağlı olarak hasta gruplarında kademeli bir artış göstermiştir, ancak glukotoksisitenin bir göstergesi olarak HbA1c düzeyleri ile inflamatuvar belirteçler arasında zayıf korelasyonlar bulunmuştur. Hemogram klinik pratikte kolay ulaşılabilen ve yaygın olarak kullanılan bir testtir. Bu nedenle hemogramdan türetilen indeksler, glukotoksisiteye bağlı inflamasyonun değerlendirilmesinde geleneksel inflamatuvar belirteçlere alternatif olabilir. HbA1c düzeyleriyle pozitif korelasyon gösteren inflamasyonun yeni indeksler aracılığıyla saptanması, diyabet komplikasyonlarının öngörülmesinde yardımcı olabilir.

Anahtar Sözcükler: Diabetes mellitus; HbA1c; sistemik immün agregat indeksi; sistemik immün inflamasyon indeksi; sistemik immün yanıt indeksi.

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Original Article

Term Pregnancy Following Uterine Prolapse Surgery, Literature Review and Case Presentation

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Keywords: Prolapsus; term pregnancy; vaginally assisted laparoscopic sacrohysteropexy.

ABSTRACT

Objective: Herniation of the pelvic organs into or outside the vagina is what is known as pelvic organ prolapse (POP). This paper was prepared in order to offer a case report of our pregnant patient who reached term after undergoing this operation, as well as to conduct a literature review on the vaginally assisted laparoscopic sacrohysteropexy (VALSH) procedure, which is a new method in the surgical treatment of POP. Both of these goals were accomplished through the writing of this article.

Methods: A patient who 32 years old was admitted to our hospital with a palpable mass in the vagina. Because our patient was planned to get pregnant in the future, we suggested that she undergo a procedure known as VALSH, which is a uterus-preserving operation. The patient, who became pregnant spontaneously one year after the operation, had a healthy baby by cesarean section on at 38 weeks of gestation.

Results: We conducted a literature review on the vaginally assisted laparoscopic sacrohysteropexy procedure, which is a new method in the surgical treatment of POP. It is unknown what kind of surgical procedure should be used to treat POP in young women who are still of childbearing age. Studies have shown that young women have an increased chance of POP recurrence following surgical treatment; however, no studies have been conducted to investigate the effect of surgical POP repair on subsequent pregnancies and the kind of delivery that occurs during those pregnancies.

Conclusion: No signs of prolapse returning were detected during the tests conducted at the 6th week, 6th month of pregnancy, and the 12th month postpartum. We believe that the surgical procedure we utilized is an appropriate treatment for women of childbearing age who plan to become pregnant. The lack of prolapse recurrence indicates that the pregnancy can progress to full term without complications.

INTRODUCTION

Herniation of the pelvic organs into or outside the vagina is what is known as pelvic organ prolapse, or POP for short. It has been claimed that the prevalence rates of POP around the world range from 1-65%. There are not enough prevalence data available for POP, and the majority of the available prevalence data are based on symptoms rather than a physical examination.[1]

Women who have symptomatic prolapse have the option of having their condition maintained conservatively or being treated surgically for their condition. The options of conservative treatment and surgical treatment should both be made available to these patients. There is no data of sufficient quality available to compare these two methods.[2]

To restore anatomy with the least amount of morbidity and the lowest possible risk of recurrence, the appropriate surgery should be undertaken. The restoration of the pelvic floor can be done using abdominal, vaginal, or laparoscopic techniques, which are the three methods that have been presented thus far. However, in the majority of instances, hysterectomy does not repair problems linked to compromised pelvic support structures such as the uterosacral and cardinal ligaments. Hysterectomy is still regarded as the primary operation to correct uterovaginal prolapse.[3] In addition, there is a rise in the number of women who are opting out of having a hysterectomy because they are under the impression that the uterus plays a part in the level of sexual satisfaction one experiences.[4]

POP patients may undergo natural tissue healing, mesh operations, or minimally invasive surgical procedures as

part of their surgical treatment. Laparoscopic or robotic procedures for POP repair are currently experiencing a surge in popularity and are continuously undergoing development.[5] There is a wide selection of surgical therapies available, but there is no consensus on which one is the most effective.[6]

At this time, it is unknown what kind of surgical procedure should be used to treat POP in young women who are still of childbearing age. Studies have shown that young women have an increased chance of POP recurrence following surgical treatment; however, to this day, no studies have been conducted to investigate the effect of surgical POP repair on subsequent pregnancies and the kind of delivery that occurs during those pregnancies.[7]

This paper was prepared to offer a case report of our pregnant patient who reached term after undergoing this operation, as well as to conduct a literature review on the vaginally assisted laparoscopic sacrohysteropexy procedure, which is a new method in the surgical treatment of POP. Both of these goals were accomplished through the writing of this article.

MATERIALS AND METHODS

The laparoscopic and vaginal combination sacrofixation technique was initially described in 1999 by Godin et al.,[8] and its long-term effects have been discussed. On December 16, 2020, we carried out this procedure following the definition provided by Fayyad et al.,[9] and all three of the definitions provided by Sanverdi et al.[10] This procedure, planned for the patient who was brought into the operating room in the lithotomy position, was carried out. Following the completion of any necessary surgical operations, the operation will be divided into three distinct stages. The first and third portions were carried out using laparoscopic techniques, whereas the second section was carried out using vaginal techniques.

The placement of the laparoscopic ports was the first step, with the 10mm port being positioned umbilically and 2 or 3 ports being positioned laterally or suprapubically. At the beginning of the procedure, an incision was made on the sacral promontory, through the peritoneum. Under the peritoneum, a tunnel measuring five centimeters in length was excavated to reach the lower cervix from the sacral promontory. After that, the mesh was positioned on the surface of the promontory.

The procedure is now in its second stage, which has just begun. In the second part of the procedure, a vaginal semicircular incision was used to access the posterior cervicovaginal junction. This was done during the vaginal portion of the procedure. A retroperitoneal tunnel was constructed using the curved ring forceps to reach right adjacent to the promontory, and the peritoneum was perforated during this process. During the process of creating this tunnel, simultaneous laparoscopic visualization was carried out. The vaginal side of the mesh was then advanced towards the posterior cervicovaginal junction with the assistance of the constructed tunnel. This was done after the vaginal side of the mesh was carried into the abdomen with the assistance of a 10-gauge trocar. After that, the process of attaching the mesh to the cervix got underway. At this stage, in contrast to Fayyad et al.,[9] to protect the tissue integrity of the cervix, instead of performing cervical dissection, suturing was conducted by creating a tunnel at the 3 and 9 o'clock positions of the cervix. This was done to prevent the cervix from being cut open during the procedure. During the third and final stage of the procedure, the uterus was tightened laparoscopically, and on the promontory, four absorbable tuckers and four non-absorbable 0 prolene sutures were used to give fixation. After that, a peritonization procedure using an absorbable 3.0 polyglactin suture was carried out. After the bleeding was brought under control, the operation was finished. During the vaginal examination that was carried out on the first postoperative day, it was determined that the patient did not have a prolapse status.

CASE

A patient who was 32 years old and had a history of two normal spontaneous vaginal deliveries was admitted to our hospital with a palpable mass in the vagina. The patient's previous deliveries had been normal. According to the POP-Q staging system, the examination revealed that the patient had uterine prolapse at the stage 4 level. During the transvaginal ultrasound, the adnexa was examined, and nothing out of the ordinary was seen. Because our patient was of childbearing age and planned to get pregnant in the near future, we suggested that she undergo a procedure known as vaginally assisted laparoscopic sacrohysteropexy (VALSH), which is a uterus-preserving operation. The procedure was carried out as stated on December 10, 2021. The duration of the operation was sixty-three minutes. At the 36th hour after surgery, the patient was released from our care because there were no difficulties. In the controls that were performed at six weeks, six months, and twelve months after surgery, we did not find any instances of recurrence or any other complications.

The patient, who became pregnant spontaneously one year after the operation, had a healthy baby by cesarean section on February 22, 2022, at 38 weeks of gestation. The procedure was performed with the indication of oligohydramnios. During the pregnancy follow-up examination, the patient did not show any signs of prolapse recurrence.

The mesh that had been inserted in the prior procedure could be seen during the cesarean section (Figure 1). After a postoperative period of 48 hours, both the mother and the infant were released from the hospital.

RESULTS

When dealing with pelvic organ prolapse, surgical options are broken down into two distinct categories. One of them supports hysterectomy for female patients who

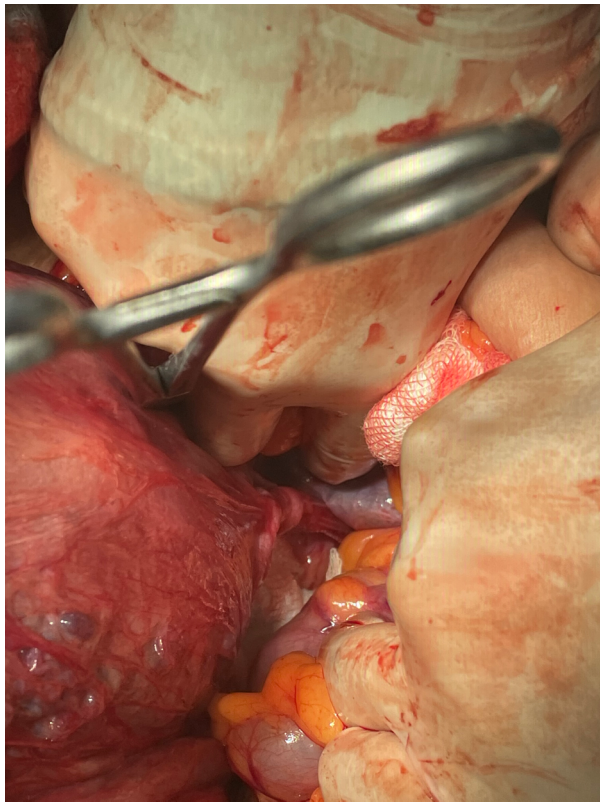

Figure 1. The mesh that had been inserted in the prior procedure could be seen during the cesarean section.

do not intend to become pregnant in the foreseeable future, while the other supports uterus-sparing surgery for female patients who do intend to become pregnant in the foreseeable future. In this particular instance, we opted for the VALSH procedure, which is a subtype of sacrohysteropexy and is one of the possibilities for surgeries that spare the uterus.

There was no evidence of a return of the prolapse in any of the examinations that were carried out during the sixth week of pregnancy, the sixth month, or the 12th month after delivery.

DISCUSSION

Currently, uterine-sparing procedures in POP are gaining popularity. The preferred surgical technique depends on the surgeon's experience, the patient's symptoms, age, comorbidities, the likelihood of pregnancy, and the desire to preserve the uterus.

The surgical technique VALSH, which is the subject of our article, is favored by the majority of surgeons due to its minimally invasive nature and low recurrence rate when literature data are followed. Since the cervix is surrounded by a membrane in the vaginal portion of our technique, its recurrence is anticipated to be lower than in other surgical procedures.

Even though it is an innovative method, it is preferable due to the decreased use of laparoscopic sutures and the fact that the majority of the surgery is conducted safely.

Reviewing the available literature, the operation was first conducted in 1999 by Godin et al.[8] In this study, 45 patients were examined, and control was attained six and thirty months after surgery. There was no recurrence of prolapse.

It was then presented in a retrospective study with 22 patients by Rae et al.[11] in 2003. At 12.5 months postoperatively, no recurrence other than cystocele was detected in 3 patients in this study.

Pechman et al.[12] presented a 2011 study comparing vaginally assisted laparoscopic sacrocolpopexy (VALS) and conventional laparoscopic sacrocolpopexy (LS) in patients undergoing concurrent hysterectomy. In this study, 44 patients underwent VALS surgery while 26 patients underwent conventional sacrocolpopexy. There was no significant difference between the complications and outcomes of the operation, and it was stated that the VALS operation required less time than the traditional sacrocolpopexy.

In 2012, Athanasiou et al.;[13] reported the postoperative 12-month outcomes of the VALS operation they performed on 27 vaginally hysterectomized patients, demonstrating that the patients' vaginal examinations improved in accordance with their anatomy.

Similarly, Zhu et al.[14] (2013) applied this technique to 21 vaginal hysterectomy patients and reported achieving 100 percent surgical success by evaluating the patients six weeks, six months, and twelve months postoperatively.

In 2014, Fayyad et al.[9] defined it. In this study, seventy patients with stages 3 and 4 uterine prolapse underwent vaginally assisted laparoscopic uterine sacropexy as surgical treatment. Patients completed the Prolapse Quality of Life Questionnaire (P-QOL) and were examined using the pelvic organ prolapse measurement system (POP-Q) preoperatively and postoperatively. The patients were evaluated three and twelve months after surgery. Sixty-four women (91.4%) reported relief in prolapse symptoms at 12 months postoperatively, and 67 women (95.7%) were determined to have POP-Q grade 0 or 1 uterine level at 12 months. Six women (8.5%) required additional surgical intervention for prolapse, three developed recurrent uterine prolapse, and the remaining three developed symptomatic recurrent anterior vaginal wall prolapse. The average vaginal length did not differ between the preoperative and postoperative periods. Two patients developed complications related to mesh. There has been an important reduction in prolapse symptoms and quality of life.

In 2014, Elvira et al.[15] shared a case series of 32 patients in a comparative study. In this study, 18 patients underwent VALSH surgery, while 14 patients underwent total laparoscopic sacrohysteropexy surgery. Although the duration and postoperative recurrence rates of both procedures are comparable, the study concluded that the VALSH procedure is safer and less invasive, which makes it preferable.

Liang et al.[16] evaluated the long-term outcomes of thirty patients in a case series after three years of follow-up. In almost all of the patients in this investigation, anatomical improvement and an increase in sexual function were observed.

Grigoriadis et al.[17] (2014) described VALS surgery in a single patient video report.

From June 2008 to July 2012, Nosti et al.[18] performed a study that was titled Transvaginal Versus Transabdominal Placement of Synthetic Mesh at Time of Sacrocolpopexy. This study was a retrospective cohort study with prospective follow-up for patients with uterovaginal prolapse who were undergoing laparoscopic supracervical hysterectomy (LSH-LSC). The results of this study were published in 2016. Participants in this research comprised 123 patients who had TVH-LSC performed, as well as 59 patients who had LSH-LSC performed. They discovered that patients did not vary from one another in terms of mesh-related issues, intraoperative or postoperative complications, or objective and subjective success. The only difference that warranted consideration was that TVH-LSC was linked with a noticeably shorter duration of time spent in surgery (256±53-344±81 minutes; P<0.01).

In the research conducted by Darwish and colleagues, the authors prospectively examined 15 patients to explore the viability, practicability, and efficacy of the vaginolaparoscopic sacrocolpopexy procedure, which they abbreviated as VLS.[19] The most important result is a postoperatively substantial improvement in prolapse, which in turn leads to an improvement in quality of life (QoL) after VLS. Six patients needed simultaneous reconstructive surgeries, and at the 6-month follow-up, the surgery was effective in 14 (93.34%) of 15 patients; however, one lady (6.66%) presented with recurrence at an earlier stage. Following the operation, there was seen considerable improvement in terms of vaginal symptoms, sexual well-being, quality of life, and clinical staging.

Aharoni et al.[20] published another comparison research in 2017. In this retrospective study, the short-term outcomes of 28 patients undergoing classical sacrocolpopexy (SCP) and 68 patients undergoing vaginolaparoscopic sacrocolpopexy (V-SCP) were compared. In addition, 11 of the patients who underwent classical laparoscopic SCP 3-7 years after the operation, and 40 of the patients who underwent V-LSCP, experienced a recurrence of the condition. One to five years after the operation, the patient was reevaluated and the long-term outcomes were examined. The short-term outcomes of the dual operation have demonstrated that it is faster without compromising patient well-being. A review of existing patients' long-term outcomes revealed that the subjective cure rate for Laparoscopic SCP patients was 73% and for combined operations, it was 88%. However, some degree of vaginal prolapse was observed in 82% (9/11) of Laparoscopic SCP surgeries, primarily cystocele or rectocele grade 1 or 2, whereas this recurrence was observed in only 30% of patients undergoing dual surgery.

Sanverdi et al.[10] presented a case series of 33 patients in which they conducted the operation in three stages as we did, however, they utilized the ascending retroperitoneal transfer approach. In these cases, there were no intraoperative complications, and no recurrence of prolapse was observed 12 months after surgery. VALSH is becoming more applicable as the peritoneal suturing is eliminated, as stated in a separate case report.[21]

Athanasiou et al.[22] shared the long-term outcomes of 114 patients with advanced POP who underwent VALS with at least 3 years of follow-up. The mean follow-up period is seven years (range: three to ten years), and the overall success rate of surgery is 95.7% (90/94). Failures (4.3%) included one (1.1%) case of anatomical recurrence (Bp: +1), one woman (1.1%), who reported vaginal swelling symptoms, and two women (1%) who underwent posterior colporrhaphy 6 and 12 months after the primary contains (2.1%).

In 2020, Tapisiz et al.[23] published an article that included a literature review and 20 cases. In this article, the authors emphasize the operation's viability and effectiveness. In numerous articles, the operation phases and short- and long-term outcomes are described. However, neither the pregnancy relationship nor its outcomes were specified. In a patient with uterine prolapse who was 12 weeks and 3 days pregnant, laparoscopic sacrohysteropexy was performed and only published as a case report.[24]

When it comes to prolapse procedures, we believe that the VALS procedure is one of the least intrusive and most simply applicable options. More research is required if we are going to have a better understanding of the connection between prolapse and pregnancy.

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: Ç.K.; Design: G.B.İ.; Supervision: Ç.K.; Fundings: E.B.; Materials: Ç.K.; Data: G.B.İ.; Analysis: E.B.; Literature search: G.B.İ.; Writing: G.B.İ.; Critical revision: E.B.

Conflict of Interest

None declared.

REFERENCES

1. Brown HW, Hegde A, Huebner M, Neels H, Barnes HC, Marquini GV, et al. International urogynecology consultation chapter 1 committee 2: Epidemiology of pelvic organ prolapse: Prevalence, incidence, natural history, and service needs. Int Urogynecol J 2022;33:173–87. [CrossRef]
2. Rogers RG, Fashokun TB. Pelvic organ prolapse in females: Epidemiology, risk factors, clinical manifestations, and management. Available at https://www.uptodate.com/contents/pelvic-organ-prolapse-in-females-epidemiology-risk-factors-clinical-manifestations-and-management#H13817287. Accessed Mar 18, 2024.
3. Maher CF, Cary MP, Slack MC, Murray CJ, Milligan M, Schluter

P. Uterine preservation or hysterectomy at sacrospinous colpopexy for uterovaginal prolapse? Int Urogynecol J Pelvic Floor Dysfunct 2001;12:381–4. [CrossRef]
4. Murphy AM, Clark CB, Denisenko AA, D'Amico MJ, Vasavada SP. Surgical management of vaginal prolapse: Current surgical concepts. Can J Urol 2021;28:22–6.
5. Ko KJ, Lee KS. Current surgical management of pelvic organ prolapse: Strategies for the improvement of surgical outcomes. Investig Clin Urol 2019;60:413–24. [CrossRef]
6. Maher C, Feiner B, Baessler K, Christmann-Schmid C, Haya N, Brown J. Surgery for women with apical vaginal prolapse. Cochrane Database Syst Rev 2016;10:CD012376. [CrossRef]
7. Tsikouras P, Dafopoulos A, Vrachnis N, Iliodromiti Z, Bouchlariotou S, Pinidis P, et al. Uterine prolapse in pregnancy: Risk factors, complications and management. J Matern Fetal Neonatal Med 2014;27:297–302. [CrossRef]
8. Godin PA, Nisolle M, Smets M, Squifflet J, Donnez J. Combined vaginal and laparoscopic sacrofixation for genital prolapse using a tacking technique: A series of 45 cases. Gynaecol Endosc 1999;8:277–85. [CrossRef]
9. Fayyad AM, Siozos CS. Safety and one year outcomes following vaginally assisted laparoscopic uterine sacropexy (VALUES) for advanced uterine prolapse. Neurourol Urodyn 2014;33:345–9. [CrossRef]
10. Sanverdi İ, Kılıççı Ç, Polat M, Özkaya E, Kılıç SG, Dizdar M, et al. A new operation technique for uterine prolapse: Vaginally-assisted laparoscopic sacrohysteropexy. Turk J Obstet Gynecol 2017;14:181–6. [CrossRef]
11. Rae D, Hawthorn R. Sacrocolpopexy for vaginal vault prolapse: A combined vaginal and laparoscopic approach. Gynaecol Endosc 2002;11:75–9. [CrossRef]
12. von Pechmann WS, Aungst MJ, Gruber DD, Ghodsi PM, Cruess DF, Griffis KR. A pilot study on vaginally assisted laparoscopic sacrocolpopexy for patients with uterovaginal prolapse. Female Pelvic Med Reconstr Surg 2011;17:115–9. [CrossRef]
13. Athanasiou S, Grigoriadis T, Chatzipapas I, Protopapas A, Antsaklis A. The vaginally assisted laparoscopic sacrocolpopexy: A pilot study. Int Urogynecol J 2013;24:839–45. [CrossRef]
14. Zhu L, Sun Z, Yu M, Li B, Li X, Lang J. Modified laparoscopic sacrocolpopexy with mesh for severe pelvic organ prolapse. Int J Gynecol Obstet 2013;121:170–2. [CrossRef]
15. Elvira BV, Brătilă PC, Negroiu AT. Vaginally-assisted laparoscopic hysterosacropexy for advanced utero-vaginal prolapse: A series of 32 cases. ARS Medica Tomitana 2014;20:63–70. [CrossRef]
16. Liang S, Zhu L, Song X, Xu T, Sun Z, Lang J. Long-term outcomes of modified laparoscopic sacrocolpopexy for advanced pelvic organ prolapse: A 3-year prospective study. Menopause 2016;23:765. [CrossRef]
17. Grigoriadis T, Protopapas A, Chatzipapas I, Athanasiou S. Vaginally assisted laparoscopic sacrocolpopexy for the treatment of complete uterovaginal prolapse. Int Urogynecol J 2015;26:449–50. [CrossRef]
18. Nosti PA, Carter CM, Sokol AI, Tefera E, Iglesia CB, Park AJ, et al. Transvaginal versus transabdominal placement of synthetic mesh at time of sacrocolpopexy. Female Pelvic Med Reconstr Surg 2016;22:151–5. [CrossRef]
19. Darwish A, Bahlol M, Ahmad A, Fekry M. Uterus-sparing vaginolaparoscopic sacrocolpopexy for apical pelvic organ prolapse. Int Urogynecol J 2018;29:1455–61. [CrossRef]
20. Aharoni A, Agranat A, Ben David M. Efficacy of vaginal and laparoscopic sacrocolpopexy, a dual approach to utero-vaginal prolapse, compared wıth laparoscopic sacrocolpopexy alone. Harefuah 2020;159:352–4.
21. Tapisiz OL, Dogan AR, Kiykac Altinbas S. Vaginal-assisted laparoscopic sacrohysterocervicopexy with retroperitoneal tunneling. Int J Gynaecol Obstet 2018;140:118–9. [CrossRef]
22. Athanasiou S, Zacharakis D, Protopapas A, Pitsouni E, Loutradis D, Grigoriadis T. Severe pelvic organ prolapse. Is there a long-term cure? Int Urogynecol J 2019;30:1697–703. [CrossRef]
23. Tapisiz OL, Altinbas SK, Dogan AR. Vaginal-assisted laparoscopic sacrohystero/colpopexy with retroperitoneal tunneling: Tips and tricks, and a review of the literature. Gynecol Pelvic Med 2020;3:6222. [CrossRef]
24. Peker BH, Ilter E, Peker H, Celik A, Gursoy A, Gunaldi O. Laparoscopic sacrohysteropexy in a woman at 12 weeks' gestation. J Minim Invasive Gynecol 2018;25:1146–7. [CrossRef]

Uterin Prolapsus Cerrahisi Sonrası Miada Ulaşan Gebelik, Literatür Taraması ve Vaka Sunumu

Amaç: Pelvik organların vajina içine veya dışına fıtıklaşması, pelvik organ prolapsusu veya kısaca POP olarak bilinen durumdur. Şu anda, henüz doğurganlık çağında olan genç kadınlarda POP'u tedavi etmek için ne tür bir cerrahi prosedürün kullanılması gerektiği bilinmemektedir. Bu yazı, bu ameliyatı geçirdikten sonra miadına ulaşan gebe hastamızı sunmak ve POP'un cerrahi tedavisinde yeni bir yöntem olan vajinal yardımlı laparoskopik sakrohisteropeksi prosedürü ile ilgili literatür taraması yapmak amacıyla hazırlanmıştır.. Bu hedeflerin her ikisi de bu makalenin yazılmasıyla gerçekleştirildi.

Gereç ve Yöntem: 32 yaşında iki normal spontan vajinal doğum öyküsü olan hasta vajinasında ele gelen kitle şikâyeti ile hastanemize başvurdu. Hastamızın doğurganlık çağında olması ve yakın gelecekte gebe kalmayı planlaması nedeniyle vajinal asiste laparoskopik sakrohisteropeksi (VALSH) olarak bilinen uterus koruyucu bir operasyon olmasını önerdik. Ameliyattan bir yıl sonra spontan gebeliği olan hasta, 38. gebelik haftasında sezaryen ile sağlıklı bir bebeğe sahip oldu.

Bulgular: POP'un cerrahi tedavisinde yeni bir yöntem olan vajinal asiste laparoskopik sakrohisteropeksi prosedürü ile ilgili literatür taraması yaptık. Şu anda, henüz doğurganlık çağında olan genç kadınlarda POP'u tedavi etmek için ne tür bir cerrahi prosedürün kullanılması gerektiği bilinmemektedir. Çalışmalar, genç kadınların cerrahi tedaviyi takiben POP nüksetme ihtimalinin arttığını göstermiştir; ancak bugüne kadar cerrahi POP onarımının sonraki gebelikler üzerindeki etkisini ve bu gebeliklerde meydana gelen doğum şeklini araştıran hiçbir çalışma yapılmamıştır.

Sonuç: Gebeliğin 6. haftasında, 6. ayında ve doğumdan sonraki 12. ayında yapılan tetkiklerin hiçbirinde prolapsus rekürrensine dair bir bulguya rastlanmadı. Uyguladığımız cerrahi yöntemin gebelik beklentisi olan fertil çağdaki hastalar için uygun bir teknik olduğunu düşünmekteyiz. Prolapsus rekürensinin olmaması, gebeliğin miada ulaşabilmesi ve komplike hale gelmemesi düşüncemizi desteklemektedir.

Anahtar Sözcükler: Prolapsus; term gebelik; vajinal yardımlı laparoskopik sakrohisteropeksi.

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Original Article

The Relationship between Serum ACE Level and Disease Severity in Patients Hospitalized Due To COVID-19 pneumonia

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Keywords: Angiotensin-converting enzyme; COVID-19; illness severity; serum ACE

ABSTRACT

Objective: The renin-angiotensin-aldosterone system (RAS) plays an important role in the pathophysiology of COVID-19. The role of the angiotensin-converting enzyme (ACE), which is part of RAS, in COVID-19 is unclear. The study aimed to investigate whether there was a relationship between serum ACE level at admission and disease severity in COVID-19.

Methods: A total of 158 patients hospitalized in our clinic between January 2021 and April 2021 due to COVID-19 pneumonia were included in this study. Patients were divided into two groups: mild-moderate and severe pneumonia, according to the severity of the disease. The two groups were compared in terms of age, gender, symptoms and signs, comorbidities, laboratory parameters, serum ACE level, and mortality. Serum ACE level was measured by a spectrophotometric method.

Results: The mean age of the patients was 61 years (min: 18, max: 89), and 85 (53.5%) were male. The most common symptoms were dyspnea (61%), cough (57.2%), and malaise (49.7%). The number of leukocytes, C-reactive protein, ferritin, D-Dimer, and days of hospitalization were higher in the severe pneumonia group compared to the mild-moderate pneumonia group, and the difference was statistically significant ($p=0.004$, $p<0.001$, $p=0.005$, $p=0.01$, $p<0.001$, respectively). The rates of intensive care unit admission, intubation, and mortality were higher in the severe pneumonia group ($p=0.035$, $p=0.035$, $p=0.035$, respectively). The mean serum ACE level of the patients was 25.14 (min: 3.39, max: 75.28) U/L; no significant difference was found between the groups ($p=0.61$).

Conclusion: No correlation was found between serum ACE levels at the time of hospitalization and COVID-19 severity. Serum ACE levels at admission did not reflect disease severity.

INTRODUCTION

In 2019, a new virus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), from the coronavirus (CoV) family, emerged in China and caused a pandemic that affected the entire world, especially with viral pneumonia.[1,2] Coronavirus disease 2019 (COVID-19) is highly contagious and has the capacity to cause more severe clinical forms such as upper airway disease to acute respiratory distress syndrome (ARDS).[3] This virus poses a greater risk, especially in the elderly and comorbid population.[4,5] The virus binds to angiotensin-converting enzyme (ACE) 2 receptors to enter cells, similar to SARS-CoV.[6,7] The lung, most affected by SARS-CoV-2 infections, is related to its large surface area and the fact that 83% of the cells expressing ACE2 are type II alveolar epithelial cells.[8-11] In addition to type II alveolar cells, ACE2 is expressed in myocardial, bladder, esophageal, ileum and colon epithelial cells and oral mucosa cells[9,10]

ACE2 and ACE, which play a role in the renin-angiotensin-aldosterone system (RAS), have a similar structure, and the imbalance between them is considered to play a role in ARDS.[12,13] ACE stimulates vasoconstriction by converting Angiotensin I (Ang ı) to Angiotensin II (Ang II) and activates thrombotic, proinflammatory, and fibrotic processes by binding to Ang II angiotensin type 1 (AT1) receptors. Ang II, converted by ACE, is an important peptide of RAS that induces vasoconstriction and exerts multiple biologic functions. Another effect of Ang II is to increase interleukin-6 (IL-6), which is one of the poor prognostic factors for COVID-19.[14] It also increases Ang II, plasminogen activator inhibitor-1, and tissue factor levels, causing thrombus in great arteries and arterioles.[15] In the non-classic RAS pathway, ACE2 has the ability to metabolize Ang II to Ang1-7.[9] Thus, it causes a decrease in inflammation, fibrosis, and thrombosis.[16,17] It has been reported that Ang(1-7) formation, which is transformed by ACE2, plays an important role in the clinic in studies conducted on ARDS models.[18]

The classic RAS route worsens impaired respiratory conditions, and the non-classic route has a protective role in ARDS. Therefore, the role of RAS in the pathogenesis of COVID-19 is useful for managing and treating. There are studies on ACE2, the cell entry receptor of SARS-CoV-2,[19] but few studies have been performed on serum ACE activity. ACE/Ang II and ACE2/Ang (1-7) routes may be associated with COVID-19 pneumonia. ACE activity may be associated with disease severity. There are conflicting results in the literature regarding ACE activity. The decrease in serum ACE activity was associated with COVID-19 severity, and serum ACE levels increased with the disease regression.[20] In another study, it was found that there was no relationship with disease severity [21]. We aimed to investigate baseline serum ACE activity and disease severity in COVID-19.

MATERIALS AND METHODS

Between January 2021 and April 2021, 159 patients aged 18 years and over who had confirmed COVID-19 pneumonia and required inpatient follow-up and treatment were admitted to City Hospital. All patients were of Caucasian origin. This research was designed as a prospective and single-center study. The Ethics Committee (Decision no: 514/192/53) approved the study, and written informed consent was obtained. Nasopharyngeal or oropharyngeal swab samples defined as positive for SARS-CoV-2 using real-time reverse transcription polymerase chain reaction (RT-PCR) were determined as confirmed cases. The disease severity was defined as mild-moderate and severe pneumonia according to the COVID-19 guide.[22]

Tachypnea (respiratory rate ≥30/minute) or oxygen levels with a pulse oximeter ≤90% in room air and bilateral diffuse pneumonia findings on radiology were classified as having severe pneumonia, and others as having mild or moderate disease. Patients under the age of 18 years, those with negative PCR tests, and pregnant women were excluded from the study. Demographic data, symptoms, comorbidities, biochemistry results, and radiologic examinations were obtained from hospital records. All data were reviewed by pulmonary physicians. Thoracic imaging, electrocardiogram, complete blood count, biochemistry, C-reactive protein, D-dimer, ferritin, and serum ACE activity were evaluated on the 1st day of hospitalization. Cases were followed up until discharge or end of life in the hospital. Blood was taken from the patients immediately after they were admitted to the clinic. Samples were drawn into 5 mL Vacutainer® SST™ II tubes (BD, Franklin Lakes, NJ, USA) for CRP and ferritin and were centrifuged at 3000g for 10 minutes. For D-dimer test analyses, 2.7-mL BD Vacutainer Plus Plastic Citrate Tubes with 3.2% (109 mmol/L) sodium citrate with a ratio of 9:1 blood/citrate were used. Blood samples were drawn into 3-mL BD Vacutainer K2EDTA Plus plastic tubes. For CBCs, measurements were performed on the day of admittance. Ferritin was measured using a UniCel DxI 800 analyzer (Beckman Coulter, Brea, CA, USA), with a 2-site immunoenzymatic ("sandwich") assay. CRP was measured on a BN II analyzer (Siemens, Germany), using an immunoturbidimetric assay. D-dimer was analyzed using a turbidimetric method on a fully automated Sysmex CS-2500 device (Sysmex Corporation, Norderstedt, Germany). Only ACE test samples were studied within 6 days.

Serum ACE Activity Assay: Peripheral blood samples were collected in BD Vacutainer® Serum Separating Tubes II

Table 1. The characteristics of the patients

COVID-19 n =158	
Sex/male n %	85 (53,5)
Age/years*	61 (18-89)
Severe pneumonia n%	68 (42.8)
BMI*	28.89 (17.78-38.95)
Cough n%	91 (57.23)
Dyspnea n %	97 (%61)
Gastrointestinal symptoms n %	35 (22)
Fatigue n %	79 (49,7)
Miyalgia n %	48 (30,2)
Headache n %	11 (7)
Comorbidity n %	106 (66.7)
Hypertension n %	50 (31.4)
Diabetes mellitus	45 (28.3)
Cardiovascular disease n %	34 (31.5)
Asthma n%	12 (7.6)
Renal disease n %	12 (7.6)
Neurological disease n %	16 (10.1)
Serum ace U/L*	25,14 (3,39-75,28)
Intensive care support n %	23 (14.5)
Intubation n %	22 (13.8)
Number of days of hospitalisation	9 (3-39)
Mortality n %	22 (13.8)

Table 2. The characteristics of the mild-moderate pneumonia and severe group

	Severe pneumonia n=68	Mild to moderate pneumonia n=90	p
Age (years)	62 (30-88)	57 (18-89)	0.194
Sex Male n (%)	40 (58.8)	45 (49.4)	0.215*
Body mass index	28,24 (20,44-38,95)	29,4 (17,78-37,87)	0.187
Cough, n (%)	41 (60.29)	50 (55.56)	0,551
Shortness of breath, n (%)	48 (70,59)	48 (53.3)	0,028
GIS symptoms, n (%)	13 (19,12)	22 (24,44)	0,425
Fatigue, n (%)	40 (58,82)	39 (43,33)	0,054
Myalgia, n (%)	27 (39,71)	21 (23,33)	0,027
Headache n (%)*	4 (5,88)	7 (7.78)	0.64
Comorbidy n (%)	45 (66.18)	60 (66,67)	0,948
Hypertension, n (%)	17 (25.00)	33 (36.67)	0,118
Diabetes mellitus, n (%)	20 (29.41)	24 (26,67)	0,703
Renal disease, n (%)	4 (5.97)	8 (8,89)	0,496
Cardiovascular diseases, n (%)	15 (22.39)	18 (20)	0,716
Asthma, n (%)	5 (7.35)	7 (7.78)	0,920
Fever	36,65 (36-39,1)	36,6 (36-39,3)	0,820
Sp02 (%)	86.68±3.79	93.80±2.16	<0.001
Systolic (mmHg)	120 (90-180)	120 (90-164)	0.195
Diastolic (mmHg)	70 (50-100)	81 (57-110)	0.757
Heart rate (min)	81,5 (60-140)	81 (57-110	0.353
Leukocytes	7300 (1110-23080)	5740 (1110-16030)	0.004
Lymphocytes	1040 (200-7800)	1065 (180-3390)	0.472
Platelets	195500 (7000-493000)	186000 (83000-756000)	0.272
CRP (mg/dL)	96,6 (2-283)	55 (1,4-230)	<0.001
Ferritin (ng/mL)	552 (31,7-2000)	326 (22,3-2000)	0.005
D-dimer (ng/mL)	770 (190-4400)	575 (190-4400)	0.010
Serum ACE (U/L)	25.6 (4.14-65.12)	24.58 (3.39-75.28)	0.612
Serum ACE (U/L)**	27.85 (4,52-65.12)	25,06 (3,39-75,28)	0.455
ACEI, n (%)	5 (7.46)	6 (6.67)	0.847
ARB blockers, n (%)	7 (10.45)	9 (10.11)	0.94
The hospitalization days	11 (4-39)	7 (3-20)	<0.001
ICU admission, n (%)	14 (20.59)	8 (8.89)	0.035
Intubation, n (%)	14 (20,59)	8 (8,89)	0,035
Mortality n (%)	14 (20,59)	8 (8,89)	0,035

Mann Whitney-U Test. * chi-square test. ** Evaluated in patients not using ACE inh or ARB blockers.

Advance Tube (SST) (Becton, Dickinson and Company, Franklin Lakes, NJ, USA). Thirty minutes after blood collection, the tubes were centrifuged at 2000 g for 10 minutes, serum was separated, and stored at 2-8°C until studied. According to the manufacturer's recommendations, samples for ACE were studied within 6 days of being taken. Serum ACE activity was measured according to the instructions (Ben S.r.l. Biochemical Enterprise, Via Pietro Toselli, 4, 20127 Milano, Italy) and analyzed using the Saturno-300 plus biochemistry analyzer (CRNOY S.R.I, Italy). Measurements were made using a kinetic spectrophotometric method.

Statistical Analysis

Analyses were performed using SPSS version 25.0 software. Histogram plots and the Kolmogorov-Smirnov test were used to analyze the conformity of the variables to the normal distribution. For descriptive analyses, mean,

Table 3. Correlation between serum ACE and inflammation parameters

	Serum ACE
CRP	
r	0.029
p	0.714
Ferritin	
r	-0.059
p	0.461
D-dimer	
r	-0.007
p	0.928

Spearman correlation test

standard deviation, and median were used. Categorical variables were compared using the Chi-square test. P values below 0.05 were considered statistically significant.

RESULTS

A total of 158 patients who were hospitalized due to definite COVID-19 were included, 85 (53.8%) of whom were male. The median age in the patient group was 61 (min: 18, max: 89) years. Dyspnea (61%), cough (57.2%), and fatigue (49.7%) were, respectively, the most common initial symptoms. Hypertension (HT) (31.4%), diabetes mellitus (DM) (28.3%), and cardiovascular disease (CVD) (21.5%) were the most common comorbidities. The mean serum ACE level was 25.14 (3.39-75.28) U/L. The mean length of stay in the hospital was 9 (3-39) days. A total of 22 (13.8%) patients died.

The characteristics of the patients are presented below (Table 1).

The characteristics of the mild-moderate pneumonia and severe group are shown in Table 2. There was no statistically significant variation observed in the sex distribution, age, and body mass index averages when comparing the groups (respectively p=0.215, p=0.194, p=0.187). The rates of shortness of breath, myalgia, need for intensive care, intubation, and mortality were significantly higher in the severe pneumonia group (respectively p=0.028, p=0.027, p=0.035, p=0.035, p=0.035). The leukocyte values of the group with mild-moderate pneumonia were lower than those of the severe group (p=0.004). Ferritin, D-dimer, and CRP values were higher in severe pneumonia than in mild-moderate pneumonia (p=0.005, p=0.010, and p<0.001, respectively). Serum ACE levels were insignificant between the groups (p=0.61). Serum ACE levels were also insignificant after patients on RAS blockers were excluded (p=0.45). No correlation was found between serum ACE activity and inflammatory parameters (CRP, ferritin, D-dimer) (Table 3).

DISCUSSION

This study aimed to evaluate the relationship between ACE activity in COVID-19 and disease severity. No correlation was observed between serum ACE levels and the severity of COVID-19 disease. The outcomes remained consistent even after excluding individuals who used RAS blockers. Similar findings are reported in the literature.[21-24]

The RAS regulates blood pressure and electrolyte balance. It is regulated by the balance between ACE and ACE2. ACE plays a role in vasoconstriction, hypoxic, oxidative, and inflammatory changes. ACE2 is responsible for counteracting the negative effects of Ang II. Therefore, the amounts of the two enzymes are the main regulators of the RAS.[23]

In the study of Güler et al.,[21] serum ACE activity was unrelated to disease severity. It was also not correlated with inflammatory markers. In their study, it was found that there was no significant difference in serum ACE levels between patients with COVID-19 and controls. In another study of 79 patients by Henry et al.,[24] similar results were obtained. In a study of 103 patients conducted by Bayyiğit et al.,[25] no difference was determined between COVID-19 patient groups in terms of serum ACE levels. These findings suggest that the role of ACE2 may be more constructive than ACE in the pathophysiology and SARS-CoV-2 infection progression. ACE activity is mainly determined by its polymorphism. Studies have shown that the D allele of the ACE I/D polymorphism is associated with increased levels of serum and tissue ACE and Ang II.[26,27] ACE gene polymorphism could not be examined in our study.

Our study showed serum ACE activity was not correlated with inflammatory markers. Similar results were also observed in the literature.[21] There are studies in the literature with different results. In a study by Chen et al.,[28] lower levels of serum ACE on admission were reported as a risk factor for COVID-19 disease progression. In addition, patients with ACE ≤33.5 U/L had higher levels of IL-2R, IL-6, IL-10, CRP, and ferritin than those with ACE >33.5 U/L.

As shown in previous studies, disease severity and mortality are associated with advanced age.[29] In a meta-analysis by Levin et al.,[29] it was demonstrated that mortality increases with age in COVID-19. In our study, the severe group was older. HT, CVD, and DM are critical risk factors in COVID-19. Approximately 66% of COVID-19 cases had comorbidities. HT, DM, and CVD were associated with RAS in our study. Consistent with current results, previous studies revealed that the most common comorbidities in patients with COVID-19 were HT and DM.[30]

In our study, leukocyte, CRP, D-dimer, and ferritin values, which are inflammation parameters, were found to be higher in the group with severe pneumonia. These findings are consistent with the literature.[31]

This study has several limitations. First, it was a single-center study with a relatively small sample size. Second, serum ACE activity was measured only at admission; serial

measurements may better define the relationship between ACE and COVID-19 severity. Third, Ang II, ACE2 levels, and ACE gene polymorphism could not be evaluated.

Conclusion

This study demonstrated that serum ACE activity decreased in COVID-19 pneumonia and there was no correlation between serum ACE level and disease severity. Serum ACE activity could not be used as a marker to determine the severity of COVID-19. Evaluation of the relationship between ACE2 activity and Ang II may help to determine the role of serum ACE in the pathogenesis, and new studies are needed.

Ethics Committee Approval

This study approved by the Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee (Date: 30.12.2020, Decision No: 514/192/53).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: B.Z.E., Z.Y., S.Ş.C., N.K., E.D., E.T.P., A.B.; Design: B.Z.E., Z.Y., S.Ş.C., N.K., E.D., E.T.P., A.B.; Supervision: B.Z.E., Z.Y., S.Ş.C., N.K., E.D., E.T.P., A.B.; Fundings: Z.Y., B.Z.E.; Materials: B.Z.E., A.B., S.Ş.C.; Data: B.Z.E., Z.Y.; Analysis: B.Z.E., N.K.; Literature search: B.Z.E., E.D.; Writing: B.Z.E., E.D.; Critical revision: S.Ş.C., N.K.

Conflict of Interest

None declared.

REFERENCES

1. World Health Organization. Naming the coronavirus disease (COVID-19) and the virus that causes it . Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it. Accessed Mar 18, 2024.
2. Munster VJ, Koopmans M, van Doremalen N, van Riel D, de Wit E. A novel coronavirus emerging in China - key questions for impact assessment. N Engl J Med 202;382:692–4. [CrossRef]
3. Esakandari H, Nabi-Afjadi M, Fakkari-Afjadi J, Farahmandian N, Miresmaeili SM, Bahreini E. A comprehensive review of COVID-19 characteristics. Biol Proced Online 2020;22:1–10. [CrossRef]
4. Richardson S, Hirsch JS, Narasimhan M, Crawford MJ, McGinnet T, Davidson KW, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA 2020;323:2052–9. [CrossRef]
5. Zheng Z, Peng F, Xu B, Zhao J, Liu H, Peng J, et al. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. J Infect 2020;81:e16–25. [CrossRef]
6. Fehr AR, Perlman S. Coronaviruses: An overview of their replication and pathogenesis. Methods Mol Biol 2015;1282:1–23. [CrossRef]
7. Li W, Moore MJ, Vasilieva N, Sui J, Wong SK, Berne MA, et al. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. Nature 2003;426:450–4. [CrossRef]
8. Ren X, Glende J, Al-Falah M, de Vries V, Schwegmann-Wessels C, Qu X, et al. Analysis of ACE2 in polarized epithelial cells: Surface expression and function as receptor for severe acute respiratory syndrome-associated coronavirus. J Gen Virol 2006;87:1691–5. [CrossRef]
9. Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. Int J Oral Sci 2020;12:8. [CrossRef]
10. Zhao Y, Zhao Z, Wang Y, Zhou Y, Ma Y, Zuo W. Single-cell RNA expression profiling of ACE2, the receptor of SARS-CoV-2. Am J Respir Crit Care Med 2020;202:756–9. [CrossRef]
11. Zhang H, Penninger JM, Li Y, Zhong N, Slutsky AS. Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: Molecular mechanisms and potential therapeutic target. Intens Care Med 2020;46:586–90. [CrossRef]
12. Imai Y, Kuba K, Penninger JM. The renin-angiotensin system in acute respiratory distress syndrome. Drug Discov Today Dis Mech 2006;3:225–9. [CrossRef]
13. Imai Y, Kuba K, Penninger JM. Angiotensin-converting enzyme 2 in acute respiratory distress syndrome. Cell Mol Life Sci 2007;64:2006–12. [CrossRef]
14. Abers MS, Delmonte OM, Ricotta EE, Fintzi J, Fink DL, de Jesus AAA, et al. An immune-based biomarker signature is associated with mortality in COVID-19 patients. JCI Insight 2021;6(1):e144455. [CrossRef]
15. Senchenkova EY, Russell J, Almeida-Paula LD, Harding JW, Granger DN. Angiotensin II-mediated microvascular thrombosis. Hypertension 2010;56:1089–95. [CrossRef]
16. Simões e Silva AC, Silveira KD, Ferreira AJ, Teixeira MM. ACE2, angiotensin-(1-7) and Mas receptor axis in inflammation and fibrosis. Br J Pharmacol 2013;169:477–92. [CrossRef]
17. Tikellis C, Thomas MC. Angiotensin-converting enzyme (ACE2) is a key modulator of the renin-angiotensin system in health and disease. Int J Pept 2012;2012:256294. [CrossRef]
18. Kuba K, Imai Y, Rao S, Gao H, Guo F, Guan B, et al. A crucial role of angiotensin-converting enzyme 2 (ACE2) in SARS coronavirus-induced lung injury. Nat Med 2005;11:875–9. [CrossRef]
19. Scialo F, Daniele A, Amato F, Pastore L, Matera MG, Cazzola M, et al. ACE2: The major cell entry receptor for SARS-CoV-2. Lung 2020;198:867–77. [CrossRef]
20. Zhu Z, Cai T, Fan L, Lou K, Hua X, Huang Z, et al. The potential role of serum angiotensin-converting enzyme in coronavirus disease 2019. BMC Infect Dis 2020;20:883. [CrossRef]
21. Guler AA, Tombul N, Yıldız P, Özger HS, Hızel K, Gulbahar O, et al. The assessment of serum ACE activity in COVID-19 and its association with clinical features and severity of the disease. Scand J Clin Lab Invest 2021;81:160–5. [CrossRef]
22. TC Sağlık Bakanlığı. COVID-19 (SARS-Cov-2 INFECTION) GUIDE. Available at: https://bidb.bingol.edu.tr/media/8718/covid-19_rehberiv5-25subat2020.pdf. Accessed Mar 18, 2024.
23. Gintoni I, Adamopoulou M, Yapijakis C. The impact of ACE and ACE2 gene polymorphisms in pulmonary diseases including COVID-19. In Vivo 2022;36:13–29. [CrossRef]
24. Henry MB, Benoit JL, Rose J, Santos de Oliveira MH, Lippi G, Benoit SW. Serum ACE activity and plasma ACE concentration in patients with SARS-CoV-2 infection. Scand J Clin Lab Invest 2021:81:272–5. [CrossRef]
25. Bayyigit A, Acar MA, Kulahli P, Simsek F, Adas M. Can Serum ACE level be used as a prognostic ındicator in COVID-19? Clin Lab 2022;68:210523. [CrossRef]
26. Woods DR, Humphries SE, Montgomery HE. The ACE I/D polymorphism and human physical performance. Trends Endocrinol Metab 2000;11:416–20. [CrossRef]

27. Çobanogullari H, Evren EU, Evren H, Suer K, Balcioglu O, Ergoren MC. Strong association between angiotensin-converting enzyme gene InDel polymorphism and COVID-19 diseases. Med Clin Barc 2023;160:489–94. [CrossRef]
28. Chen Y, Huang D, Yuan W, Chang J, Yuan Z, Wu D, et al. Lower serum angiotensin-converting enzyme level in relation to hyperinflammation and ımpaired antiviral ımmune response contributes to progression of COVID-19 infection. Infect Dis Ther 2021;10:2431–46. [CrossRef]
29. Levin AT, Hanage WP, Owusu-Boaitey N, Cochran KB, Walsh SP, Meyerowitz-Katz G. Assessing the age specificity of infection fatality rates for COVID-19: Systematic review, meta-analysis, and public policy implications. Eur J Epidemiol 2020;35:1123–38. [CrossRef]
30. Hu Y, Sun J, Dai Z, Deng H, Li X, Huang Q, et al. Prevalence and severity of coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. J Clin Virol 2020;127:104371. [CrossRef]
31. Huang I, Pranata R, Lim MA, Oehadian A, Alisjahbana B. C-reactive protein, procalcitonin, D-dimer, and ferritin in severe coronavirus disease-2019: A meta-analysis. Ther Adv Respir Dis 2020;14:1–14. [CrossRef]

COVID-19 Nedeniyle Yatan Hastalarda Serum ACE Düzeyi ile Hastalık Şiddeti Arasındaki İlişki

Amaç: Renin-anjiyotensin-aldosteron sistemi (RAS) COVID-19 patofizyolojisinde önemli bir rol oynamaktadır. RAS'ın bir parçası olan anjiyotensin dönüştürücü enzimin (ACE) COVID-19'daki rolü belirsizdir. Bu çalışma, COVID-19'da başvuru sırasındaki serum ACE düzeyleri ile hastalık şiddeti arasında bir ilişki olup olmadığını araştırmayı amaçlamıştır.

Gereç ve Yöntem: COVID-19 pnömonisi nedeniyle Ocak 2021-Nisan 2021 tarihleri arasında kliniğimize yatırılan toplam 158 hasta çalışmaya dahil edilmiştir. Hastalar hastalığın şiddetine göre hafif-orta ve ağır pnömoni olarak iki gruba ayrılmıştır. İki grup yaş, cinsiyet, semptom ve bulgular, komorbiditeler, laboratuvar parametreleri, serum ACE düzeyi ve mortalite açısından karşılaştırılmıştır. Serum ACE düzeyi spektrofotometrik yöntemle ölçülmüştür.

Bulgular: Hastaların ortalama yaşı 61 (min: 18 maks: 89) olup 85 (%53.5)'i erkekti. 106 (%66.7) hastada ek hastalık mevcuttu. En sık semptom sırayla dispne (%61), öksürük (%57.2) ve halsizlikti (%49.7). Ağır pnömoni olan grupta lökosit, C-reaktif protein, Ferritin, D-Dimer ve yattığı gün sayısı hafif-orta pnömoni grubuna göre daha yüksek olup fark istatistiksel olarak anlamlı bulundu (sırayla p=0.004, p<0.001, p=0.005, p=0.01, p<0.001). Ağır pnömoni grubunda yoğun bakım ünitesine gidiş, entübasyon ve mortalite oranları daha yüksekti(sırayla p=0.035, p=0.035, p=0.035). Hastaların ortalama serum ACE düzeyi 25.14 (min: 3.39- max: 75.28) U/L olup her iki grup arasında anlamlı fark saptanmadı (p=0.61).

Sonuç: Hastaneye yatış sırasındaki serum ACE düzeyleri ile COVID-19 şiddeti arasında herhangi bir ilişki bulunmadı. Başvuru anındaki serum ACE düzeyinin hastalık şiddetini yansıtmadığı saptanmıştır.

Anahtar Sözcükler: Anjiyotensin dönüştürücü enzim; COVID-19; hastalık şiddeti; serum ACE.

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Original Article

Subcoracoid Effusion in Subscapularis Tears Is it a Radiological Marker?

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Keywords: Subcoracoid; effusion; subscapularis; rotator cuff tear.

ABSTRACT

Objective: Diagnosing subscapularis tendon rupture in preoperative MRI slices can be challenging. This study investigated whether subcoracoid effusion (SE) is more common in subscapularis tendon injuries and whether it can serve as a marker.

Methods: Patients with subscapularis tendon rupture were categorized as Group 1, consisting of 26 patients, while patients with intact subscapularis tendon but other cuff pathologies were classified as Group 2, consisting of 116 patients. We evaluated the presence of effusion in the subcoracoid bursa, effusion in the subscapular bursa, acromiohumeral distance, and coracohumeral distance. We examined retrospectively 208 patients who underwent shoulder arthroscopy in the same clinic between January 2021 and August 2023. We included 142 patients in the study who underwent surgery due to rotator cuff rupture. cuff rupture. We reviewed preoperative MRI images and surgical notes of the patients. Patients with subscapularis rupture were categorized as Group 1, consisting of 26 patients, while patients with intact subscapularis but other cuff pathologies were classified as Group 2, consisting of 116 patients.

Results: No statistically significant differences were observed between the groups regarding sex, age, and gender. Of 142 patients, 26 (18%) had arthroscopically confirmed Ssc tears. Among these, 22 were repaired, and 4 underwent debridement. There was no significant difference between the groups regarding acromiohumeral distance (p=0.253) and coracohumeral distance (p=0.12). No significant difference was found in subscapular bursa effusion between the groups (p=0.81). The difference in SE between the groups was statistically significant (p=0.0003).

Conclusion: In our study, we showed the relationship between the sub finding and Ssc tears. We found no relationship between coracohumeral and acromiohumeral distance and subscapularis tears.

INTRODUCTION

However, in recent years, with an understanding of its biomechanical significance and advancements in surgical techniques, there has been an increased focus on diagnosis and treatment.[1,2] Subscapularis tendon (Ssc) ruptures are injuries that can quickly go unnoticed. Diagnosing Ssc rupture in preoperative MRI slices can be challenging.[3] As a result, indirect indicators such as biceps dislocation and subscapularis muscle atrophy are used to estimate whether a tear is present.[4] Cases where the rupture goes undetected in preoperative MRI slices but is identified and repaired during surgery can also occur. Establishing an accurate preoperative diagnosis is crucial for surgical planning.

In the anterior shoulder, there are two bursae: subcoracoid and subscapular bursae. The subscapular bursa is between the subscapularis muscle and the shoulder capsule, and effusion in this region can be physiological. The subcoracoid bursa is beneath the inferior aspect of the coracoid process on the anterior surface of the subscapularis muscle, and effusion in this area can be associated with intra-articular pathologies.[5] This study investigated whether subcoracoid effusion (SE) is more common in Ssc injuries and whether it can serve as a marker.

MATERIALS AND METHODS

We obtained ethical approval from the local ethics committee (Decision No: 2023/514/258/33 Date: 27.09.2023). We examined retrospectively 208 patients who underwent shoulder arthroscopy in the same clinic between January 2021 and August 2023. Patients who were operated on due to rotator cuff pathology, whose MRI sections were taken completely and appropriately, and whose subscapu-

laris evaluation during the operation was clearly stated in the operating note were included in the study. Patients with inadequate or inappropriate preoperative MRI images, those with instability, and those with a history of previous shoulder surgery were excluded. Among them, we included 142 patients in the study who underwent surgery due to rotator cuff rupture. We reviewed preoperative MRI images and surgical notes of the patients. Patients with Ssc rupture were categorized as Group 1, consisting of 26 patients, while patients with intact Ssc but other cuff pathologies were classified as Group 2, consisting of 116 patients. There were no isolated Ssc ruptures. We examined all patients' preoperative MRI images. We evaluated the presence of effusion in the subcoracoid bursa, effusion in the subscapular bursa, acromiohumeral distance, and coracohumeral distance. We assessed the presence of Ssc tears from the surgical notes. We performed the measurements by an orthopaedic surgeon with seven years of arthroscopic surgical experience. With the assistance of a particular shoulder device, MRI images were evaluated with the patient in a supine position using a 1.5 Tesla MRI machine. We evaluated axial, sagittal, and coronal sections in oblique coronal MRI. The normality of distributions was assessed using the Shapiro-Wilk test and found to be normally distributed. The data were analyzed using SPSS version 22.0 software (IBM Corporation, Armonk, NY, United States). Independent t-tests and Chi-Square tests were conducted for demographic data and measurement results.

RESULTS

No statistically significant differences were observed between the groups regarding sex, age, and gender (Table 1). Of 142 patients, 26 (18%) had arthroscopically confirmed Ssc tears. Among these, 22 were repaired, and 4 underwent debridement. There was no significant difference between the groups regarding acromiohumeral distance (p=0.253) and coracohumeral distance (p=0.12). In 8 out of the 26 patients with Ssc tears (30.7%), preoperative MRI evaluations failed to detect the Ssc tear. Among the 26 patients with Ssc ruptures, 17 (65.3%) had effusion in the subscapular bursa, while among the 116 patients without Ssc tears, 73 (62.9%) had subscapular bursa effusion. No significant difference was found in subscapular bursa effusion between the groups (p=0.81). In 14 out of the 26 patients with Ssc tears (53.8%), SE was observed, whereas 23 out of the 116 patients without Ssc tears (19.8%) had SE. The difference in SE between the groups was statistically significant (p=0.0003) (Table 2).

Table 1. Demographic comparison of groups

	Group 1 n: 26	Group 2 n:116	p value
Age	57.73	55.38	0.95
Sex			0.59
Male	9	34	-
Female	17	82	-

DISCUSSION

With this study, we demonstrated the effectiveness of seeing SE on MRI images taken in the preoperative period in diagnosing Ssc tears. Although we observed SE in some rotator cuff patients with intact Ssc, we found it to be significantly more frequent in patients with Ssc tears. Ssc tears were injuries not previously considered a major cause of shoulder problems. Orthopaedic surgeons generally treat partial tears conservatively and open repaired total tears.[6] However, in recent years, subscapular tears have begun to be diagnosed and treated more frequently.[1] In a study published in 2005 with 84 patients, patients with isolated Ssc rupture were treated. Open repair was applied. It has been demonstrated that Ssc repair provides a functional contribution in selected patient.[7] Arthroscopic interventions on the Ssc began in the early 2000s. In 2001, the Ssc was visualized arthroscopically, and it was stated that not all lesions could be seen arthroscopically.[8] Then, arthroscopic repair methods of the Ssc began to be applied, and their clinical benefits were demonstrated.[9-11] We performed a surgical intervention on all patients. We detected Ssc tears, including debridement in 4 and repair in the others. As a result of biomechanical and clinical studies, the effectiveness of repairing the Ssc tear on shoulder functions, especially in forward elevation, has been demonstrated. For this reason, more studies have begun to be conducted on the diagnosis and treatment of Ssc rupture. In order not to miss Ssc tears that are difficult to diagnose, new examination techniques[12] and new indirect findings in MRI sections and arthroscopic images were stated.[13-17] In another study dated 2006, it was stated that out of 1345 patients who underwent rotator cuff repair,

Table 2. Radiological measurements of the groups

	Group 1 n: 26 (%)	Group 2 n:116 (%)	p value
Subcoracoid effusion	14	23	0.000355
Subscapular effusion	17	73	0.81
Acromiohumeral distance (mm.)	8.01	8.26	0.25
Coracohumeral distance (mm.)	6.13	6.58	0.12

isolated or combined Ssc tear was detected in only 73 patients. Open surgery was applied to these patients, and it was stated that there was an improvement in constant scores.[18] Arai R et al. found a Ssc tear in 19 (27.4%) of 435 patients in whom they performed rotator cuff surgery.[19]

Siddhant K. Mehta detected Ssc tear in 14% of 354 asymptomatic patients with rotator cuff rupture due to USG and physical examination.[20] However, since it was performed with asymptomatic patients and there was no surgical confirmation, Ssc tear was detected in patients with rotator cuff syndrome who presented symptomatically. It should be kept in mind that tears may occur more frequently than this.

Ismail Turkmen et al. detected Ssc rupture in 44 (38%) of 114 patients to whom they performed arthroscopic rotator cuff repai.[5] In the literature, the rate of Ssc tear in patients with rotator cuff pathology varies between 14-38%. In our study, we found Ssc tears in 26 (18%) of 142 patients. In this respect, this rate is compatible with the literature.

Burkhart et al. performed repair on 25 patients with Ssc tears, 8 of whom were isolated, and reported excellent results after 11 months of follow-up.[9] Adams et al. operated on 40 Ssc tears, 7 of which were isolated, and published their mid-term results. They achieved satisfactory clinical results after five years.[21] Denard et al. published the long-term results of 79 patients. ASES reported improvements in UCLA scores and forward flexion.[22]

As recent studies have shown, repairing subscapularis muscle ruptures provides significant clinical improvement and has been accepted by orthopaedic surgeons. In our study, we applied debridement (partial tear) to 4 of 26 Ssc tears and repair to 22.

In Ssc tears, MRI is not as practical as it is for posterosuperior tears. In studies, writers found MRI sensitivity low in subscapular tears.[2,23] Pfirrmann et al. found it more effective to evaluate subscapular tears with MR arthrography: 95%-100% sensitivity and 55%-62% specificity for detecting Ssc tears using MRA.[24] Furukawa et al. reported that sensitivity and specificity increased by using MRI sections from different angles.[3] Large retracted tears are more accessible to spot on MRI, and there is a lack of tendon continuity in axial sections. Fat infiltration may be visible in sagittal sections. However, it is more challenging to detect non-retracted tears on MR.[23]

Meyer et al. stated in their study that an increase in tendon length in axial MRI sections may indicate a tear.[25] In their study, Shi et al. examined the relationship between Ssc tears and biceps luxation. They stated there is a high probability of an Ssc tear if the biceps are luxated, but there is also an Ssc tear when the biceps are in place.[26]

The comma sign is a known finding in patients with retracted supraspinatus and Ssc tear in arthroscopic view.[27,28] There are studies in the literature that evaluate comma signs in MRI sections. Zappia Marcello, in his study, examined the MRI with comma sign findings of 110 patients who underwent arthroscopy. Jung et al. similarly mentioned the MRI finding and found it useful in full-thickness supraspinatus and Ssc ruptures.[29,30]

As the literature shows, many studies have shown that detecting Ssc tears is more accessible on MRI. We stated in our study that the finding of SE would help diagnose an Ssc tear.

Yamamoto et al. discussed the findings of Neer and Hawkins. They reported that there were different compression findings in both findings. They stated that there is compression under the subscapularis and coracoacromial arch in the Hawkins manoeuvre.[31] From this, there may be a relationship between the decrease in acromiohumeral distance and the Ssc tear. However, in our study, we did not detect any difference in acromiohumeral distance between the Ssc torn and intact groups (p=0.25).

Studies show that correlating decreased coracohumeral distance and subcoracoid impingement with Ssc tears. The narrowing of the coracohumeral distance may be related to the anterior translation of the humeral head.[32] There are opinions that superior migration of the humeral head due to a supraspinatus tear puts the Ssc at risk and narrows the coracohumeral space. However, some patients have a narrow coracohumeral distance and an intact Ssc.[33] In our study, we did not detect any difference between the groups in terms of coracohumeral distance (p=0.12). The effectiveness of coracoplasty is controversial. Therefore, the relationship between coracohumeral distance and Ssc tear is unclear.[32,34]

Studies have revealed the importance of diagnosis and treatment of Ssc tear. Indirect findings, especially on MRI scans, come to the fore in the preoperative period regarding these injuries, which are difficult to diagnose. In our study, we showed the relationship between the SE finding and Ssc tears. We found no relationship between coracohumeral and acromiohumeral distance and Ssc tears.

Our limitations include the retrospective nature of the study and the limited number of patients. New studies on this subject are necessary, with more patients prospectively correlating with arthroscopic images.

Conclusion

Diagnosing Ssc tears is challenging, and neglecting them causes insufficient clinical results. Detection of SE in MRI images taken in the preoperative period makes diagnosis easier.

Ethics Committee Approval

This study approved by the Dr. Lutfi Kirdar Kartal City Hospital Ethics Committee (Date: 27.09.2023, Decision No: 2023/514/258/33).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: E.Ş., E.E.; Design: E.Ş., E.E.; Supervision: E.E.; Fundings: E.Ş.; Materials: E.Ş.; Data: E.Ş.; Analysis: E.Ş.; Literature search: E.Ş.; Writing: E.Ş., E.E.; Critical revision: E.Ş., E.E.

Conflict of Interest

None declared.

REFERENCES

1. Lee J, Shukla DR, Sanchez-Sotelo J. Subscapularis tears: Hidden and forgotten no more. JSES Open Access 2018;2:74-83. [CrossRef]
2. Foad A, Wijdicks CA. The accuracy of magnetic resonance imaging and magnetic resonance arthrogram versus arthroscopy in the diagnosis of subscapularis tendon injury. Arthroscopy 2012;28:636-41. [CrossRef]
3. Furukawa R, Morihara T, Arai Y, Ito H, Kida Y, Sukenari T, et al. Diagnostic accuracy of magnetic resonance imaging for subscapularis tendon tears using radial-slice magnetic resonance images. J Shoulder Elbow Surg 2014;23:e283-90. [CrossRef]
4. Tung GA, Yoo DC, Levine SM, Brody JM, Green A. Subscapularis tendon tear: Primary and associated signs on MRI. J Comput Assist Tomogr 2001;25:417-24. [CrossRef]
5. Turkmen I, Altun G, Celik H, Bilsel K. Can subcoracoid cyst formation be a sign of anterosuperior rotator cuff tears and biceps pulley lesions? A prospective radiologic and arthroscopic correlation study. J Shoulder Elbow Surg 2020;29:1665-70. [CrossRef]
6. Lyons RP, Green A. Subscapularis tendon tears. J Am Acad Orthop Surg 2005;13:353-63. [CrossRef]
7. Edwards TB, Walch G, Sirveaux F, Molé D, Nové-Josserand L, Boulahia A, et al. Repair of tears of the subscapularis. J Bone Joint Surg Am 2005;87:725-30. [CrossRef]
8. Wright JM, Heavrin B, Hawkins RJ, Noonan T. Arthroscopic visualization of the subscapularis tendon. Arthroscopy 2001;17:677-84. [CrossRef]
9. Burkhart SS, Tehrany AM. Arthroscopic subscapularis tendon repair: Technique and preliminary results. Arthroscopy 2002;18:454-63. [CrossRef]
10. Lo IK, Burkhart SS. Subscapularis tears: Arthroscopic repair of the forgotten rotator cuff tendon. Tech Shoulder Elb Surg 2002;3:282-91. [CrossRef]
11. Lafosse L, Lanz U, Saintmard B, Campens C. Arthroscopic repair of subscapularis tear: Surgical technique and results. Orthop Traumatol Surg Res 2010;96:S99-108. [CrossRef]
12. Rhee SM, Youn SM, Park JH, Chang GW, Rhee YG. The scissors sign: A provocative test for detecting the leading-edge tear of subscapularis tendon: A diagnostic study. BMC Musculoskeletal Disorders 2022;23:1-9. [CrossRef]
13. Scheibel M, Magosch P, Pritsch M, Lichtenberg S, Habermeyer P. The belly-off sign: A new clinical diagnostic sign for subscapularis lesions. Arthroscopy 2005;21:1229-35. [CrossRef]
14. Barth JR, Burkhart SS, De Beer JF. The bear-hug test: A new and sensitive test for diagnosing a subscapularis tear. Arthroscopy 2006;22:1076-84. [CrossRef]
15. Lo IK, Burkhart SS. The comma sign: An arthroscopic guide to the torn subscapularis tendon. Arthroscopy 2003;19:334-7. [CrossRef]
16. Koo SS, Burkhart SS. Subscapularis tendon tears: Identifying mid to distal footprint disruptions. Arthroscopy 2010;26:1130-4. [CrossRef]
17. Walch G, Nové-Josserand L, Boileau P, Levigne C. Subluxations and dislocations of the tendon of the long head of the biceps. J Shoulder Elbow Surg 1998;7:100-8. [CrossRef]
18. Flury MP, John M, Goldhahn J, Schwyzer HK, Simmen BR. Rupture of the subscapularis tendon (isolated or in combination with supraspinatus tear): When is a repair indicated? J Shoulder Elbow Surg 2006;15:659-64. [CrossRef]
19. Arai R, Sugaya H, Mochizuki T, Nimura A, Moriishi J, Akita K. Subscapularis tendon tear: An anatomic and clinical investigation. Arthroscopy 2008;24:997-1004. [CrossRef]
20. Mehta SK, Teefey SA, Middleton W, Steger-May K, Sefko JA, Keener JD. Prevalence and risk factors for development of subscapularis and biceps pathology in shoulders with degenerative rotator cuff disease: A prospective cohort evaluation. J Shoulder Elbow Surg 2020;29:451-8. [CrossRef]
21. Adams CR, Schoolfield JD, Burkhart SS. The results of arthroscopic subscapularis tendon repairs. Arthroscopy 2008;24:1381-9. [CrossRef]
22. Denard PJ, Jiwani AZ, Lädermann A, Burkhart SS. Long-term outcome of a consecutive series of subscapularis tendon tears repaired arthroscopically. Arthroscopy 2012;28:1587-91. [CrossRef]
23. Adams CR, Schoolfield JD, Burkhart SS. Accuracy of preoperative magnetic resonance imaging in predicting a subscapularis tendon tear based on arthroscopy. Arthroscopy 2010;26:1427-33. [CrossRef]
24. Pfirrmann CW, Zanetti M, Weishaupt D, Gerber C, Hodler J. Subscapularis tendon tears: Detection and grading at MR arthrography. Radiology 1999;213:709-14. [CrossRef]
25. Meyer DC, Zimmermann SM, Wieser K, Bensler S, Gerber C, Germann M. Lengthening of the subscapularis tendon as a sign of partial tearing in continuity. J Shoulder Elbow Surg 2016;25:31-7. [CrossRef]
26. Shi LL, Mullen MG, Freehill MT, Lin A, Warner JJ, Higgins LD. Accuracy of long head of the biceps subluxation as a predictor for subscapularis tears. Arthroscopy 2015;31:615-9. [CrossRef]
27. Dilisio MF, Neyton L. Comma sign-directed repair of anterosuperior rotator cuff tears. Arthrosc Tech 2014;3:e695–8. [CrossRef]
28. Garofalo R, Flanagin BF, Castagna A, Krishnan SG. Subscapularis tear: Intraoperative evaluation and treatment. In Gumina S, editors. Rotator Cuff Tear. New York City: Springer; 2017. p. 345–51. [CrossRef]
29. Zappia M, Ascione F, Romano AM, Di Pietto F, Nastrucci G, Collina A, et al. Comma sign of subscapularis tear: Diagnostic performance and magnetic resonance imaging appearance. J Shoulder Elbow Surg 2021;30:1107-16. [CrossRef]
30. Jung JY, Yoon YC, Cha DI, Yoo JC, Jung JY. The "bridging sign": An MR finding for combined full-thickness tears of the subscapularis tendon and the supraspinatus tendon. Acta Radiologica 2013;54:83-8. [CrossRef]
31. Yamamoto N, Muraki T, Sperling JW, Steinmann SP, Itoi E, Cofield RH, et al. Impingement mechanisms of the Neer and Hawkins signs. J Shoulder Elbow Surg 2009;18:942-7. [CrossRef]
32. Suenaga N, Minami A, Kaneda K. Postoperative subcoracoid impingement syndrome in patients with rotator cuff tear. J Shoulder Elbow Surg 2000;9:275-8. [CrossRef]
33. Cetinkaya M, Ataoglu MB, Ozer M, Ayanoglu T, Kanatli U. Subscapularis tendon slip number and coracoid overlap are more related parameters for subcoracoid impingement in subscapularis tears: A magnetic resonance imaging comparison study. Arthroscopy 2017;33:734-42. [CrossRef]
34. Kim SJ, Choi YR, Jung M, Yoon YK, Chun YM. Concomitant coracoplasty during arthroscopic subscapularis repair does not yield better clinical outcomes and structural integrity. Knee Surg Sports Traumatol Arthrosc 2018;26:56-62. [CrossRef]

Subkorakoid Efüzyon, Subskapularis Yırtıklarında Radyolojik Bir Belirteç Midir?

Amaç: Ameliyat öncesi MR kesitlerinde subscapularis tendon rüptürünün teşhis edilmesi zor olabilir. Bu çalışmada subscapularis tendon yaralanmalarında subkorakoid efüzyonun (SE) daha sık görülüp görülmediği ve bunun bir belirteç olarak kullanılıp kullanılamayacağı araştırıldı.

Gereç ve Yöntem: Çalışmada rotator manşet yırtığı nedeniyle ameliyat edilen 142 hastayı retrospektif olarak inceledik. Subskapularis tendon yırtığı olan hastalar 26 hastadan oluşan Grup 1 olarak sınıflandırılırken, subskapularis tendonu sağlam ancak diğer manşet patolojileri olan hastalar 116 hastadan oluşan Grup 2 olarak sınıflandırıldı. Tüm hastaların ameliyat öncesi MR kesitleri incelendi. Subkorakoid bursada efüzyon varlığını, subskapular bursada efüzyonu, akromiohumeral mesafeyi ve korakohumeral mesafeyi değerlendirdik.208 hastayı retrospektif olarak inceledik. Çalışmaya rotator manşet yırtığı nedeniyle ameliyat edilen 142 hastayı dahil ettik. Hastaların ameliyat öncesi MR görüntülerini ve ameliyat notlarını inceledik. Subskapularis rüptürü olan hastalar 26 hastadan oluşan Grup 1 olarak sınıflandırılırken, subskapularis sağlam ancak diğer manşet patolojileri olan hastalar 116 hastadan oluşan Grup 2 olarak sınıflandırıldı.

Bulgular: Gruplar arasında cinsiyet, yaş ve cinsiyet açısından istatistiksel olarak anlamlı bir fark gözlenmedi. 142 hastanın 26'sında (%18) artroskopik olarak doğrulanmış Ssc yırtığı vardı. Bunlardan 22'si onarıldı, 4'üne debridman uygulandı. Akromiohumeral mesafe (p: 0.253) ve korakohumeral mesafe (p: 0.12) açısından gruplar arasında anlamlı fark yoktu. Gruplar arasında subskapular bursa efüzyonu açısından anlamlı fark bulunamadı (p: 0.81). Gruplar arasındaki SE farkı istatistiksel olarak anlamlıydı (p: 0.0003).

Sonuç: Bu çalışma ile ameliyat öncesi dönemde çekilen MR görüntülerinde subkorakoid efüzyon görülmesinin subskapularis yırtıklarının tanısındaki etkinliğini ortaya koyduk. Subskapularis yırtığı olan hastalarda anlamlı olarak daha sık görüldüğünü bulduk.

Anahtar Sözcükler: Efüzyon; rotator manşet yırtığı; subkorakoid; subskapularis.

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Original Article

Efficacy of Cyclocryotherapy on Pain in Patients with Absolute Glaucoma

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Keywords: Cyclocryotherapy; absolute glaucoma; pain control; phthisis; evisceration.

ABSTRACT

Objective: The aim of this study was to evaluate the short-term efficacy of cyclocryotherapy in pain control in 63 patients with absolute glaucoma who had pain and no vision despite maximum medical treatment.

Methods: 63 eyes of 63 glaucoma patients defined as absolute glaucoma were included in the study. The intraocular pressures, number of drops used, pain status and need for recur-rent therapy were compared before and after the procedure at 1 and 3 months.

Results: 13 of the patients were female and 40 were male. The mean age was 59.4±17.5 years. 50 of the patients were diagnosed with neovascular glaucoma, 3 with congenital glaucoma, 1 with primary open-angle glaucoma and 9 with angle-closure glaucoma. Preoperative mean intraocular pressure was 50.7±12 mmHg, while it was found to be 37.9±15.4 mmHg in the 1st month and 28.5±15.8 mmHg in the 3rd month postoperatively. The decrease in intraocular pressure before and after the procedure was statistically significant at 1 and 3 months. ($p<0.0001$) Pain control was received 85% at the first month and 96% at the third month after the procedure. Number of medications that were used was found 3.00 and 2.3±0.9 respectively before and after the procedure and this was statistically significant. ($p<0.0001$) While no phthisis was observed in any patient, evisceration was applied to 2 patients because of uncontrolled pain.

Conclusion: Cyclocryotherapy may be a preferred treatment option before evisceration, as it is a non-invasive, inexpensive and easily applicable method in patients whose pain control cannot be achieved, although it has lost its former popularity with the discovery of new options in the surgical and medical treatment of glaucoma.

INTRODUCTION

Glaucoma is one of the most common causes of blindness in the world. Absolute glaucoma can be defined as end-stage glaucoma in which there is no vision and there is pain despite maximum medical treatment. While it is aimed to protect the visual field and visual acuity in the treatment of glaucoma, the goal in absolute glaucoma patients is to relieve the pain and to ensure the quality of life of the patient. Evisceration or enucleation can be applied for the control of glaucoma, but these options are left to the last due to cosmetic concerns. Although cyclocryotherapy lost its popularity in current glaucoma treatment, it still has validity to control pain in patients with absolute glaucoma. In our study, we evaluated the effectiveness of cyclocryotherapy on intraocular pressure and pain in patients with painful absolute glaucoma in our clinic between 2017 and 2019.

MATERIALS AND METHODS

The records of patients with absolute glaucoma who underwent cyclocryotherapy between 2017 and 2019 were retrospectively reviewed. Sixty-three eyes of 63 patients who were older than 18 years of age had no light perception, had eye pain despite maximum medical treatment, and had an intraocular pressure above 21 mmHg were included in the study. Patients were evaluated in terms of intraocular pressure before and after the 1st and 3th months of the procedure, number of eye drops used, pain status before and after the procedure, and repeatability of the procedure. Cyclocryotherapy was applied to all patients under retrobulbar anesthesia with the 2.5-mm probe of the Bimed Universal cryo device, 2 mm behind the limbus, for 60s at −80°C in 6 quadrants. Subconjunctival steroid injection was applied at the end of the procedure and topical antibiotics, steroids, and cycloplegics were used in tapering doses within 1 month after the procedure. The

Table 1. Pre and post operative IOP and medication status of patients

	n	Minimum	Maximum	Mean	Standard Deviation
Age	63	17	86	59.4	17.5
Pre-operative IOP	63	27	72	50.7	12
Post-operative 1. month IOP	63	8	64	37.9	15.4
Post-operative 3. month IOP	63	9	64	28.5	15.8
Number of drops pre-operative	63	3	3	3	0
Number of drops post-operative	63	0	3	2.3	0.9

IOP: Intraocular pressure (mmHg).

intraocular pressures (Goldmann applanation tonometry) before and at the 1st and 3rd months after the procedure, presence of pain, and the number of eye drops used before and after the procedure were recorded.

Statistics

Statistical analysis was performed using SPSS (version 21.0, SPSS, Inc., Chicago, IL, USA). Data were expressed as mean±standard deviation or percent where appropriate. $p<0.05$ was considered statistically significant. The normal distribution of the data distribution in the groups was evaluated using the Shapiro–Wilk test. Friedman test was used to compare intraocular pressures at pre-operative, 1st, and 3rd months. Wilcoxon test was used for pairwise comparisons.

RESULTS

The cyclocryotherapy procedure applied to 63 eyes of 63 patients with absolute glaucoma whose pain persisted despite maximum medical treatment and who were not suitable for glaucoma surgery was evaluated. 13 of the patients were female and 40 were male. The mean age was 59.4±17.5 years. Diagnoses of patients were neovascular glaucoma in 50 patients, congenital glaucoma in 3 patients, and primary open-angle glaucoma and angle closure glaucoma in 9 patients. Pre-operative mean intraocular pressure was 50.7±12 mmHg, while post-operative was 37.9±15.4 mmHg in 1st month and 28.5±15.8 mmHg in 3rd month. The decrease in intraocular pressure before and 1 and 3 months after the procedure was statistically significant. The descriptive information of the patients is summarized in Table 1. The difference in intraocular pressure between 1st and 3rd months after the procedure was also significant. All of the patients used 3 antiglaucomatous drops pre-operatively, and this number was found to be 2.3±0.9 after the procedure. 54 patients had never undergone surgery. Ahmed glaucoma valve implantation was performed in 4 patients, trabeculectomy in 2 patients, diode laser cyclophotocoagulation in 1 patient, and pars plana vitrectomy in 2 patients before the procedure. Pain control was achieved in 54 patients in the post-operative 1st month. Because of pain persistence, 6 patients underwent the same procedure in post-operative 1st month while 9 underwent in post-operative 2nd month. Evisceration was performed in 2 patients due to uncontrolled pain.

DISCUSSION

Cyclocryotherapy was first defined by Bietti[1] in 1950 and started to be used more frequently after Roeth[2] reported 73% success after the application. Although it is an easy procedure, the most important and feared complication is phthisis. Boniuk[3] and Bellows[4] reported the rate of phthisis as 10%, while this rate was 34% in the study of Croup.[5] With the increase in vision-saving options in glaucoma surgery, cyclocryotherapy has almost completely lost its use, especially in patients with good visual acuity. However, no matter how new options are defined in the medical treatment and surgical treatment of glaucoma, the disease still progresses aggressively in some patients, and eventually, despite maximum medical treatment, blindness develops and severe pain is experienced. The primary goal in these patients is to increase their quality of life by providing pain control. For this, the chosen method should have the lowest risk in terms of complications and should be less invasive. Cyclocryotherapy is an easy, repeatable, and non-invasive method and its costs are low. Humor aqueous is produced by non-pigmented ciliary epithelium. With a probe placed 2.5–3 mm behind the limbus over the conjunctiva at −80°C for about 60s, provides ablation in the ciliary body and deteriorates the blood flow of the ciliary body. Thus, aqueous humor production is reduced. Meantime, an increase in outflow can be achieved by causing damage to the trabecular meshwork. It takes about 3–4 weeks for damage to the ciliary epithelium, so this time should be considered when evaluating the effectiveness of the procedure. With the regeneration of the ciliary epithelium, the effectiveness of cyclocryotherapy decreases. Therefore, repeated applications may be required. Damage in the suprachoroidal space affects both ciliary nerves and long posterior ciliary artery. Damage to arteries can cause phthisis and vision loss. Destruction of the ciliary nerves, on the other hand, reduces the feeling of pain. In our study, the rate of intraocular pressure ≤21 mmHg with or without medication in the post-operative 1st month was 12%, while pain control was 85%. Although the aimed intraocular pressure cannot be achieved, the decrease in pain after the procedure can be explained by

damage to the ciliary nerves in the suprachoroidal area. In a study by Ruixue et al.[3] in 2020 comparing the effectiveness of ultrasound cycloplasty and cyclocryotherapy, reduction in pain in the 6th month after cyclocryotherapy was found 73%. Kim et al.[4] showed that the cyclocryotherapy procedure, which was applied to 6 quadrants and 3 and 9 o'clock position, provided pain control in all patients. Baykara et al.[5] evaluated the effectiveness of cyclocryotherapy in 39 eyes with painful and absolute glaucoma and found the success of pain control to 79%. In our study, similar results were found with respect to other studies. There was no loss of vision because patients with any vision acuity were not included in our study. Phthisis is the most devastating complication of cyclocryotherapy. In particular, application to more than 6 quadrants, application to the 3 and 9 o'clock lines, and repetitive applications increase the risk of phthisis. While Heuring[6] reported the rate of phthisis as 6.7% in his study in 1998, this rate was 11.7% in the study of Benson and Nelson.[7] In the study of Kim,[4] even though cyclocryotherapy was applied to the 3 and 9 o'clock quadrants, phthisis developed in only one of 20 eyes. In our study, phthisis was not seen in any patient. This situation can be explained by the fact that cyclocryotherapy is applied only 6 quadrants and the rate of recurrent treatment is low (23%). While the expectation from cryotherapy was to provide both effective intraocular pressure and protection of vision in the past, today, cryotherapy is mostly used to control pain as last chance. Rates of feared complications have decreased as a result of the almost non-applicability of the procedure in eyes with vision acuity in the current studies. Pain which does not respond to medical treatment seriously affects the quality of life of glaucoma patients. Furthermore, it is very difficult to use eye drops many times a day for patients who take maximum medical treatment but do not have light perception. Reduction in the number of drops can be included in the success criteria for this procedure. In our study, the decrease in the number of drops was found to be statistically significant. In the study by Gorsler[8] published in 2015, a significant decrease was found in the number of drops used after cyclocryotherapy and the need for drops was completely eliminated in 2% of the patients. In our study, the rate of complete elimination of the drop requirement was 3%. With the help of the results we have obtained, it can be said that cyclocryotherapy is successful in pain control, regardless of the decrease in intraocular pressure in patients with absolute glaucoma and can be a last chance before evisceration or enucleation.

Conclusion

Cyclocryotherapy may be a preferred treatment option before evisceration, as it is a non-invasive, inexpensive and easily applicable method in patients whose pain control cannot be achieved, although it has lost its former popularity with the discovery of new options in the surgical and medical treatment of glaucoma.

Ethics Committee Approval

This study approved by the Kartal Dr. Lütfi Kırdar City Hospital, Clinical Research Ethics Committee (Date: 27.10.2021, Decision No: 2021/514/212/9).

Informed Consent

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Authorship Contributions

Concept: B.Y.; Design: B.Y., Ş.Ş.; Supervision: B.Y., Ş.Ş.; Fundings: B.Y., A.A.; Materials: B.Y., A.A.; Data: B.Y., A.A.; Analysis: B.T.; Literature search: B.T., A.A.; Writing: B.Y.; Critical revision: B.Y., Ş.Ş.

Conflict of Interest

None declared.

REFERENCES

1. Bietti G. Surgical intervention on the ciliary body: New trends for the relief of glaucoma. JAMA 1950;142:889–97. [CrossRef]
2. De Roetth A Jr. Cryosurgery for the treatment of advanced chronic simple glaucoma. Am J Ophthalmol 1968;66:1034–41. [CrossRef]
3. Ruixue W, Tao W, Ning L. A comparative study between ultrasound cycloplasty and cyclocryotherapy for the treatment of neovascular glaucoma. J Ophthalmol 2020;2020:4016536. [CrossRef]
4. Kim BS, Kim YJ, Seo SW, Yoo JM, Kim SJ. Long-term results from cyclocryotherapy applied to the 3o'clock and 9o'clock positions in blind refractory glaucoma patients. Korean J Ophthalmol 2015;29:47–52. [CrossRef]
5. Baykara M, Başkaya K, Yayla U, Budak BA, İncebıyık İ. Cyclocryotherapy in painful eyes wıth end stage glaucoma. Uludağ Univ Tıp Fak Derg [Article in Turkish] 2014;40:49–51.
6. Heuring AH, Hütz WW, Hoffmann PC, Eckhardt HB. Cyclocryotherapy in neovascular glaucoma and non-neovascular glaucoma. Klin Monbl Augenheilkd [Article in German] 1998;213:213–9. [CrossRef]
7. Benson MT, Nelson ME. Cyclocryotherapy: A review of cases over a 10-year period. Br J Ophthalmol 1990;74:103–5. [CrossRef]
8. Gorsler I, Thieme H, Meltendorf C. Cyclophotocoagulation and cyclocryocoagulation as primary surgical procedures for open-angle glaucoma. Graefes Arch Clin Exp Ophthalmol 2015;253:2273–7. [CrossRef]

Absolu Glokom Hastalarında Siklokriyoterapi Tedavisinin Ağrı Üzerine Etkinliği

Amaç: Bu çalışmanın amacı maksimum medikal tedaviye rağmen ağrısı olan ve görme hissi olmayan 63 absolu glokom hastasına ağrı kontrolü için uygulanan siklokriyoterapi tedavisinin kısa dönem etkinliğini değerlendirmektir.

Gereç ve Yöntem: Absolu glokom olarak tanımlanan 63 glokom hastasının 63 gözü çalışmaya dahil edildi. Hastaların işlem öncesi ve sonrasındaki 1 ve 3. aydaki göz içi basınçları, kullandıkları ilaç sayıları, ağrı durumları ve tekrar uygulama gereksinimleri karşılaştırıldı.

Bulgular: Hastaların 13'ü kadın 40'ı erkekti. Yaş ortalaması 59.4+-17.5 idi. Hastaların 50 si neovasküler glokom, 3ü konjenital glokom, 1'i primer açık açılı glokom ve 9'u açı kapanması glokomu tanılıydı. Preoperatif ortalama göz içi basıncı 50,7 mmHg +-12 mm-Hg iken post operatif 1. ayda 37.9+-15 mm-Hg, 3. ayda 28.5+-15.8 mm-Hg olarak bulundu. İşlem öncesi ve sonrasında 1 ve 3. ayda göz içi basıncında elde edilen düşüş istatistiksel olarak anlamlıydı. ($p<0.0001$) Ağrı kontrolü işlem sonrası birinci ayda %85, üçüncü ayda %96 olarak bulundu. İşlem öncesi ve sonrası kullanılan ilaç miktarları sırasıyla 3 ve 2.3±0.9 olarak bulundu ve bu değer istatstiksel olarak anlamlı görüldü. ($p<0.0001$) Hiçbir hastada fitizis görülmezken ağrı kontrolü sağlanamaması nedeniyle 2 hastaya eviserasyon uygulandığı tespit edildi.

Sonuç: Siklokriyoterapi glokomun cerrahi ve medikal tedavisinde yeni seçeneklerin bulunmasıyla eski popülerliğini kaybetmesine rağmen ağrı kontrolü sağlanamayan hastalarda non invazif, ucuz ve kolay uygulanabilir bir yöntem olmasıyla eviserasyon öncesi tercih edilebilir bir tedavi seçeneği olabilir.

Anahtar Sözcükler: Absolu glokom; ağrı kontrolü; eviserasyon; fitizis; siklokriyoterapi.

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Original Article

The Relationship Between Lactate Level and Fluid Management After Hepatectomy

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Keywords: Fluid therapy; hepatectomy; lactate; postoperative management.

ABSTRACT

Objective: After surgeries such as hepatectomy, careful monitoring of various physiological measurements is crucial for successful outcomes. Among these measurements are lactate levels, which are significant indicators of tissue perfusion and oxygenation. Particularly in the postoperative period, arterial blood lactate (ABL) levels are important for monitoring tissue perfusion. Maintaining an optimal fluid balance is critical for sustaining tissue perfusion and preventing potential complications. The aim of this study is to examine the relationship between patients' ABL levels and fluid therapy in the postoperative period.

Methods: This study was designed as a retrospective analysis to examine the outcomes of patients treated in the intensive care unit following hepatectomy. To assess the impact of fluid therapy on patients' clinical outcomes, the amounts of fluids administered were calculated. Initial arterial blood lactate levels, peak lactate levels, the rate of lactate clearance, acidosis status, and base deficit values in arterial blood gas analyses were recorded. The Pearson Correlation Test was used to determine the relationship between arterial blood gas parameters, ABL trend parameters, and fluid therapy, considering $p<0.05$ as statistically significant.

Results: In this study, 108 patients who underwent hepatectomy were examined. Patients were administered 42.3 cc/kg of fluid until their ABL levels returned to the normal range. Additionally, a significant correlation was found between the highest ABL levels and the total amount of fluid administered ($r=0.385$, $p<0.01$).

Conclusion: The study identified a relationship between ABL levels and fluid intake. We believe that high lactate levels indicate a sepsis-like condition requiring intensive fluid therapy. These results suggest that monitoring ABL levels in patients who have undergone hepatectomy can be an important tool for predicting the need for fluid therapy and the duration of close monitoring. Arterial blood lactate monitoring can play a critical role in the postoperative management and monitoring of patients.

INTRODUCTION

Hepatectomy is a major surgical procedure that requires careful monitoring of various physiological parameters to ensure successful outcomes.[1] One of the important parameters closely monitored in the postoperative period is the lactate levels in the blood, which can serve as indicators of tissue perfusion and oxygenation.[2]

During hepatectomy, there is a significant risk of blood loss, which can lead to hypovolemia and impaired tissue perfusion.[3,4] This can result in the accumulation of lactate in the blood, which can lead to metabolic acidosis and impaired organ function. Therefore, close monitoring of lactate levels is essential to detect and address any abnormalities in tissue perfusion.[5,6]

Fluid management is also a critical aspect of postoperative care after hepatectomy. Proper fluid balance is crucial to maintaining adequate tissue perfusion and preventing complications.[7,8]

After hepatectomy, the patient may be under metabolic stress, which can cause an increase in blood lactate levels. However, fluid therapy can increase blood volume and carry more oxygen to the tissues, thereby reducing lactate levels. Therefore, this study aims to investigate the effect of fluid therapy on improving the metabolic status of the patient during the postoperative period after hepatectomy. The results of this study may impact clinical practices in fluid management after liver and biliary tract tumor surgery and improve patient outcomes.

MATERIALS AND METHODS

This study utilized a retrospective cohort study design and was conducted by examining the medical records of pa-

tients between January 2021 and April 2023. A total of 108 patients who underwent surgery due to liver and biliary tract tumors were included in the study. In this study, parameters such as initial arterial blood lactate (ABL) levels, peak lactate levels, lactate clearance, presence of acidosis, and base deficit in arterial blood gas analysis were retrospectively evaluated concerning the amount of fluid administered to the patients. The study was performed in a tertiary intensive care unit specific to hepatobiliary surgery and liver transplantation. All data were obtained from the hospital's records system and intensive care unit observation notes.

Intensive Care Follow-Up Protocol and Definitions

In the postoperative period following hepatectomy, patients require close monitoring and fluid therapy. Upon admission to the intensive care unit, arterial blood gas, hemogram, and blood biochemistry tests are conducted within the first 15 minutes. Arterial blood gas examination is then repeated at regular intervals, initially every two hours and later at wider intervals. The amount of fluid given per hour as 0.9% saline and 10% dextrose is determined until stability is achieved, as assessed by the attending physician. The first day after the operation is defined as the time from the patient's arrival in the intensive care unit until 07:00 AM the next day.

Arterial blood gas values were determined through samples taken from the radial artery cannula or femoral artery cannula. The highest ABL level recorded during the follow-up period in the intensive care unit was documented, and the time to this value was defined as the maximum ABL value time. A normal ABL concentration was defined as 2 mmol/L or less, and the time to reach this level was also noted. The amount of fluid given to patients was calculated as mL/kg, and the amount of fluid administered until the ABL level returned to normal was recorded. These protocols and definitions are crucial for the accurate assessment and management of critically ill patients in the postoperative period following hepatectomy.

Statistical Analysis

Statistical analysis was performed using SPSS Statistics version 20 (IBM, Armonk, NY). The normality of the study data was assessed using the Kolmogorov-Smirnov analysis. Vital signs of patients upon admission to the intensive care unit and laboratory values were reported as median (Q1)

Table 1. Characteristics of patients

Age*	58.5 (41-66)
Gender (%)	
Male	69 (%64)
Female	39 (%36)
Etiology (%)	
Metastasis	35 (%19.4)
Cholangiocarcinoma	24 (%17.4)
Adenoma/adenocarcinoma	21 (%17.4)
Hepatocellular carcinoma	19 (%11.6)
Gallbladder tumor	7 (%6.7)
Hemangioendothelioma	2 (%1.9)
Vital signs at admission*	
Heart beat/minute	106 (92-121)
Respiratory rate/minute	18 (16-20)
Oxygen saturation (%)	98 (97-100)
Systolic blood pressure (mmHg)	114 (105-122)
Diastolic blood pressure (mmHg)	68 (60-76)
Long of stay ICU*	1 (1-13)
Number of Inotropic / vasopressor support (%)	7 (%6.7)
Number of invasive mechanical ventilation support (%)	6 (%5.8)
Laboratory values at admission*	
Hemoglobin (g/dL)	12 (10.5-14,5)
Platelets (10^9/L)	224 (181-279)
INR	1.1 (1.04-1.18)
AST(U/L)	334 (203-508)
ALT(U/L)	254 (146-433)
Total bilirubin (mg/dL)	1.03 (0,56-1.76)

*Median (Q1-Q3); ALT: Alanine transaminase; AST: Aspartate aminotransferase ICU: Intensive care unit; INR: International normalised ratio.

Table 2. Patients arterial blood gas values and arterial lactate trend

	Adult*
ABG pH	7.38 (7.37-7.40)
ABG BE	-2.9{(-4.3)-(-1.5)}
A.lactate at admisson (mmol/L)	3.7 (2-4.5)
A.lactate maximum value (mmol/L)	6 (4.1-7.8)
A.lactate maximum value time (hours)	7.4(5.6-9.2)
A.lactate value under 2 time (hours)	11(7.2-14.6)

*Mean (%95 Confidence interval). ABG: Arterial blood gas; A. Lactate: Arterial blood lactate; BE: Base excess.

and third (Q3) quartiles. Arterial blood gas values and ABL trend parameters were reported as mean and 95% Confidence Interval (CI). The Pearson Correlation test was used to determine the correlation between arterial blood gas parameters, ABL trend parameters, and fluid therapy, with a significance level of $p<0.05$. These findings have implications for the management of critically ill patients in the intensive care unit.

Ethical Statement

The study was approved by the Başakşehir Çam and Sakura City Hospital's ethics committee with number 2022-389.

RESULTS

A total of 108 patients were included, all over 18 years old. Among the participants, 69 were male and 39 were female. Table 1 provides an overview of the characteristics of the patients upon admission to the intensive care unit. An analysis of blood gas values at admission and ABL trend parameters was performed, as shown in Table 2. The mean amount of fluid required to return the ABL level to normal was found to be 42.3 cc/kg (95% CI, 38.5-45.9). The study also examined the correlation between arterial blood gas parameters, ABL trend, and the amount of fluid administered, which is presented in Table 3. The results showed that only one patient died, and one patient required re-operation. The 30-day survival rate was 99%, indicating favorable outcomes for the majority of patients.

DISCUSSION

Our research aimed to scrutinize the influence of fluid therapy on the postoperative metabolic status of patients undergoing hepatectomy. We assessed various factors, including initial and peak lactate levels, lactate clearance, the presence of acidosis, and base deficit from arterial blood gas analysis, in relation to the volume of fluid administered to patients.

Table 3. Correlation arterial blood gas parametres, lactate trend and fluid

	pH	BE	Lactate at admisson	Max lactate	Max lactate time	Lactate<2 time	Fluid
pH							
r	-	0.17	0.09	0.05	0.36	0.05	0.06
p	-	0.15	0.46	0.68	0.02	0.68	0.64
BE							
r	0.17		0.31	0.39	0.01	0.32	0.04
p	0.15		0.01	<0.01	0.93	0.01	0.73
Lactate at admisson							
r	0.09	0.31		0.68	0.15	0.5	0.11
p	0.46	0.01		<0.01	0.34	<0.01	0.41
Max lactate							
r	0.05	0.39	0.68		0.16	0.65	0.38
p	0.68	<0.01	<0.01		0.32	<0.01	<0.01
Max lactate time							
r	0.36	0.01	0.15	0.16		0.18	0.19
p	0.02	0.93	0.34	0.32		0.31	0.29
Lactate<2 time							
r	0.05	0.32	0.50	0.65	0.18		0.484
p	0.68	0.01	0<.01	<0.01	0.31		<0.01
Fluid							
r	0.06	0.04	0.11	0.385	0.19	0.48	
p	0.68	0,73	0.41	<0.01	0.29	<0.01	

p: p value (significant the 0.05); r: Pearson correlation; BE: ABG base excess at admission; Fluid: Amount of fluid given on the first day (ml/kg); Lactate<2 time: Time until arterial lactate value<2 mmol/L; Lactate at admisson: Arterial lactate at admission; Max lactate: Maximum value of arterial lactate; Max lactate time: Time until maximum value of arterial lactate; pH: ABG pH at admission.

Our findings indicated that arterial lactate levels exhibited an uptrend post-hepatectomy, with a significant correlation between the ABL values and the volume of fluid intake. The surge in lactate levels could be attributed to tissue hypoperfusion, diminished activity of the pyruvate dehydrogenase enzyme, and reduced lactate clearance owing to hepatic dysfunction.[9] Although there are no direct studies in the existing literature drawing a correlation between increased lactate levels post-hepatectomy and fluid therapy, we propose that this correlation may indicate a sepsis-like metabolic state following hepatectomy. Tissue hypoperfusion can potentially occur during hepatectomy, contributing to lactate elevation, similar to sepsis.[10,11] Increased levels of proinflammatory cytokines have been noted post-hepatectomy, akin to sepsis.[12-14] Another commonality between hepatectomy and sepsis is the perception of low lactate clearance as an unfavorable prognostic marker.[10-15] Thus, we surmise that patients with elevated lactate levels post-hepatectomy are possibly in a sepsis-like state, necessitating higher volumes of fluid therapy.

Remarkably, we observed that the elevation in lactate levels persisted for an additional 7.4 hours in patients, and a return to normal levels was evident after approximately 11 hours. These insights underscore the necessity for vigilant monitoring of patients post-hepatectomy as the metabolic stress process persists in the postoperative period. Timely detection and management of potential complications are thereby crucial.

Our study stands as one of the pioneering pieces of research elucidating the relationship between fluid therapy and arterial lactate levels following liver surgery. Moreover, it demonstrates the trend of ABL levels post-hepatectomy. However, certain limitations warrant mention. Primarily, the retrospective nature of the study and the reliance on data from medical records can potentially influence the outcomes. Additionally, the absence of data on intraoperative variables and the long-term follow-up of patients in a surgical ward, as opposed to an intensive care unit, constitute other notable limitations.

Conclusion

This research investigated the trend of ABL levels in patients following hepatectomy and their relationship with administered fluid therapy. The findings indicate a significant correlation between ABL levels and the volume of fluid administered to patients. Our study reveals that elevated lactate levels may indicate a sepsis-like metabolic state arising post-hepatectomy and an associated increase in the need for fluid therapy. These results emphasize that close monitoring of ABL levels after hepatectomy can be a critical indicator for effectively determining patients' fluid therapy requirements and monitoring duration. Therefore, regular tracking of arterial blood lactate levels can be important in managing and monitoring patients in the postoperative period.

Ethics Committee Approval

This study approved by the Çam ve Sakura City Hospital's Ethics Committee (Date: 14.12.2022, Decision No: 2022.12.389).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: M.Ç.; Design: M.Ç.; Supervision: M.Ç.; Fundings: M.Ç.; Materials: İ.O.; Data: İ.O.; Analysis: M.Ç.; Literature search: İ.O.; Writing: M.Ç.; Critical revision: M.Ç.

Conflict of Interest

None declared.

REFERENCES

1. Tsim NC, Frampton AE, Habib NA, Jiao LR. Surgical treatment for liver cancer. World J Gastroenterol 2010;16:927–33. [CrossRef]
2. Connolly C, Stättner S, Niederwieser T, Primavesi F. Systematic review on peri-operative lactate measurements to predict outcomes in patients undergoing liver resection. J Hepatobiliary Pancreat Sci 2020;27:359–70. [CrossRef]
3. de Boer MT, Molenaar IQ, Porte RJ. Impact of blood loss on outcome after liver resection. Dig Surg 2007;24:259–64. [CrossRef]
4. van Genderen ME, Paauwe J, de Jonge J, van der Valk RJ, Lima A, Bakker J, et al. Clinical assessment of peripheral perfusion to predict postoperative complications after major abdominal surgery early: A prospective observational study in adults. Crit Care 2014;18:R114. [CrossRef]
5. Watanabe I, Mayumi T, Arishima T, Takahashi H, Shikano T, Nakao A, et al. Hyperlactemia can predict the prognosis of liver resection. Shock 2007;28:35–8. [CrossRef]
6. Meregalli A, Oliveira RP, Friedman G. Occult hypoperfusion is associated with increased mortality in hemodynamically stable, high-risk, surgical patients. Crit Care 2004;8:R60–5. [CrossRef]
7. Correa-Gallego C, Tan KS, Arslan-Carlon V, Gonen M, Denis SC, Langdon-Embry L, et al. Goal-directed fluid therapy using stroke volume variation for resuscitation after low central venous pressure-assisted liver resection: A randomized clinical trial. J Am Coll Surg 2015;221:591–601. [CrossRef]
8. Melloul E, Hübner M, Scott M, Snowden C, Prentis J, Dejong CH, et al. Guidelines for perioperative care for liver surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations. World J Surg 2016;40:2425–40. [CrossRef]
9. Arnold RC, Shapiro NI, Jones AE, Schorr C, Pope J, Casner E, et al; Emergency Medicine Shock Research Network (EMShockNet) Investigators. Multicenter study of early lactate clearance as a determinant of survival in patients with presumed sepsis. Shock 2009;32:35–9. [CrossRef]
10. Lemke M, Karanicolas PJ, Habashi R, Behman R, Coburn NG, Hanna SS, et al. Elevated lactate is independently associated with adverse outcomes following hepatectomy. World J Surg 2017;41:3180–8. [CrossRef]
11. Casserly B, Phillips GS, Schorr C, Dellinger RP, Townsend SR, Osborn TM, et al. Lactate measurements in sepsis-induced tissue hypoperfusion: Results from the Surviving Sepsis Campaign database. Crit Care Med 2015;43:567–73. [CrossRef]
12. Murtha-Lemekhova A, Fuchs J, Ghamarnejad O, Nikdad M, Probst P, Hoffmann K. Influence of cytokines, circulating markers and growth factors on liver regeneration and post-hepatectomy liver fail-

ure: A systematic review and meta-analysis. Sci Rep 2021;11:13739. [CrossRef]

13. Sasturkar SV, David P, Sharma S, Sarin SK, Trehanpati N, Pamecha V. Serial changes of cytokines and growth factors in peripheral circulation after right lobe donor hepatectomy. Liver Transpl 2016;22:344–51. [CrossRef]
14. Blackwell TS, Christman JW. Sepsis and cytokines: Current status. Br J Anaesth 1996;77:110–7. [CrossRef]
15. Sandal ÖS, Ceylan G, Sarı F, Atakul G, Çolak M, Topal S, et al. Could lactate clearance be a marker of mortality in pediatric intensive care unit? Turk J Med Sci 2022;52:1771–8. [CrossRef]

Hepatektomi Sonrası Laktat Seviyesi ile Sıvı Yönetimi Arasındaki İlişki

Amaç: Hepatektomi gibi cerrahi işlemlerin ardından başarılı sonuçlar elde edebilmek için çeşitli fizyolojik ölçümlerin dikkatlice izlenmesi gerekmektedir. Bu ölçümler arasında, doku perfüzyonu ve oksijenasyonunun önemli bir göstergesi olan laktat seviyeleri de yer almaktadır. Özellikle postoperatif dönemde, arteriyel kan laktat (ABL) düzeyleri, doku perfüzyonunun izlenmesi açısından öenmli bir yere sahiptir. Optimal bir sıvı dengesinin korunması ise, doku perfüzyonunun sürdürülmesi ve potansiyel komplikasyonların önlenmesi için kritik öneme sahiptir. Bu çalışmanın amacı, postoperatif dönemde hastaların ABL düzeyleri ile sıvı tedavisi arasındaki ilişkiyi incelemektir.

Gereç ve Yöntem: Bu çalışma, hepatektomi sonrası yoğun bakım ünitesinde tedavi gören hastaların sonuçlarını incelemek için retrospektif bir çalışma olarak tasarlandı. Sıvı tedavisinin hastaların klinik sonuçları üzerindeki etkisini değerlendirmek için hastaların aldığı sıvı miktarları hesaplandı. Başlangıç arteriyel kan laktat seviyeleri, en yüksek laktat seviyeleri, laktatın vücuttan atılma hızı, asidoz durumu ve arteriyel kan gazı analizlerindeki baz açığı değerleri kaydedildi. Arteriyel kan gazı parametreleri, ABL trend parametreleri ve sıvı tedavisi arasındaki ilişkiyi belirlemek için Pearson Korelasyon Testi kullanıldı ve $p<0.05$ anlamlı olarak olarak kabul edildi.

Bulgular: Bu çalışmada, hepatektomi operasyonu geçirmiş toplam 108 hasta incelenmiştir. Hastaların ABL seviyelerini normal aralığa düşene kadar ortalama olarak 42.3cc/kg sıvı verilmiştir. Ayrıca, izlem süresince gözlemlenen en yüksek ABL değerleri ile verilen toplam sıvı miktarı arasında anlamlı bir korelasyon saptanmıştır (r: 0.385, $p<0.01$).

Sonuç: Çalışmada, ABL düzeyleri ve sıvı alımı arasında bir ilişki olduğunu tespit edilmiştir. Yüksek laktat seviyelerinin, sepsis benzeri bir durumu ve yoğun sıvı tedavisi gerektiren bir metabolik durumu işaret ettiği düşünülmektedir. Bu sonuçlar, hepatektomi geçiren hastalarda ABL seviyelerinin takibinin, sıvı tedavisi ihtiyacını ve hastanın yakın izlem süresini tahmin etmede kullanılabilecek önemli bir araç olduğuna işaret etmektedir. Arteriyel kan laktat takibi, hastaların postoperatif dönemdeki yönetimi ve takibinde kritik bir rol oynayabilir.

Anahtar Sözcükler: Hepatektomi; laktat; postoperatif yönetim; sıvı tedavisi.

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Original Article

Relationship Between Serum Adiponectin and Kisspeptin Levels and Insulin Resistance in Patients With Pcos

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Keywords: Adiponectin; insulin resistance; kisspeptin; PCOS; polycystic ovarian syndrome.

ABSTRACT

Objective: In this study, it is aimed to investigate the relationship between serum adiponectin and kisspeptin levels and insulin resistance in patients with PCOS.

Methods: 144 patients diagnosed with PCOS in a tertiary center, were included in the study. At the first visit, the height and weight measurements were recorded and menstrual functions were questioned. After ultrasonographic evaluation and hormonal assessment, patients were divided into groups according to insulin resistance (IR), then were compared in terms of hormonal parameters.

Results: Weight and BMI were significantly higher in the insulin-resistant group (p=0.018, p=0.012). Mean fasting glucose, fasting insulin levels and HOMA indexes of the insulin-resistant group were significantly higher than the non-resistant group, respectively (p<0.001). LH/FSH ratios were significantly lower in the IR+ group (1.33 vs 1.58, p<0.05). No significant difference was observed between the groups in terms of adiponectin and kisspeptin levels, but the mean kisspeptin level in the IR- group was higher than the IR+ group (32.72 vs 19.36, p=0.067). Adiponectin and kisspeptin were both found to have a very weak positive relationship with FSH (r=0.169 and 0.171).

Conclusion: Adiponectin is known to decrease in obesity and type 2 diabetes, but does not show the difference in insulin-resistant PCOS patients. Kisspeptin, which is a hypothalamic peptide and associated with increased LH levels in patients with PCOS, was found to be lower in the IR+ group. In order to clarify the role of kisspeptin and adiponectin in the mechanisms of PCOS and insulin resistance, it is needed to be examined in a larger sample with BMI-matched healthy controls.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a prevalent metabolic and endocrine condition that affects 5–22% of reproductive-age women and is known for its features of chronic anovulation, hyperandrogenism, and ovaries with multiple cysts.[1,2] The cause of PCOS has not been fully understood, however, factors such as disruptions in ovarian steroid production and gonadotropin secretion, genetic predisposition, as well as hyperinsulinemia/insulin resistance (IR) are mechanisms that focused on.[3]

Kisspeptin, a peptide produced in the hypothalamus that is important in regulating the Hypothalamic–Pituitary–Gonadal axis,[4] is been reported to increase luteinizing hormone (LH) levels by more than double, with only a minor or no change in follicle-stimulating hormone (FSH) levels after intravenous administration.[5,6] In addition, it has been suggested that the effects of the kisspeptin molecule on the gonadal axis may be the cause of hyperandrogenism, reproductive and metabolic changes in PCOS.[7,8] It has been shown that kisspeptin-10 administered to rats had increased insulin levels in a dose-dependent manner.[9]

Adiponectin, first described in the mid-1990s,[10] has a crucial role in regulating the sensitivity of insulin and has been

Table 1. Demographic characteristics comparisons between the groups

	IR[+] Group n=69 Mean±SD	IR[-] Group n=75 Mean±SD	p-value
Age	28.35±3.95	28.16±4.28	0.785
Weight (kg)	72.68±12.88	67.24±14.28	0.018*
Height (m)	162.67±5.68	162.16±6.39	0.617
BMI (kg/m²)	27.45±4.53	25.49±4.68	0.012*

*: p<0.05; t-test; SD: Standard Deviation; BMI: Body Mass Index; IR[+]: Insulin Resistant; IR[-]: Non-insulin Resistant.

Table 2. Comparison of fasting glucose and fasting insulin levels and HOMA indices between the groups

	IR[+] Group n=69 Mean±SD	IR[-] Group n=75 Mean±SD	p-value
Fasting Glucose (mg/dL)[2]	95.33±16.30	87.04±6.22	0.000*
Fasting Insulin (mIU/mL)[1]	17.08±7.06	6.93±1.85	0.000*
HOMA index[2]	4.04±2.27	1.47±0.38	0.000*

*p<0.001; 1:t test; 2: Mann–Whitney U test; SD: Standard Deviation; IR[+]: Insulin Resistant; IR[-]: Non-insulin Resistant.

shown to have protective effects against type 2 diabetes.[11,12] It has also been suggested that adiponectin may have an effect on the metabolic background of PCOS and was found to be low in PCOS patients with high insulin levels.[13,14] In the study, it was determined that adiponectin level was negatively correlated with fasting insulin, HOMA model sensitivity, BMI, and testosterone, but not with LH/FSH ratio in patients both with and without PCOS.[15]

The purpose of this study is to look into the association between serum adiponectin and kisspeptin levels and IR in PCOS patients.

MATERIALS AND METHODS

This study included 144 patients with PCOS at the ages of 18 and 40 years, who applied to the infertility polyclinic of Zeynep Kamil Women and Children Disease Training and Research Hospital between January 2019 and 2022. At the first visit, the height and weight measurements of the patients were recorded, and body mass indices (BMI) were calculated. Ultrasonographic assessments were done by the transvaginal probe and patients were questioned in terms of menstrual functions. Patients with polycystic ovaries are instructed to give blood test to evaluate fasting glucose, fasting insulin, adiponectin, kisspeptin, FSH, estradiol (E2), LH, thyroid-stimulating hormone (TSH), free thyroxine (FT4), and prolactin (PRL) levels on the 2nd and 4th days of menstruation.

IR was used to divide the patients into two groups. HOMA index was calculated for each patient according to [Fasting glucose (mg/dL) X Fasting insulin (mIU/mL) X 0,055]/22,5 formula, the value <2.1 were considered to have no IR[-], and those with a HOMA index value equal to or >2.1 were considered to have IR[+]. Serum adiponectin and kisspeptin levels were compared with patients with and without IR and it was also examined whether there was a significant difference in terms of age, BMI, HOMA indices, FSH, LH, LH/FSH, E2, TSH, FT4, and PRL levels.

Statistical Analysis

The data analysis was done using the IBM SPSS program. Since the data were analyzed in two groups' patients with and without IR, the t-test, which is one of the parametric analyses, was used to compare the data with normal distribution, and the Mann–Whitney test, which is one of the non-parametric analyses, was used to compare the data that did not comply with the normal distribution.

RESULTS

There was not a significant difference in the groups' average ages and heights(p>0.05). Weight and BMI of the insulin-resistant group were significantly higher than those of the non-insulin-resistant patients (72.68±12.88 vs. 67.24±14.28 and 27.45±4.53 vs. 25.49±4.68, respectively) (p<0.05) (Table 1).

On account of higher mean fasting glucose (95.33±16.30) and fasting insulin (17.08±7.06) levels of the insulin-resistant group, HOMA indices were significantly higher in them than those in the non-resistant group (4.04±2.27 vs. 1.47±0.38) (p<0.001) (Table 2).

Early follicular phase assessments of FSH, LH, E2, TSH, and PRL levels of the groups were similar (p>0.05). LH/FSH ratios were lower (1.33±0.58 vs. 1.58±0.83) and free T4 values were higher (1.22±0.19 vs. 1.14±0.17) in

Table 3. Hormone parameter comparisons between the groups

	IR[+] Group n=69 Mean±SD	IR[-] Group n=75 Mean±SD	p-value
FSH (mIU/mL)[1]	5.69±1.71	5.77±1.81	0.785
LH (mIU/mL)[1]	7.39±3.55	8.68±4.37	0.055
LH/FSH[1]	1.33±0.58	1.58±0.83	0.043*
E2[2]	41.79±14.47	45.16±21.21	0.555
TSH[1]	2.46±1.14	2.42±1.29	0.846
FT4[1]	1.22±0.19	1.14±0.17	0.010*
PRL[2]	18.02±8.34	17.85±9.30	0.517

*: p<0.05; 1:t.test; 2:Mann–Whitney U test; SD: Standard Deviation; FSH: Follicle-stimulating Hormone; LH: Luteinizing Hormone; E2: Estradiol Hormone; TSH: Thyroid-stimulating Hormone; FT4: Free Thyroxine Hormone; PRL: Prolactin Hormone.

Table 4. Serum adiponectin and kisspeptin levels comparisons between the groups

	IR[+] Group n=69 Mean±SD	IR[-] Group n=75 Mean±SD	p-value
Adiponectin (mg/dL) 1	9.53±7.25	8.93±8.20	0.646
Kisspeptin (mIU/mL) 1	19.36±29.80	32.72±52.92	0.067

1: t-test; SD: Standard Deviation.

Table 5. Correlation analysis of serum adiponectin and kisspeptin levels with other hormones

	Weight	BMI	Fasting Insulin	Fasting Glucose	HOMA	FSH	LH	LH/FSH	E2	TSH	PRL
Adiponectin											
r	−0.058	−0.009	0.072	0.001	0.063	0.169	0.016	−0.109	−0.032	−0.045	−0.068
p	0.492	0.919	0.393	0.993	0.456	0.042*	0.848	0.194	0.701	0.590	0.416
n	144	144	144	144	144	144	144	144	144	144	144
Kisspeptin											
r	−0.067	−0.078	−0.022	−0.007	−0.007	0.171	−0.017	−0.064	−0.018	−0.132	−0.089
p	0.423	0.353	0.795	0.933	0.937	0.040*	0.841	0.443	0.834	0.115	0.290
n	144	144	144	144	144	144	144	144	144	144	144

*: p<0.05; r: Pearson Correlation; For r<0.20=weak correlation; FSH: Follicle-stimulating Hormone; LH: Luteinizing Hormone; E2: Estradiol Hormone; TSH: Thyroid-stimulating Hormone; PRL: Prolactin Hormone.

the insulin-resistant group compared to the IR[-] group, (p<0.05) (Table 3).

As presented in Table 4, no significant difference was observed between the groups in terms of serum adiponectin levels (IR[+]: 9.53±7.25 vs. IR[-]: 8.93±8.20). Although it was not significant, serum kisspeptin levels in the insulin-resistant group were found to be quite lower than in the other group (IR[+]:19.36±29.80 vs. IR[−]: 32.72±52.92) (p>0.05).

When correlation analyses were done for serum adiponectin and kisspeptin levels and other hormones; adiponectin was found to be positively correlated with FSH, very weakly (p=0.042, Table 5 and Figure 1a). Similarly, kisspeptin was found to have a very weak positive correlation with FSH (0.171, p=0.040, Table 5 and Figure 1b). Adiponectin or kisspeptin had no significant relationship with weight, BMI, fasting insulin, fasting glucose, HOMA index, and other hormones (Table 5).

DISCUSSION

There is broad agreement that the majority of women with PCOS is insulin resistant and have a higher incidence of obesity.[16,17] In line with the literature, our data revealed that weight and BMI were significantly higher in the group with IR than in age-matched PCOS patients who had normal glucose tolerance. In the studies, it was declared that obesity and IR resulted from decreased insulin-mediated glucose disposal (IMGD).[18] Dunaif et al.[19] showed in

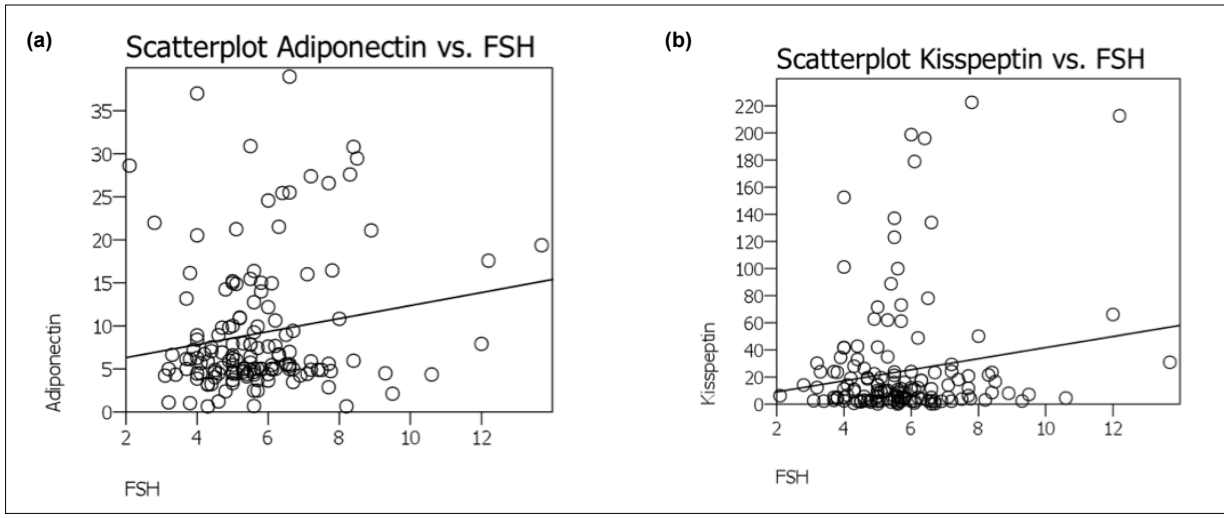

Figure 1. (a) Scatterplots for adiponectin vs FSH. **(b)** Scatterplots for kisspeptin vs. FSH.

1989 that IMGD was significantly decreased in 35–40% of women with PCOS than control women of comparable BMI. Thus, IR seems to be increased in PCOS independently from BMI.

The studies which investigated the relationship between body fat topography and insulin sensitivity suggested that the increase in upper body obesity is associated with IR in PCOS.[20,21] Since then, indirect evaluation of adipose tissue like the measurement of adipokines had come to the fore. Adiponectin is an adipokine that is expressed and secreted by adipocytes and presented to play an important role in the pathogenesis of obesity, IR, and type 2 diabetes mellitus.[14,15,22] It has been shown that obese subjects expressed lower levels of adiponectin; however, the relationship between hypoadiponectinemia and IR was stronger than that of obesity.[23]

In the study of Sepilian and Nagamani adiponectin level had been reported to be negatively correlated with BMI in the control group where there was no correlation between BMI and adiponectin in the patients with PCOS. They have presented IR as a main determinant of hypoadiponectinemia and not adiposity in patients with PCOS.[14] In another case-control study conducted by Spranger et al.[15] in 2005, plasma levels of adiponectin were linked to BMI, HOMA index, and fasting insulin in both PCOS women and healthy controls. It was revealed by multiple regression analysis that circulating adiponectin concentrations were independently correlated with the level of obesity and IR. Despite these findings, we observed that adiponectin levels were similar in PCOS patients with and without IR, and there was no relationship between IR and adiponectin levels (9.53 vs. 8.93 mg/dL, p=0.646).

Studies investigating the relationship between serum adiponectin and the hormonal axis have reported opposing results. Spranger et al.[15] have declared an increased LH/FSH ratio in patients with PCOS with no correlation with the adiponectin levels (r=−0.05, p=0.7). Two studies reported a positive correlation between adiponectin and LH and LH/FSH ratio and put forward the hypothesis of LH and gonadotropin-releasing hormone (GnRH) secretion were inhibited by adiponectin.[24,25] In our study, while the FSH and LH levels of the groups did not differ, the LH/FSH ratios were significantly higher in the group without IR (1.58 vs. 1.33, p=0.043), but there was no correlation with the adiponectin levels (r=0.016, p=0.848).

In a recent study by Artimani et al.,[26] a positive correlation between the expressions of adiponectin and FSH was found at a strong (r=0.84) and significant (p=0.001) level. Similarly, in our study, adiponectin was found to have a positive and significant relationship with FSH, but this relationship was very weak (r=0.169). In addition, we have noticed a positive correlation between kisspeptin and FSH, similarly (r=0.171, p=0.040). Contrarily, Gorkem et al.[27] reported a negative relationship between kisspeptin and FSH, while another study found no significant relationship between these two in patients with PCOS.[28]

According to our data, in the group without IR, the mean LH levels were higher than that of the patients with IR (8.68 vs. 7.39 IU, p=0.055), and although not significant, it was observed that the mean kisspeptin level in the IR-negative group was approximately 69% (32.72 vs. 19.36 mIU/mL, p=0.067) higher than IR+ group. In addition, we have found no correlation between LH and LH/FSH ratio with kisspeptin levels (r=0.017, r=−0.064).

Previous studies in the literature reported that an increase in kisspeptin significantly increases LH levels, thus more than twice the LH/FSH ratio, with little or no change in FSH levels.[6,29] While several investigators have noticed a positive correlation between kisspeptin and LH levels, they have failed to find significantly higher kisspeptin levels in patients with PCOS compared with non-PCOS women,[30] Daghestani et al.[28] found a negative significant relationship between these two in obese PCOS patients. Therefore, the association between kisspeptin and LH secretion in PCOS patients is unclear due to the varied constitution of participants in various research.[30]

Strengths and Limitations

The short sample size and lack of healthy controls are the study's principal limitations. If the groups were chosen by randomization and the control group was added, the study power would increase, and more significant differences would be produced. On the other hand, this is thought to be the first prospective study to look into the relationship between kisspeptin and adiponectin and IR and PCOS.

Conclusion

In this study, it was concluded that adiponectin levels, which are known to decrease in obesity and type 2 diabetes, do not show a difference in insulin-resistant PCOS patients compared to those without IR. Kisspeptin, which is a hypothalamic peptide and associated with increased LH levels in patients with polycystic ovarian syndrome, was not significantly affected by insulin levels, but kisspeptin levels in the insulin-resistant group were lower than the IR-group. To clarify the role of kisspeptin and adiponectin in the mechanisms of PCOS and IR, it is needed to be examined in a larger sample with BMI-matched healthy controls.

Ethics Committee Approval

This study approved by the Zeynep Kamil Women and Children's Disease Training and Research Hospital Ethics Committee (Date: 29.04.2020, Decision No: 63).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: M.B.Y., S.Ş., B.D.; Design: M.B.Y., S.Ş., B.D.; Supervision: M.B.Y., S.Ş., B.D.; Fundings: M.N.C.K., Z.C., B.N.O.; Materials: M.N.C.K., Z.C., B.N.O.; Data: M.B.Y., M.N.C.K., Z.C., B.N.O.; Analysis: S.Ş., M.B.Y., B.N.O., E.M.G., E.K.; Literature search: M.B.Y., S.Ş., B.D., M.N.C.K., Z.C., B.N.O., E.M.G., E.K.; Writing: M.B.Y., S.Ş., B.D., M.N.C.K.; Critical revision: M.B.Y., S.Ş., B.D., M.N.C.K., Z.C., B.N.O., E.M.G., E.K.

Conflict of Interest

None declared.

REFERENCES

1. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril 2004;81(1):19–25. [CrossRef]
2. Tsilchorozidou T, Overton C, Conway GS. The pathophysiology of polycystic ovary syndrome. Clin Endocrinol 2004;60(1):1–17. [CrossRef]
3. Barbieri RL, Smith S, Ryan KJ. The role of hyperinsulinemia in the pathogenesis of ovarian hyperandrogenism. Fertil Steril 1988;50(2):197–212. [CrossRef]
4. Ohtaki T, Shintani Y, Honda S, Matsumoto H, Hori A, Kanehashi K, et al. Metastasis suppressor gene KiSS-1 encodes peptide ligand of a G-protein-coupled receptor. Nature 2001;411(6837):613–7. [CrossRef]
5. Xie C, Jonak CR, Kauffman AS, Coss D. Gonadotropin and kisspeptin gene expression, but not GnRH, are impaired in cFOS deficient mice. Mol Cell Endocrinol 2015;411:223–31. [CrossRef]
6. Dhillo WS, Chaudhri OB, Patterson M, Thompson EL, Murphy KG, Badman MK, et al. Kisspeptin-54 stimulates the hypothalamic-pituitary gonadal axis in human males. J Clin Endocrinol Metab 2005;90(12):6609–15. [CrossRef]
7. Panidis D, Rousso D, Koliakos G, Kourtis A, Katsikis I, Farmakiotis D, et al. Plasma metastin levels are negatively correlated with insulin resistance and free androgens in women with polycystic ovary syndrome. Fertil Steril 2006;85(6):1778–83. [CrossRef]
8. Jeon YE, Lee KE, Jung JA, Yim SY, Kim H, Seo SK, et al. Kisspeptin, leptin, and retinol-binding protein 4 in women with polycystic ovary syndrome. Gynecol Obstet Invest 2013;75(4):268–74. [CrossRef]
9. Matsui H, Takatsu Y, Kumano S, Matsumoto H, Ohtaki T. Peripheral administration of metastin induces marked gonadotropin release and ovulation in the rat. Biochem Biophys Res Commun 2004;320(2):383–8. [CrossRef]
10. Hu E, Liang P, Spiegelman BM. AdipoQ Is a novel Adipose-specific gene dysregulated in obesity. J Biol Chem. 1996;271(18):10697–703. [CrossRef]
11. Takahashi M, Arita Y, Yamagata K, Matsukawa Y, Okutomi K, Horie M, et al. Genomic structure and mutations in adipose-specific gene, adiponectin. Int J Obes Relat Metab Disord 2000;24(7):861–8. [CrossRef]
12. Lindsay RS, Funahashi T, Hanson RL, Matsuzawa Y, Tanaka S, Tataranni PA, et al. Adiponectin and development of type 2 diabetes in the Pima Indian population. Lancet 2002;360(9326):57–8. [CrossRef]
13. Lillioja S, Nyomba BL, Saad MF, Ferraro R, Castillo C, Bennett PH, et al. Exaggerated early insulin release and insulin resistance in a diabetes-prone population: A metabolic comparison of Pima Indians and Caucasians. J Clin Endocrinol Metab 1991;73(4):866–76. [CrossRef]
14. Sepilian V, Nagamani M. Adiponectin levels in women with polycystic ovary syndrome and severe insulin resistance. J Soc Gynecol Investig 2005;12(2):129–34. [CrossRef]
15. Spranger J, Möhlig M, Wegewitz U, Ristow M, Pfeiffer AF, Schill T, et al. Adiponectin is independently associated with insulin sensitivity in women with polycystic ovary syndrome. Clin Endocrinol 2004;61(6):738–46. [CrossRef]
16. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: The complete task force report. Fertil Steril 2009;91(2):456–88. [CrossRef]
17. Yildiz BO, Knochenhauer ES, Azziz R. Impact of obesity on the risk for polycystic ovary syndrome. J Clin Endocrinol Metab 2008;93(1):162–8. [CrossRef]
18. Diamanti-Kandarakis E, Dunaif A. Insulin resistance and the polycystic ovary syndrome revisited: An update on mechanisms and implications. Endocr Rev 2012;33(6):981–1030. [CrossRef]
19. Dunaif A, Segal KR, Futterweit W, Dobrjansky A. Profound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome. Diabetes 1989;38(9):1165–74. [CrossRef]
20. Pasquali R, Vicennati V. The abdominal obesity phenotype and insulin resistance are associated with abnormalities of the hypothalamic-pituitary-adrenal axis in humans. Horm Metab Res 2000;32(11):521–5. [CrossRef]
21. Mannerås-Holm L, Leonhardt H, Kullberg J, Jennische E, Odén A, Holm G, et al. Adipose tissue has aberrant morphology and function

in PCOS: Enlarged adipocytes and low serum adiponectin, but not circulating sex steroids, are strongly associated with insulin resistance. J Clin Endocrinol Metab 2011;96(2):e304–11. [CrossRef]

22. Berg AH, Combs TP, Scherer PE. ACRP30/adiponectin: An adipokine regulating glucose and lipid metabolism. Trends Endocrinol Metab 2002;13(2):84–9. [CrossRef]
23. Kern PA, Di Gregorio GB, Lu T, Rassouli N, Ranganathan G. Adiponectin expression from human adipose tissue: Relation to obesity, insulin resistance, and tumor necrosis factor-alpha expression. Diabetes 2003;52(7):1779–85. [CrossRef]
24. Atanasova Boshku A, Ivanova Panova D, Zafirova Ivanovska B. Adiponectin as a serum marker of adipose tissue dysfunction in women with polycystic ovary syndrome: Correlation with indicators of metabolic disturbances. Acta Endocrinol Buchar 2018;14(3):346–52. [CrossRef]
25. Olszanecka-Glinianowicz M, Kuglin D, Dąbkowska-Huć A, Skałba P. Serum adiponectin and resistin in relation to insulin resistance and markers of hyperandrogenism in lean and obese women with polycystic ovary syndrome. Eur J Obstet Gynecol Reprod Biol 2011;154(1):51–6. [CrossRef]
26. Artimani T, Saidijam M, Aflatoonian R, Ashrafi M, Amiri I, Yavangi M, et al. Downregulation of adiponectin system in granulosa cells and low levels of HMW adiponectin in PCOS. J Assist Reprod Genet 2016;33(1):101–10. [CrossRef]
27. Gorkem U, Togrul C, Arslan E, Oruç A, Büyükkayacı Duman N. Is there a role for kisspeptin in pathogenesis of polycystic ovary syndrome? Gynecol Endocrinol 2017;34:1–4. [CrossRef]
28. Daghestani MH, Daghestani MH, Warsy A, El-Ansary A, Omair MA, Omair MA, et al. Adverse effects of selected markers on the metabolic and endocrine profiles of obese women with and without PCOS. Front Endocrinol Lausanne 2021;12:665446. [CrossRef]
29. Jayasena CN, Abbara A, Veldhuis JD, Comninos AN, Ratnasabapathy R, De Silva A, et al. Increasing LH pulsatility in women with hypothalamic amenorrhoea using intravenous infusion of Kisspeptin-54. J Clin Endocrinol Metab 2014;99(6):e953–61. [CrossRef]
30. Emekci Ozay O, Ozay AC, Acar B, Cagliyan E, Seçil M, Küme T. Role of kisspeptin in polycystic ovary syndrome (PCOS). Gynecol Endocrinol 2016;32(9):718–22. [CrossRef]

PKOS'lu Hastalarda Serum Adiponektin ve Kisspeptin Düzeyleri ile İnsülin Direnci Arasındaki İlişki

Amaç: Bu çalışmada PKOS'lu hastalarda serum adiponektin ve kisspeptin düzeyleri ile insülin direnci arasındaki ilişkinin araştırılması amaçlanmıştır.

Gereç ve Yöntem: Üçüncü basamak bir merkezde PKOS tanısı alan 144 hasta çalışmaya dahil edildi. İlk ziyarette boy ve kilo ölçümleri kaydedildi ve adet fonksiyonları sorgulandı. Ultrasonografik değerlendirme ve hormonal değerlendirme sonrasında hastalar insülin direncine (IR) göre gruplara ayrılarak hormonal parametreler açısından karşılaştırıldı.

Bulgular: Ağırlık ve VKİ insülin dirençli grupta anlamlı olarak yüksekti (p=0.018, p=0.012). İnsüline dirençli grubun ortalama açlık glukozu, açlık insülin düzeyi ve HOMA indeksi sırasıyla dirençli olmayan gruba göre anlamlı olarak yüksekti (p<0.001). LH/FSH oranları IR+ grupta anlamlı derecede düşüktü (1.33'e karşı 1.58, p<0.05). Adiponektin ve kisspeptin düzeyleri açısından gruplar arasında anlamlı bir fark gözlenmedi, ancak IR- grubundaki ortalama kisspeptin düzeyi IR+ grubuna göre daha yüksekti (32.72'ye karşı 19.36, p=0.067). Adiponektin ve kisspeptinin FSH ile çok zayıf bir pozitif ilişkisi olduğu bulundu (r=0.169 ve 0.171).

Sonuç: Adiponektinin obezite ve tip 2 diyabette azaldığı bilinmekte olup, insülin direnci olan PKOS hastalarında farklılık göstermemektedir. Hipotalamik bir peptit olan ve PKOS'lu hastalarda artmış LH seviyeleri ile ilişkili olan Kisspeptin, IR+ grubunda daha düşük bulundu. Kisspeptin ve adiponektinin PKOS ve insülin direnci mekanizmalarındaki rolünü netleştirmek için BMI eşleşmiş sağlıklı kontrollerle daha geniş bir örneklemde incelenmesine ihtiyaç vardır.

Anahtar Sözcükler: Adiponektin; insülin direnci; kisspeptin; PKOS; polikistik over sendromu.

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Original Article

The Relationship Between Microalbuminuria and Serum Uric Acid Levels in Patients With Type 2 Diabetes Mellitus

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Keywords: Albuminuria; diabetic nephropathy; proteinuria; type 2 diabetes mellitus; uric acid.

ABSTRACT

Objective: Increasing evidence suggests that oxidants from uric acid synthesis may cause renal dysfunction and cardiovascular diseases by inducing inflammation and endothelial dysfunction. Variations in the correlations between inflammation and albuminuria due to race and ethnicity have been noted in diabetic patients. However, studies on this topic among Turkish patients with type 2 diabetes remain limited. This study aimed to investigate the relationship between serum uric acid levels and microalbuminuria in patients with type 2 DM.

Methods: This prospective cross-sectional study included 80 patients with T2DM, divided into two groups: 40 with microalbuminuria (30–300 mg in 24-hour urine proteinuria) and 40 without (<30 mg in 24-hour urine proteinuria). Biochemical parameters were assessed through the analysis of venous blood samples, which were collected following a 12-hour fasting period during outpatient evaluations.

Results: The study population had a mean age of 57.8±11.6 years. The mean uric acid levels (4.7±1.5 vs. 4.0±1.1, P=0.036) and the mean creatinine clearance (114.6±5.8 vs. 98.1±3.4, P=0.050) were higher in the group with microalbuminuria compared to the group without. The 24-hour urinary protein levels were positively correlated with HbA1C (r=0.305, P=0.036), uric acid (r=0.308, P=0.032), and creatinine clearance (r=0.294, P=0.050).

Conclusion: Individuals with T2DM and microalbuminuria tend to display elevated levels of uric acid. Considering the potential effects of increased uric acid levels on diabetic nephropathy, end-stage renal disease, and the development of cardiovascular disease, routine monitoring of uric acid levels in T2DM patients may be important from a prognostic perspective.

INTRODUCTION

Diabetes mellitus (DM), a major health concern, is projected to impact 578 million individuals worldwide by 2030 and escalate to 700 million by 2045.[1] Diabetes is a significant metabolic disease known for causing macrovascular complications such as cardiovascular disease (CVD) and atherosclerosis, as well as microvascular complications such as nephropathy.[2] These complications are well-established factors for the increased risk of mortality in patients with type-2 DM (T2DM).[3,4] Therefore, studies concerning the pathogenesis of diabetes and its complications are gaining increased importance.

Uric acid, a product of purine metabolism, is generated through the enzymatic actions of xanthine oxidase. This process also results in the production of oxidants, which have been implicated in cardiovascular diseases and renal dysfunction.[5] This can also induce an inflammatory response, leading to organ dysfunction. Therefore, in clinical practice, uric acid can serve as a significant marker for predicting elevated levels of oxidative stress.[6] Oxidative stress can increase reactive oxygen species (ROS), leading to renal vascular endothelial damage and the production of proteinuria.[7,8] Albuminuria, defined as the presence of an excessive amount of serum protein in the urine, is a significant indicator of kidney damage, including impaired reabsorption and filtration by the kidneys.[9] On the other hand, it has been suggested that race and ethnicity could cause significant variations in the relationship between inflammation and albuminuria in patients with diabetic diseases.[10] Globally, recent studies in patients with cardiovascular or diabetic diseases have demonstrated a significant association between uric acid levels and albuminuria levels.[11-14] However, studies on this topic among Turkish patients with T2DM remain limited.

The objective of this research was to explore the associ-

ation between microalbuminuria and serum uric acid concentrations in patients with T2DM.

MATERIALS AND METHODS

This prospective cross-sectional investigation, carried out at the DM Clinic of HaydarpaşaNumune Training and Research Hospital between January 2006 and May 2007, was in alignment with the Helsinki Declaration and Good Clinical Practice Guidelines.This study is a specialization thesis, it was conducted with institutional approval before 2020, the ethics committee decision was not taken at that time

The study was conducted 80 patients with T2DM, aged between 28 and 77 years, all of whom presented to the DM outpatient clinic. Each patient was undergoing treatment with oral antidiabetic medication. Patients with secondary and type-1 DM, suspected pregnancy, and an estimated glomerular filtration rate (eGFR) less than 60 mg/dL/1.173 m^2 were excluded from the study. Those suspected of pregnancy were tested for beta human chorionic gonadotropin. Patients with hypertension who were using antihypertensive drugs known to affect uric acid levels (such as losartan, various diuretics including hydrochlorothiazide, furosemide, and ethacrynic acid) were also excluded from the study.

Operational definitions

Patients with a significant increase in urine albumin-creatinine ratio (ACR) in the range of 30-299 mg/g of creatinine or with a urine albumin excretion rate (UAE) in the range of 30-299 mg/24 hours were considered to have microalbuminuria.

Study protocol

The demographic and clinical data of all patients were recorded during the outpatient examination. Biochemical parameters were assessed through the analysis of venous blood samples, which were collected following a 12-hour fasting period during outpatient evaluations. The analysis of all samples was conducted in a single laboratory, utilizing a uniform methodology detailed later in the text. Patients with T2DM were categorized into two distinct groups: those with microalbuminuria (n=40) and those without (n=40). Measurements of fat mass and body fat percentage were conducted using the Tanita Body Composition Analyzer TBF-300, following a 30-minute rest period for the subjects.

Biochemical analysis

The Hitachi Modular autoanalyzer (Roche Diagnostics Corp., Indianapolis, IN, USA) was used for the analysis of patients' venous blood and 24-hour urine samples. Levels of 24-hour urine protein (microalbumin turbidimetric method), hemoglobin A1C (HbA1C) (turbidimetric inhibition immunoassay, TINIA), fasting blood glucose (FBG), and lipid parameters (enzymatic colorimetric method) were measured. The determination of low-density lipoprotein cholesterol (LDL-C) was carried out employing the Friedewald formula.[15] Creatinine clearance was determined using the Cockcroft-Gault equation. For female patients, the obtained value was adjusted by multiplying by a factor of 0.85. The formula for creatinine clearance (mL/min) is: (140 - age) × weight / (72 × serum creatinine level).[16]

Statistical Analysis

All data were analyzed with MINITAB RELEASE 14 (Minitab Inc., Pennsylvania, USA). The assessment of normal distribution was conducted through the Anderson-Darling test. Numerical data were represented in terms of mean ± standard deviation. Depending on the distribution's normality, the comparison of numerical data between the two groups was conducted using either the Student's T-test or the Mann-Whitney U test. The correlations among numerical data sets were assessed through Pearson or Spearman correlation analysis, depending on the normality of distribution. Categorical variables were displayed in the form of numbers and percentages, with group comparisons conducted through the Chi-square test. A p-value of less than 0.05 (*) was considered statistically significant for all analyses.

RESULTS

The study population consisted of 80 cases including 49 women (61.3%) and 31 men (38.7%), with a mean age of 57.8±11.6 years. The mean weight was higher in the group with microalbuminuria compared to the group without (89.5±12.0 vs. 75.0±12.6, P=0.002), while the mean BMI was lower (35.1±9.6 vs. 40.0±9.6, P=0.024). The mean high-density lipoprotein cholesterol (HDL-C) was lower in the group with microalbuminuria compared to the group without (40.6±8.6 vs. 47.3±9.3, P=0.001), while the mean uric acid (4.7±1.5 vs. 4.0±1.1, P=0.036) (Figure 1) and the mean creatinine clearance (114.6±5.8 vs. 98.1±3.4, P=0.050) were higher. There were no significant variances in other demographic and clinical findings between the groups with and without microalbuminuria (Table 1).

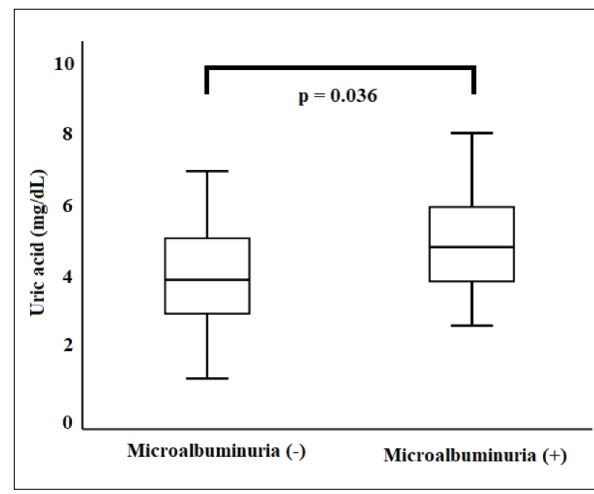

Figure 1. Distribution of uric acid levels in patients with type 2 diabetes mellitus based on the presence of microalbuminuria.

Table 1. Demographic and laboratory findings of patients with type 2 diabetes mellitus

Variables	Type 2 DM		P-value
	With MA n = 40	Without MA n = 40	
Age, years	57.0±11.8	58.0±12.6	0.833
Gender, n (%)			
Male	16 (40.0)	15 (37.5)	0.820
Female	24 (60.0)	25 (62.5)	
Weight, kg	89.5±12.0	75.0±12.6	0.002*
Height, m	1.7±3.5	1.6±2.8	0.131
Waist circumference, cm	104.1±9.6	99.4±14.0	0.079
BMI, kg/m2	35.1±9.6	40.0±9.6	0.024*
Smoker, n (%)	6 (15.0)	8 (20.0)	0.559
Duration of DM, years	7.8 ±1.0	9.5±1.3	0.279
Hypertension, n (%)	21 (52.5)	18 (45.0)	0.505
Cholesterol, mg/dL	207.0±57.7	196.0±51.0	0.353
LDL-C, mg/dL	122.0±39.8	118.0±37.0	0.634
HDL-C, mg/dL	40.6±8.6	47.3±9.3	0.001*
Triglyceride, mg/dL	229.0±60.3	161.0±40.4	0.197
HbA1C, %	8.5±2.4	10.6±3.0	0.409
Uric acid, mg/dL	4.7±1.5	4.0±1.1	0.036*
Creatinine clearance, mL/min	114.6±5.8	98.1±3.4	0.050*

Data are mean ± standard deviation or median (IQR), or number (%). *p<0.05 indicates statistical significance. Abbreviations: BMI: Body mass index; DM: Diabetes mellitus; HbA1C: Hemoglobin A1C; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; MA: Microalbuminuria.

Table 2. Parameters associated with 24-hour urinary protein levels in patients with type 2 diabetes mellitus

Variables	r	P-value
Age	0.102	0.862
Weight	0.258	0.301
Waist circumference	0.271	0.109
BMI	0.282	0.126
Duration of DM	0.125	0.354
Cholesterol	0.233	0.422
LDL-C	0.105	0.711
HDL-C	-0.318	0.011*
Triglyceride	0.251	0.258
HbA1C	-0.305	0.036*
Uric acid	0.308	0.032*
Creatinine clearance	0.294	0.050*

*p<0.05 indicates statistical significance. Abbreviations: BMI: Body mass index; DM: Diabetes mellitus; HbA1C: Hemoglobin A1C; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol.

The 24-hour urinary protein levels were positively correlated with HbA1C (r=0.305, P=0.036), uric acid (r=0.308, P=0.032), and creatinine clearance (r=0.294, P=0.050), whereas they showed a negative correlation with HDL-C levels (r=-0.318, P=0.011) (Table 2).

DISCUSSION

Even with the latest advancements in the treatment of diabetes, nephropathy continues to be a leading cause of end-stage renal disease. Increasing evidence indicates that oxidants generated in the process of uric acid synthesis contribute to the pathogenesis of renal dysfunction and the development of cardiovascular diseases by triggering inflammation and leading to endothelial dysfunction.[17] Moreover, studies propose that endothelial dysfunction resulting from hyperuricemia promotes the proliferation of afferent vascular smooth muscle cells and diminishes renal perfusion. This suggests that increased levels of uric acid may play a crucial role in the progression of renal damage.[18]

Observations indicated that patients with microalbuminuria had increased uric acid levels. A study by Behradmanesh et al.[19] suggested that higher levels of serum uric acid might significantly contribute to the development of diabetic nephropathy. In another study conducted in patients with T2DM, a positive correlation was reported between serum uric acid concentration and urinary albumin excretion.[20] A study involving healthy Korean men demonstrated that elevated serum uric acid levels independently increased the risk of microalbuminuria development over a period of five years.[21] Studies have shown that even mild hyperuricemia has an independent relationship with microalbumin.[22] Furthermore, in patients with T2DM who

have preserved renal function, an elevation in serum uric acid levels by one standard deviation is associated with a 21% increased risk of initiating chronic kidney disease.[23] These findings are supported by a meta-analysis involving patients with T2DM, which also revealed a link between high uric acid levels and an increased risk of diabetic kidney disease.[24] On the other hand, a Japanese two-year cohort study indicated that higher levels of serum uric acid in diabetic patients correlate with a greater risk of diabetic nephropathy worsening, characterized by a transition from microalbuminuria to albuminuria. However, the study also revealed no association between uric acid levels and the probability of progression either from normoalbuminuria to microalbuminuria or from microalbuminuria to albuminuria.[25] An Italian 4-year cohort study identified a significant correlation between the levels of serum uric acid and the onset risk of albuminuria, specifically in instances where the estimated GFR was under 60 mL/min per 1.73 m^2.[26] These differences between studies may be attributable to potential variations in patients' age ranges, follow-up durations, race, and ethnic background.[27]

A significant finding of this study was the negative correlation between serum uric acid and HDL-C levels. Several studies have demonstrated a significant relationship between serum uric acid and the lipid profile, particularly indicating a negative correlation with HDL.[28-30] These findings are also consistent with previous studies that indicate an overlap in the pathogenesis between hyperuricemia and dyslipidemia.[31,32] Furthermore, studies have indicated that in patients with T2DM, higher HDL-C levels are associated with a lower likelihood of microalbuminuria.[33,34] Similarly, in this study, HDL-C levels were found to be lower in T2DM patients with microalbuminuria. The hypothesized mechanisms by which HDL-C contributes to the pathogenesis of microalbuminuria encompass the facilitation of glomerular sclerosis and renal tubular interstitial damage, in addition to the exacerbation of systemic oxidative stress consequent to augmented oxidized LDL concentrations.[35,36]

Numerous studies have indicated that HbA1C is an independent predictor in the development of microalbuminuria.[37-39] In this study, the study observed a tendency towards lower HbA1C levels in T2DM patients with microalbuminuria. This may be associated with the elevated levels of uric acid observed in these patients. Previous studies have indicated that there is a negative correlation between serum uric acid and HbA1C levels.[40,41] The inverse transport of uric acid and glucose in the renal tubules could be responsible for these correlations.[40]

There are notable limitations to this study. Firstly, the study was single-center with a small sample size. Secondly, the collection of uric acid levels was limited to outpatient examinations, and there was no longitudinal monitoring of uric acid levels. Therefore, the influence of uric acid on the development of diabetic nephropathy over an extended period could not be evaluated in this study. Thirdly, medications including urate-lowering, anti-diabetic, and antihypertensive drugs were not accounted for. This might limit the generalizability of the study.

Conclusion

In patients with T2DM, a positive correlation exists between levels of uric acid and 24-hour urinary protein. Individuals with T2DM and microalbuminuria tend to display elevated levels of uric acid. Considering the potential effects of increased uric acid levels on diabetic nephropathy, end-stage renal failure, and the development of cardiovascular disease, routine monitoring of uric acid levels in T2DM patients may be important from a prognostic perspective.

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: N.A., F.M.T.; Design: N.A.; Supervision: N.A.; Fundings: N.A.; Materials: N.A.; Data: N.A.; Analysis: N.A.; Literature search: N.A.; Writing: N.A.; Critical revision: N.A., F.M.T.

Conflict of Interest

None declared.

REFERENCES

1. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract 2019;157:107843. [CrossRef]
2. Chawla A, Chawla R, Jaggi S. Microvasular and macrovascular complications in diabetes mellitus: Distinct or continuum? Indian J Endocrinol Metab 2016;20:546–51. [CrossRef]
3. Hirakawa Y, Ninomiya T, Kiyohara Y, Murakami Y, Saitoh S, Nakagawa H, et al. Age-specific impact of diabetes mellitus on the risk of cardiovascular mortality: An overview from the evidence for Cardiovascular Prevention from Observational Cohorts in the Japan Research Group (EPOCH-JAPAN). J Epidemiol 2017;27:123–9. [CrossRef]
4. Salinero-Fort MÁ, San Andrés-Rebollo FJ, de Burgos-Lunar C, Abánades-Herranz JC, Carrillo-de-Santa-Pau E, Chico-Moraleja RM, et al. Cardiovascular and all-cause mortality in patients with type 2 diabetes mellitus in the MADIABETES Cohort Study: Association with chronic kidney disease. J Diabetes Complications 2016;30:227–36. [CrossRef]
5. Sekizuka H. Uric acid, xanthine oxidase, and vascular damage: Potential of xanthine oxidoreductase inhibitors to prevent cardiovascular diseases. Hypertens Res 2022;45:772–4. [CrossRef]
6. Kurajoh M, Fukumoto S, Yoshida S, Akari S, Murase T, Nakamura T, et al. Uric acid shown to contribute to increased oxidative stress level independent of xanthine oxidoreductase activity in MedCity21 health examination registry. Sci Rep 2021;11:7378. [CrossRef]
7. Duni A, Liakopoulos V, Roumeliotis S, Peschos D, Dounousi E. Oxidative stress in the pathogenesis and evolution of chronic kidney disease: Untangling Ariadne's thread. Int J Mol Sci 2019;20:3711. [CrossRef]
8. Schei J, Fuskevåg OM, Stefansson VTN, Solbu MD, Jenssen TG,

Eriksen BO, et al. Urinary markers of oxidative stress are associated with albuminuria but not GFR decline. Kidney Int Rep 2018;3:573–82. [CrossRef]
9. Gonzalez Suarez ML, Thomas DB, Barisoni L, Fornoni A. Diabetic nephropathy: Is it time yet for routine kidney biopsy? World J Diabetes 2013;4:245–55. [CrossRef]
10. Sinha SK, Shaheen M, Rajavashisth TB, Pan D, Norris KC, Nicholas SB. Association of race/ethnicity, inflammation, and albuminuria in patients with diabetes and early chronic kidney disease. Diabetes Care 2014;37:1060–8. [CrossRef]
11. Lai YJ, Chen YY, Ku PW, Chen LJ, Yen YF. Association between uric acid level and incidence of albuminuria in patients with type 2 diabetes mellitus: A 4.5-year cohort study. Medicine Baltimore 2021;100:e27496. [CrossRef]
12. Kocak MZ, Aktas G, Duman TT, Atak BM, Savli H. Is uric acid elevation a random finding or a causative agent of diabetic nephropathy? Rev Assoc Med Bras 2019;65:1155–60. [CrossRef]
13. Chuengsamarn S, Rattanamongkolgul S, Jirawatnotai S. Association between serum uric acid level and microalbuminuria to chronic vascular complications in Thai patients with type 2 diabetes. J Diabetes Complications 2014;28:124–9. [CrossRef]
14. Latif H, Iqbal A, Rathore R, Butt NF. Correlation between serum uric acid level and microalbuminuria in type-2 diabetic nephropathy. Pak J Med Sci 2017;33:1371–5. [CrossRef]
15. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499–502. [CrossRef]
16. Matz R. Cockcroft-Gault equation and estimation of creatinine clearance. Am J Med 2002;112:684. [CrossRef]
17. Gherghina ME, Peride I, Tiglis M, Neagu TP, Niculae A, Checherita IA. Uric acid and oxidative stress-relationship with cardiovascular, metabolic, and renal impairment. Int J Mol Sci 2022;23:3188. [CrossRef]
18. Park JH, Jo YI, Lee JH. Renal effects of uric acid: Hyperuricemia and hypouricemia. Korean J Intern Med 2020;35:1291–304. [CrossRef]
19. Behradmanesh S, Horestani MK, Baradaran A, Nasri H. Association of serum uric acid with proteinuria in type 2 diabetic patients. J Res Med Sci 2013;18:44–6.
20. Neupane S, Dubey RK, Gautam N, Agrawal KK, Jayan A, Shrestha S, et al. Association between serum uric acid, urinary albumin excretion, and glycated hemoglobin in Type 2 diabetic patient. Niger Med J 2016;57:119–23. [CrossRef]
21. Oh CM, Park SK, Ryoo JH. Serum uric acid level is associated with the development of microalbuminuria in Korean men. Eur J Clin Invest 2014;44:4–12. [CrossRef]
22. Viazzi F, Leoncini G, Ratto E, Falqui V, Parodi A, Conti N, et al. Mild hyperuricemia and subclinical renal damage in untreated primary hypertension. Am J Hypertens 2007;20:1276–82. [CrossRef]
23. Zoppini G, Targher G, Chonchol M, Ortalda V, Abaterusso C, Pichiri I, et al. Serum uric acid levels and incident chronic kidney disease in patients with type 2 diabetes and preserved kidney function. Diabetes Care 2012;35:99–104. [CrossRef]
24. Ji P, Zhu J, Feng J, et al. Serum uric acid levels and diabetic kidney disease in patients with type 2 diabetes mellitus: A dose-response meta-analysis. Prim Care Diabetes 2022;16:457–465. [CrossRef]
25. Hayashino Y, Okamura S, Tsujii S, Ishii H. Association of serum uric acid levels with the risk of development or progression of albuminuria among Japanese patients with type 2 diabetes: A prospective cohort study [Diabetes Distress and Care Registry at Tenri (DDCRT 10)]. Acta Diabetol. 2016;53:599–607. [CrossRef]
26. De Cosmo S, Viazzi F, Pacilli A, Giorda C, Ceriello A, Gentile S, et al. Serum uric acid and risk of CKD in type 2 diabetes. Clin J Am Soc Nephrol 2015;10:1921–9. [CrossRef]
27. Bhalla V, Zhao B, Azar KM, Wang EJ, Choi S, Wong EC, et al. Racial/ethnic differences in the prevalence of proteinuric and nonproteinuric diabetic kidney disease. Diabetes Care 2013;36:1215–21. [CrossRef]
28. Ali N, Rahman S, Islam S, Haque T, Molla NH, Sumon AH, et al. The relationship between serum uric acid and lipid profile in Bangladeshi adults. BMC Cardiovasc Disord 2019;19:42. [CrossRef]
29. Peng TC, Wang CC, Kao TW, Chan JY, Yang YH, Chang YW, et al. Relationship between hyperuricemia and lipid profiles in US adults. Biomed Res Int 2015;2015:127596. [CrossRef]
30. Maloberti A, Vanoli J, Finotto A, Bombelli M, Facchetti R, Redon P, et al. Uric acid relationships with lipid profile and adiposity indices: Impact of different hyperuricemic thresholds. J Clin Hypertens Greenwich 2023;25:78–85. [CrossRef]
31. Lu W, Song K, Wang Y, Zhang Q, Li W, Jiao H, et al. Relationship between serum uric acid and metabolic syndrome: An analysis by structural equation modeling. J Clin Lipidol 2012;6:159–67. [CrossRef]
32. Conen D, Wietlisbach V, Bovet P, Shamlaye C, Riesen W, Paccaud F, et al. Prevalence of hyperuricemia and relation of serum uric acid with cardiovascular risk factors in a developing country. BMC Public Health 2004;4:9. [CrossRef]
33. Sun X, Xiao Y, Li PM, Ma XY, Sun XJ, Lv WS, et al. Association of serum high-density lipoprotein cholesterol with microalbuminuria in type 2 diabetes patients. Lipids Health Dis 2018;17:229. [CrossRef]
34. Zoppini G, Targher G, Chonchol M, Perrone F, Lippi G, Muggeo M. Higher HDL cholesterol levels are associated with a lower incidence of chronic kidney disease in patients with type 2 diabetes. Nutr Metab Cardiovasc Dis 2009;19:580–6. [CrossRef]
35. Vaziri ND. Lipotoxicity and impaired high density lipoprotein-mediated reverse cholesterol transport in chronic kidney disease. J Ren Nutr 2010;20:S35–43. [CrossRef]
36. Li C, Gu Q. Protective effect of paraoxonase 1 of high-density lipoprotein in type 2 diabetic patients with nephropathy. Nephrology Carlton 2009;14:514–20. [CrossRef]
37. Chiu WC, Lai YR, Cheng BC, Huang CC, Chen JF, Lu CH. HbA1C variability is strongly associated with development of macroalbuminuria in normal or microalbuminuria in patients with type 2 diabetes mellitus: A six-year follow-up study. Biomed Res Int 2020;2020:7462158. [CrossRef]
38. Lian H, Wu H, Ning J, Lin D, Huang C, Li F, et al. The risk threshold for hemoglobin A1c associated with albuminuria: A population-based study in China. Front Endocrinol Lausanne 2021;12:673976. [CrossRef]
39. Hsu CC, Chang HY, Huang MC, Hwang SJ, Yang YC, Lee YS, et al. HbA1c variability is associated with microalbuminuria development in type 2 diabetes: A 7-year prospective cohort study. Diabetologia 2012;55:3163–72. [CrossRef]
40. Wei F, Chang B, Yang X, Wang Y, Chen L, Li WD. Serum uric acid levels were dynamically coupled with hemoglobin A1c in the development of type 2 diabetes. Sci Rep 2016;6:28549. [CrossRef]
41. Cui Y, Bu H, Ma X, Zhao S, Li X, Lu S. The relation between serum uric acid and HbA1c Is dependent upon hyperinsulinemia in patients with newly diagnosed type 2 diabetes mellitus. J Diabetes Res 2016;2016:7184123. [CrossRef]

Tip 2 Diyabetli Hastalarda Mikroalbuminüri ile Serum Ürik Asit Seviyeleri Arasındaki İlişki

Amaç: Giderek artan kanıtlar, ürik asit sentezindeki oksidanların, inflamasyonu ve endotel disfonksiyonunu indükleyerek böbrek fonksiyon bozukluğuna ve kardiyovasküler hastalıklara neden olabileceğini düşündürmektedir. Diyabetik hastalarda ırk ve etnik kökene bağlı olarak inflamasyon ve albüminüri korelasyonlarında farklılıklar kaydedilmiştir. Ancak tip 2 diyabetli Türk hastalarda bu konuda yapılan çalışmalar sınırlı kalmaktadır. Bu çalışmada tip 2 DM hastalarında serum ürik asit düzeyleri ile mikroalbüminüri arasındaki ilişkinin araştırılması amaçlandı

Gereç ve Yöntem: Bu prospektif kesitsel çalışmaya T2DM'li 80 hasta dahil edildi ve iki gruba ayrıldı: mikroalbüminürisi olan 40 hasta (24 saatlik idrar proteinürisinde 30-300 mg) ve olmayan 40 hasta (24 saatlik idrar proteinürisinde <30 mg). 12 saatlik açlık sonrası hastalardan alınan venöz kan örneklerinin analizi ile biyokimyasal parametreler değerlendirildi.

Bulgular: Çalışma popülasyonunun yaş ortalaması 57.8±11.6 yıldı. Ortalama ürik asit (4.7±1.5 vs. 4.0±1.1, P=0.036) ve ortalama kreatinin klirensi (114.6±5.8 vs. 98.1±3.4, P=0,050) mikroalbüminürisi olmayan gruba göre mikroalbuminürisi olan grupta daha yüksekti. 24 saatlik idrar protein düzeyleri HbA1C (r=0.305, P=0.036), ürik asit (r=0.308, P=0.032) ve kreatinin klirensi (r= 0,294, P=0.050) ile pozitif korelasyon gösterdi.

Sonuç: Mikroalbuminürisi olan Tip2 DM hastaların ürik asit seviyesi daha yüksek değerdeydi. Artan ürik asit düzeylerinin diyabetik nefropati, son dönem böbrek yetmezliği ve kardiyovasküler hastalık gelişimi üzerindeki potansiyel etkileri göz önüne alındığında, T2DM hastalarında ürik asit düzeylerinin rutin olarak izlenmesi prognostik açıdan önemli olabilir.

Anahtar Sözcükler: Albuminüri; diyabetik nefropati; proteinüri; ürik asit; tip 2 diyabetes mellitus.

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Original Article

Lower Gastrointestinal Endoscopy in Elderly: A Single-center Experience

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Keywords: Aged; colonoscopy; elderly; proctoscopy; rectosigmoidoscopy.

ABSTRACT

Objective: Endoscopic procedures are frequently applied to the elderly population over 65, with the increased population of this age group. The comorbidities of this population are thought to be increased risk factors for endoscopic interventions. We need more literature on applying lower gastrointestinal (GI) endoscopy to the elderly population. This study aims to analyze the efficiency and safety of lower GI endoscopy in the aged population.

Methods: We performed a retrospective observational study of patients over 65 who underwent lower GI endoscopy from January 2016 to January 2021 at the Istanbul Sultanbeyli State Hospital Endoscopy Unit. This study was approved by the local Ethics Committee and registered with ClinicalTrials.gov (NCT05012527). A total of 564 patients' following parameters were analyzed: indications, endoscopic findings, histopathological findings, and complications of lower GI endoscopy.

Results: The cecal intubation rate was 90% in colonoscopies. The inadequate bowel cleansing rate was 12.4% in colonoscopies and 13% in all lower endoscopy procedures. There was a six percent malignancy detected. The polyp detection rate is approximately 45% in colonoscopies, and polyps are seen mainly left side of the colon. The overall diagnostic yield rate is 48.7%, and colorectal cancer yield is 5.9% on colonoscopies. The complication rate was 1.2%.

Conclusion: This study showed that colonoscopy in the elderly has a high diagnostic yield and can be applied safely.

INTRODUCTION

Lower gastrointestinal (GI) endoscopy is the most important diagnostic tool used in colorectal system disease diagnosis and screening.[1] All over the world, millions of colonoscopies are performed annually for GI bleeding, colon cancer screening or surveillance, diagnosis of other GI diseases, and therapeutic applications such as a colonoscopic polypectomy, hemostasis, decompression, or dilation.[2]

With the rapid increase in the elderly population worldwide, the number of people over 65 is expected to double in the next 25 years. The incidence of colorectal cancer (CRC) increases with age; therefore, the number of endoscopies performed on the elderly will gradually increase. The colonoscopy procedure performed in the elderly population has some difficulties, and the risk of developing complications is thought to be higher.[3,4]

We need more literature on applying lower GI endoscopy to the elderly population. Therefore, in this article, we evaluated lower GI system endoscopic interventions that were performed in our hospital over 65 years of patients. This study aimed to analyze the indications, endoscopic findings, histopathological findings, and complications of lower GI endoscopy.

MATERIALS AND METHODS

We performed a retrospective observational study of patients who underwent lower GI endoscopy from January 2016 to January 2021 at the Istanbul Sultanbeyli State Hospital Endoscopy Unit. This study was approved by the Marmara University Faculty of Medicine Clinical Research Ethics Committee (Number: 09.2021-724) and registered with ClinicalTrials.gov (NCT05012527). This study was to determine inadequate bowel cleansing rate, cecal intubation rate, the prevalence of polyps/cancer, and total complications rate.

We used patients' endoscopy and hospital records for data acquisition. Patients with missing data and duplicate records were excluded from the study. Patients over the age of 65 who underwent colonoscopy and rectosigmoidoscopy were included in the analysis.

The following parameters were analyzed: age and gender, type of endoscopy, examination date, indication, endoscopic results, completeness of the procedures, polyp/tumor localization, histopathological examination of biopsies, and complications.

For further analysis, patients were stratified according to age into three groups: 65–74 (youngest-old), 75–84 (middle-old), and ≥85 (oldest-old), and also into two groups as symptomatic and screening.

CRC, polyps, diverticula, and inflammation are clinically important endoscopic findings.[5] We calculate the overall diagnostic yield according to these parameters.

The patients were suggested on a grain-free, pulp-free, and liquid diet for three days before the colonoscopy. One day before the colonoscopy, patients were given two doses of oral sodium phosphate (45 ml) as a laxative, and enemas were administered twice. All endoscopies were performed using standard video-colonoscopes (Fujinon EC-530WL, ES-530WE-sigmoidoscope) by six general surgeons who have at least five years of experience in endoscopy.

Almost all colonoscopy procedures were performed under sedation, but rectosigmoidoscopy without drugs. Conscious sedation was achieved with Propofol 1% 10 mg/ml by an anesthetic technician under the supervision of an anesthesiologist. Continuous monitoring was provided by recording oxygen saturation, blood pressure, and pulse rate.

The endoscopy indications were classified by the American Society for GI Endoscopy guideline.[6] Pathological results were evaluated according to the World Health Organization criteria.[7]

The primary outcome of this study was to determine inadequate bowel cleansing rate, cecal intubation rate, prevalence of polyps/cancer, and total complications rate.

All authors had access to the study data and reviewed and approved the final manuscript.

Statistical Analysis

We performed statistical analysis using the Statistical Package for the Social Sciences (Version 24 for Mac, IBM Corporation). Chi-square or Fisher exact tests were used to compare categorical variables. For quantitative variables, the t-test, Mann–Whitney or Kruskal–Wallis, and ANOVA are applied. $p<0.05$ were considered statistically significant.

RESULTS

From January 2016 to January 2021, 5214 lower GI en-

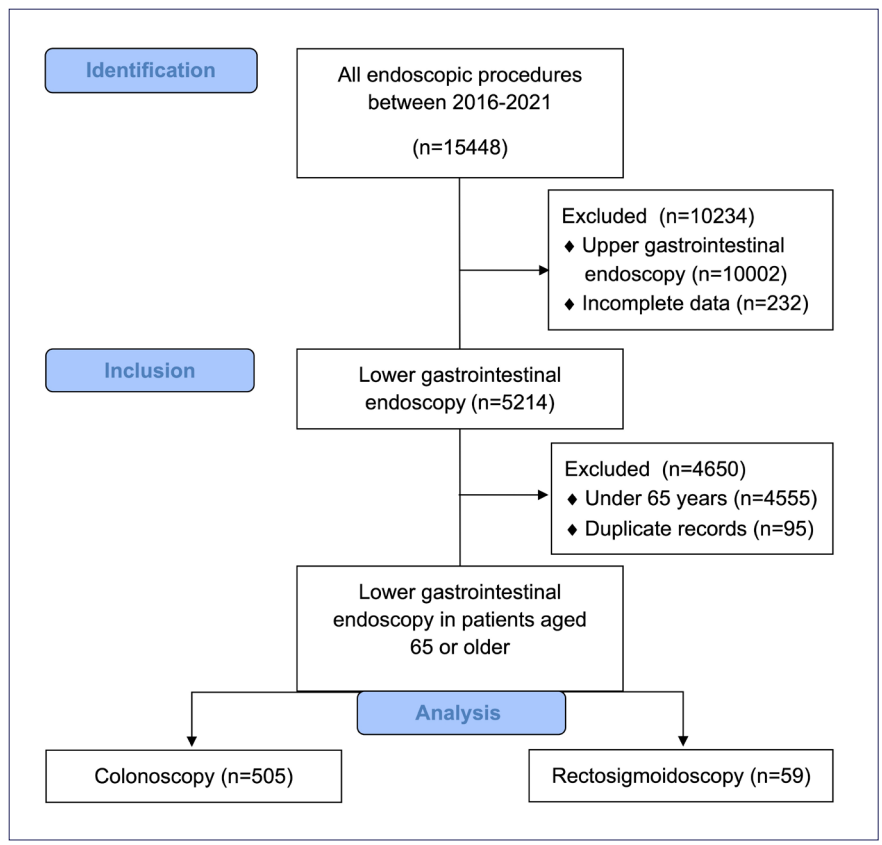

Figure 1. Flowchart of patient selection

Table 1. General characteristics of the elderly patients

Procedure	n (%)
Colonoscopy	
Sex	
Male	261 (51.7)
Female	244 (48.3)
Total	505 (100.0)
Age (years)	
65–74	396 (78.4)
75–84	93 (18.4)
≥85	16 (3.2)
Total	505 (100)
Minimum–maximum	65–93
Mean–SD	71.09–5.585
Rectosigmoidoscopy	
Sex	
Male	33 (55.9)
Female	26 (44.1)
Total	59 (100.0)
Age (years)	
65–74	43 (72.9)
75–84	11 (18.6)
≥85	5 (8.5)
Total	59 (100)
Minimum–maximum	65–96
Mean–SD	72.49–6.655

SD: Standard deviation.

doscopies were performed at Istanbul Sultanbeyli State Hospital Endoscopy Unit. After exclusion criteria, 564 (11%) patients were analyzed aged 65 years or older (Figure 1). Patient demographics by age subgroups are detailed in Table 1. The cecal intubation rate was 90% in colonoscopies. The inadequate bowel cleansing rate was 12.4% in colonoscopies and 13% in all lower endoscopy procedures.

The major indications for lower GI endoscopy were identified GI bleeding symptoms, screening, and surveillance. Detailed indications are given in Table 2. Major endoscopic findings identified hemorrhoids, colonic polyps, diverticular disease, and normal examination. There was a six percent malignancy detected (Table 2). Synchronous tumors were seen in one patient on an ascending and descending colon.

We detected a total of 204 polyps on colonoscopies. In order of polyps/cancer, location and frequency were; rectum 20.1%, sigmoid colon 23%, descending colon 8.3%, splenic flexure 5.4%, transverse colon 8.8%, hepatic flexure 2%, ascending colon 6.4%, caecum 2.9%, multiple localization 21.6%, and unspecified 1.5%. Furthermore, we detected a total of 18 polyps with rectosigmoidoscopy, and their location was rectum 50%, sigmoid colon 27.8%, descending colon 16.7%, and multiple localization 5.6%.

Regarding the results of histopathological examination (total of 307 biopsies), neoplastic (adenomatous) polyps 172 (53.4%) and non-neoplastic polyps 40 (13%) were the major pathological findings. In addition, intramucosal carcinoma was detected in 4 patients with adenomatous

Table 2. Indications and endoscopic findings for lower gastrointestinal endoscopy

Procedure	Indications	n (%)	Findings	n (%)
Colonoscopy	Abnormal imaging	31 (6.1)	Normal findings	166 (32.9)
	GI bleeding	144 (28.5)	Colorectal polyps	154 (30.5)
	Anemia	47 (9.3)	Hemorrhoids	61 (12.1)
	Screening and surveillance	125 (24.8)	Diverticular disease	57 (11.3)
	Diarrhea	9 (1.8)	Cancer	30 (5.9)
	Constipation	57 (11.3)	Findings secondary to operation	10 (2.0)
	Abdominal pain	72 (14.3)	Perianal findings (fissure/fistula/abscess)	10 (2.0)
	Weight loss	15 (3.0)	Angiodysplasia	7 (1.4)
	Other	5 (1.0)	Inflammation-ulceration	5 (1.0)
	-	Other	5 (1.0)	
	Total	505 (100)	Total	505 (100)
Rectosigmoidoscopy	Abnormal imaging	3 (5.1)	Hemorrhoids	20 (33.9)
	GI bleeding	46 (78.0)	Normal findings	15 (25.4)
	Screening and surveillance	5 (8.5)	Colorectal polyps	11 (18.6)
	Constipation	1 (1.7)	Cancer	4 (6.8)
	Other	4 (6.8)	Inflammation-ulceration	3 (5.1)
	Total	59 (100)	Diverticular disease	2 (3.4)
			Angiodysplasia	1 (1.7)
			Other	3 (5.1)
			Total	59 (100)

GI: Gastrointestinal.

Table 3. Results of pathological examinations

Diagnosis	n (%)
Adenocarcinoma	26 (8.5)
Neoplastic (adenomatous) polyp	
Tubular adenoma	
Without dysplasia	84 (27.4)
With low-grade dysplasia	59 (19.2)
With high-grade dysplasia	8 (2.6)
Tubulovillous adenoma	
Without dysplasia	4 (1.3)
With low-grade dysplasia	8 (2.6)
With high-grade dysplasia	7 (2.3)
Villous adenoma	
With low-grade dysplasia	1 (0.3)
With high-grade dysplasia	1 (0.3)
Intramucosal carcinoma	4 (1.3)
Nonneoplastic polyp	
Hyperplastic polyp	36 (11.7)
Inflammatory polyp	4 (1.3)
Nonspecific colitis	26 (8.5)
Normal findings	13 (4.2)
Nonspecific proctitis	11 (3.6)
Active colitis	9 (2.9)
Malignant melanoma (anal canal)	1 (0.3)
Malignant invasion (prostate cancer)	1 (0.3)
Other	4 (1.3)
Total	307 (100)

polyps. Adenocarcinoma was detected in 26 of all biopsies. According to histopathological features, tubular adenoma was the most common type of adenomatous polyp, as expected. Normal colorectal mucosal findings were seen in 13 (4.2%) cases of all biopsies. The results of pathological examinations are detailed in Table 3.

According to the diagnostic yield definition, our overall diagnostic yield rate is 48.7%, and CRC yield is 5.9% on colonoscopies.

The comparison of age groups showed no difference between gender, presence of polyps and/or cancer and location, bowel preparation rate, and cecal intubation rate. Diverticular disease prevalence is increasing with age: youngest-old: 9.6%, middle-old: 12.5%, and oldest-old: 19% (Table 4).

The patients were divided into two groups: symptomatic and screening in terms of colonoscopy indications. The mean age of the screening group was significantly higher (71.4 vs. 69.8, p=0.005). Benign diseases were seen at a rate of 63% in the screening group. The incidence of polyps and/or cancer was significantly higher in the symptomatic group (p=0.001) (Table 5).

The complication rate was 1.2%. During the colonoscopy, three cardiac arrhythmias occurred and were treated medically. One patient was readmitted for rectal bleeding four hours after discharge, in an endoscopic examination showed hemorrhage at the polypectomy site, and it was controlled by endoscopic clipping. Two colonic perforations (80-year-old female, 69-year-old male) occurred and were treated by emergency surgery. The 80-year-old female patient was treated with primary suture repair, and she was discharged with no other complications. A 69-year-old male patient was in the intensive care unit because of his comorbidities (kidney failure, pneumonia). Colonoscopy was requested due to rectal bleeding. Colonoscopy revealed a rectosigmoid tumoral mass before perforation. He was operated on and applied just colostomy without resection was done due to his general

Table 4. Comparisons by age groups

Parameters	n=396, n (%)	n=93, n (%)	n=16, n (%)	p
Age (years)	65–74	75–84	≥85	
Sex				
Female	184 (46)	54 (58)	6 (37.5)	0.08
Male	212 (54)	39 (42)	10 (62.5)	
Polyp detection	151 (40)	43 (46)	7 (43)	0.7
Benign findings				
Hemorrhoids	60 (13.7)	18 (17.3)	3 (14.3)	0.6
Diverticular disease	42 (9.6)	13 (12.5)	4 (19)	
Polyp location				
Right colon	30 (20)	9 (21)	2 (29)	0.47
Left colon	87 (57)	27 (63)	2 (29)	
Both side	34 (23)	7 (16)	3 (42)	
Bowel preparation				
Optimal	341 (86)	83 (89)	14 (87.5)	0.72
Suboptimal	55 (14)	10 (11)	2 (12.5)	
Cecal intubation rate	357 (90)	83 (89)	14 (87.5)	0.7

Table 5. Comparisons by screening and symptomatic groups

Parameters	Screening group (n=380), n (%)	Symptomatic group (n=125), n (%)	p
Age	71.4	69.8	0.005
Sex			
Female	186 (49)	67 (53)	0.34
Male	194 (51)	58 (47)	
Pathology			
Polyp/cancer	142 (37)	62 (49)	0.001
Benign disorders	238 (63)	63 (51)	

condition. He died 19 days after the operation. Unfortunately, we could not obtain information about delayed complications of colonoscopies.

DISCUSSION

Endoscopic procedures are frequently applied to the elderly population over 65, with the increased population of this age group.[8,9] The comorbidities of this population are thought to be increased risk factors for endoscopic interventions. On the other hand, it is emphasized that special attention should be paid to endoscopic procedures in this age population with the possible problems that the patients may experience during the preparation phase. In the current study, 564 patients who had colonoscopy and rectosigmoidoscopy were evaluated in this single center. In most of the patients, the cecum was successfully reached with adequate cleaning, and the colonoscopy was completed safely. Endoscopy was performed on most patients due to rectal bleeding, screening, and surveillance, and polyps were detected in approximately one-third of them.

In this study, major colonoscopy indications are lower GI bleeding and screening. The main part of the population in our study was aged 65–74. Studies that emphasize a high diverticular disease rate had a study population over 75. Therefore, We consider that this affects our main findings, which the majority are the normal result, and a low rate of diverticular disease compared to the other published data.[3,10]

Some studies showed younger patients have higher bowel preparation rates rather than the elderly. Therefore, inadequate bowel cleansing is related to low completion rates. Our result that cecal intubation (90%) and poor preparation (12.4%) in colonoscopies is similar to other studies.[11-13] In comparison by age groups, we did not detect statistically insignificant cecal intubation and bowel preparation rates between youngest-old, middle-old, and oldest-old.

The prevalence of colorectal malignancy increases with age, so lower GI endoscopy plays a major role in cancer detection in the elderly population. The yield of colonoscopy in the elderly is reported differently in many studies. Our data showed lower GI endoscopy in the elderly has a high diagnostic yield.[10,12,14]

The colonoscopy results of the symptomatic groups are compared to the screening group. Screening groups were older than symptomatic patients, and there was no difference between the two groups in terms of gender. Our results showed the detection rate of polyp/cancer was symptomatic group (49%) higher than the screening group (37%) and statistically significant. This result is compatible with other published data.[3,5,12,13,15,16]

There is no difference in gender and polyp detection between age groups. Our polyp detection rate is approximately 45% in colonoscopies, and polyps are seen mainly on the left side of the colon. However, in some studies, more polyps were detected in the screening group, and another study showed that the symptomatic group had more polyp detection rate. In this study, polyp detection was seen more in the symptomatic groups. The polyp detection rate increased with age, but in the present study, we could not find a correlation between age with polyp detection rate.[3,17-20]

In the elderly population, less considered symptoms, including abdominal pain, weight loss, diarrhea, and constipation, should be reckoned for endoscopic investigation.

Our complication rate of 1.2% is similar to published data.[3] The most common complications have been reported as bleeding and perforation. The published review reported perforation rate was 0.005–0.085% and bleeding in 0.001–0.687%, and the incidence of post-colonoscopy complications increased in elderly patients.[21] The post-colonoscopy mortality rate was reported at 0.0029% for all indications.[22] Therefore, before deciding to perform a colonoscopy on the elderly, we should consider their general condition and comorbidities. The literature and our study show lower GI endoscopy is a safe procedure for elderly patients.[23]

Our study has certain limitations. It is a retrospective, single-center, and low-volume study. Our center is a secondary care hospital. So might be our patient population has a low morbidity rate, and its related to low complication rates. Due to retrospective design, we do not know the surveillance colonoscopy result on these patients.

Conclusion

With the increase in the population over 65, the application of screening and therapeutic colonoscopy is increasing in the elderly. We need to take precautions for prepa-

ration and during the procedure due to the frailty of this population. The present study showed colonoscopy in the elderly has a high diagnostic yield and can be applied safely.

Ethics Committee Approval

This study approved by the Marmara University School of Medicine Ethics Committee (Date: 16.07.2021, Decision No: 09.2021.724).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: M.E., T.K.U.; Design: M.E., T.K.U.; Supervision: M.E., T.K.U.; Fundings: M.E., T.K.U.; Materials: M.E., T.K.U.; Data: M.E., T.K.U.; Analysis: M.E., T.K.U.; Literature search: M.E., T.K.U.; Writing: M.E., T.K.U.; Critical revision: M.E., T.K.U.

Conflict of Interest

None declared.

REFERENCES

1. Pignone M, Rich M, Teutsch SM, Berg AO, Lohr KN. Screening for colorectal cancer in adults at average risk: a summary of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med 2002;137:132–41. [CrossRef]
2. Cappell MS, Friedel D. The role of sigmoidoscopy and colonoscopy in the diagnosis and management of lower gastrointestinal disorders: endoscopic findings, therapy, and complications. Med Clin North Am 2002;86:1253–88. [CrossRef]
3. Lippert E, Herfarth HH, Grunert N, Endlicher E, Klebl F. Gastrointestinal endoscopy in patients aged 75 years and older: risks, complications, and findings--a retrospective study. Int J Colorectal Dis 2015;30:363–6. [CrossRef]
4. Ma WT, Mahadeva S, Kunanayagam S, Poi PJ, Goh KL. Colonoscopy in elderly Asians: a prospective evaluation in routine clinical practice. J Dig Dis 2007;8:77–81. [CrossRef]
5. Loffeld RJ, Liberov B, Dekkers PE. Yearly diagnostic yield of colonoscopy in patients age 80 years or older, with a special interest in colorectal cancer. Geriatr Gerontol Int 2012;12:298–303. [CrossRef]
6. Committee ASoP, Early DS, Ben-Menachem T, Decker GA, Evans JA, Fanelli RD, et al. Appropriate use of GI endoscopy. Gastrointest Endosc 2012;75:1127–31. [CrossRef]
7. Hamilton S, Vogelstein B, Kudo S, Riboli E, Nakamura S, Hainaut P, et al. Tumours of the colon and rectum: Carcinoma of the colon and rectum. In: World Health Organization classification of tumours: Pathology and genetics of tumours of the digestive system. Lyon, France: IARC Press. p. 105–19.
8. Ergenç M, Uprak TK. Esophagogastroduodenoscopy in patients aged 75 years and older: a single-center study. Cureus 2022;14:e21846.
9. Ergenç M, Derici ST, Uprak TK. Percutaneous endoscopic gastrostomy: A secondary care hospital experience. Laparosc Endosc Surg Sci 2021;28:210–4. [CrossRef]
10. Duncan JE, Sweeney WB, Trudel JL, Madoff RD, Mellgren AF. Colonoscopy in the elderly: low risk, low yield in asymptomatic patients. Dis Colon Rectum 2006;49:646–51. [CrossRef]
11. Travis AC, Pievsky D, Saltzman JR. Endoscopy in the elderly. Am J Gastroenterol 2012;107:1495–501; quiz 1494, 1502. [CrossRef]
12. Karajeh M, Sanders D, Hurlstone D. Colonoscopy in elderly people is a safe procedure with a high diagnostic yield: a prospective comparative study of 2000 patients. Endoscopy 2006;38:226–30. [CrossRef]
13. Lin OS. Performing colonoscopy in elderly and very elderly patients: Risks, costs and benefits. World J Gastrointest Endosc 2014;6:220–6. [CrossRef]
14. Arora A, Singh P. Colonoscopy in patients 80 years of age and older is safe, with high success rate and diagnostic yield. Gastrointest Endosc 2004;60:408–13. [CrossRef]
15. Lin OS, Kozarek RA, Schembre DB, Ayub K, Gluck M, Drennan F, et al. Screening colonoscopy in very elderly patients: prevalence of neoplasia and estimated impact on life expectancy. JAMA 2006;295:2357–65. [CrossRef]
16. Tran AH, Man Ngor EW, Wu BU. Surveillance colonoscopy in elderly patients: a retrospective cohort study. JAMA Intern Med 2014;174:1675–82. [CrossRef]
17. Ferlitsch M, Reinhart K, Pramhas S, Wiener C, Gal O, Bannert C, et al. Sex-specific prevalence of adenomas, advanced adenomas, and colorectal cancer in individuals undergoing screening colonoscopy. JAMA 2011;306:1352–8. [CrossRef]
18. Baker FA, Mari A, Hosadurg D, Suki M, Ovadia B, Gal O, et al. The impact of colonoscopy indication on polyp detection rate. Ann Gastroenterol 2019;32:278–82. [CrossRef]
19. Zhou L, Zhang H, Sun S, Huang M, Liu J, Xu D, et al. Clinical, endoscopic and pathological characteristics of colorectal polyps in elderly patients: Single-center experience. Mol Clin Oncol 2017;7:81–7. [CrossRef]
20. Singhal S, Verma A, Anand K. Colonoscopy for colorectal cancer screening above age 75: outcomes in symptomatic african american and Hispanic adults. J Gastrointest Cancer 2011;42:212–6.
21. Kim SY, Kim HS, Park HJ. Adverse events related to colonoscopy: Global trends and future challenges. World J Gastroenterol 2019;25:190–204. [CrossRef]
22. Reumkens A, Rondagh EJ, Bakker CM, Winkens B, Masclee AA, Sanduleanu S. Post-colonoscopy complications: a systematic review, time trends, and meta-analysis of population-based studies. Am J Gastroenterol 2016;111:1092–101. [CrossRef]
23. Inagaki Y, Yoshida N, Hasegawa D, Kassai K, Yasuda R, Inoue K, et al. The efficacy and safety of colonoscopy in nonagenarians: A multicenter study. Indian J Gastroenterol 2020;39:557–64. [CrossRef]

Yaşlılarda Alt Gastrointestinal Endoskopi: Tek Merkez Deneyimi

Amaç: Endoskopik işlemler, bu yaş grubunun artan nüfusu ile birlikte 65 yaş üstü hastalarda sıklıkla uygulanmaktadır. Bu popülasyonda komorbiditelerin endoskopik girişimler için esktra risk oluşturduğu düşünülmektedir. Bu çalışma, yaşlı popülasyonda alt gastrointestinal endoskopinin etkinliğini ve güvenliğini değerlendirmeyi amaçlamıştır.

Gereç ve Yöntem: İstanbul Sultanbeyli Devlet Hastanesi Endoskopi Ünitesinde Ocak 2016-Ocak 2021 tarihleri arasında alt gastrointestinal endoskopi yapılan 65 yaş üstü hastaların verileri retrospektif olarak incelendi. Bu çalışma yerel Etik Kurul tarafından onaylandı ve ClinicalTrials.gov'a (NCT05012527) kaydedildi. Toplam 564 hastanın sıralanan parametreleri analiz edildi: Endikasyonlar, endoskopik bulgular, histopatolojik bulgular ve alt gastrointestinal endoskopi komplikasyonları.

Bulgular: Kolonoskopilerde çekal entübasyon oranı %90 olarak saptandı. Yetersiz barsak temizliği oranı kolonoskopilerde %12.4 ve tüm alt gastrointestinal endoskopi işlemlerinde %13 saptandı. Yüzde 6 malignite tespit edildi. Kolonoskopilerde polip görülme oranı yaklaşık %45 idi ve polipler ağırlıklı olarak kolonun sol tarafında tespit edildi. Kolonoskopilerde genel tanı verimi %48,7 ve kolorektal kanser tanı koyma oranı %5.9 saptandı. Komplikasyon oranı %1.2 idi.

Sonuç: Bu çalışma, kolonoskopinin yüksek tanısal verime sahip olduğunu ve yaşlı hastalarda güvenle uygulanabileceğini göstermiştir.

Anahtar Sözcükler: Kolonoskopi; rektosigmoidoskopi; proktoskopi; yaşlı hasta; yaşlılık.