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Patient and healthcare provider burden due to conventional measurement of the international normalized ratio: From a multi-dimensional perspective

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ABSTRACT

Objectives: In this study, we aimed to investigate the healthcare burden associated with hospital visits for international normalized ratio (INR) measurement from a multi-dimensional perspective.

Patients and methods: A total of 415 patients (198 males, 217 females; mean age: 54±12.7 years; range, 14 to 84 years) who were admitted to the cardiovascular surgery (CVS) outpatient clinic between March 2015 and June 2015 were included. The burden of INR measurement was assessed in two main categories: social and clinical. Data including educational status, occupational status and accompanying persons, indications for warfarin use, history of warfarin-related complications, expenses made by the patient and the accompanying persons, and the time spent were recorded.

Results: A total of 1,259 laboratory entries were found for the overall study population. Of these entries, 99.4% were only for INR measurements. An INR outside the target therapeutic range (TTR) was detected in 53.7% of the patients. Among all patients attending to the CVS outpatient clinic during the study, the sole reason for attendance was the INR measurement in 23%. The rate of complications requiring intervention was 2.1%. The daily clinical cost per patient was \$22.14, the social monetary cost was \$9.77, and the total cost was \$31.91.

Conclusion: Conventional INR measurements have a significant social and economic impact on patients and are associated with significantly increased workload and loss of resources from the perspective of the healthcare provider.

Keywords: Cost of illness, management, medication therapy, Warfarin.

The number of patients requiring oral anticoagulant therapy (OAT) has been steadily increasing worldwide, mainly due to the presence of a wide spectrum of indications for OAT therapy, most of which require lifelong use of these agents.^[1] Although novel oral anticoagulants (NOACs) are commonly used for the treatment of atrial fibrillation (AF), data from the randomized studies regarding their safety and efficacy in patients with mechanical cardiac valves (MCVs) or those with mechanical cardiac support (MCS) devices are scarce, despite initial promising studies.^[2-5] One study examining NOACs in MCV patients was terminated prematurely due to adverse effects.^[6] Thus, warfarin remains the most commonly prescribed OAT currently.^[7]

Tight and regular international normalized ratio (INR) monitoring is a prerequisite after the initiation of warfarin treatment.^[8] Conventional INR measurement methods require the attendance of the patient to a healthcare facility for blood sampling,

leading to an increased workload and costs. In this study, we aimed to investigate the workload, loss of productivity, and associated costs of the monitoring of patients on warfarin treatment from a multi-dimensional perspective.

PATIENTS AND METHODS

This prospective, observational study was conducted at Ankara Türkiye Yüksek İhtisas Training and Research Hospital, Department of Cardiovascular

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Surgery (CVS) between March 2015 and June 2015. Initially 418 patients who were on warfarin treatment and admitted to the CVS outpatient clinic were screened. Three patients were excluded due to coagulopathy confirmed by genetic testing. Finally, a total of 415 patients (198 males, 217 females; mean age: 54 ± 12.7 years; range, 14 to 84 years) were included. Exclusion criteria included treatment with additional anticoagulant agents rather than warfarin, having a diagnosis of coagulopathy, unwillingness to participate in the study, inability to follow the warfarin treatment regimen, and inability to answer the questions in the quality of life questionnaire. A written informed consent was obtained from each patient. The study protocol was approved by the Ankara Numune Training and Research Hospital Ethics Committee (date, no: 09/02/2015, E-15-541). The study was conducted in accordance with the principles of the Declaration of Helsinki.

The following parameters were examined in patients attending to the unit for conventional INR measurements: time spent for official procedures at the laboratory, the monitoring frequency and interval, costs associated with the transportation, accommodation, examination, and laboratory work-up, INR-related complications, and treatment costs associated with the treatment of these complications. Also, a questionnaire was filled out to determine whether patients received any education on warfarin use, as well as to find out whether the quality of life was an important factor for the level of INR stability. Additionally, quality of life tools (EuroQoL-5 Dimensions [EQ-5D], Turkish Version) were administered and information on portable point-of-care devices (POCDs) were gathered.^[9,10] Patients were classified into two categories based on their location of residence: those residing in Ankara province or other provinces. The distance covered by those paying a visit to the healthcare facility from outside the Ankara province was calculated as the distance from the district/village of residence to Ankara provincial center. The time spent on transportation was recorded based on the patients' declaration. The mean INR target values of anticoagulation therapy were as follows: 2.5 ± 0.5 for aortic valve replacement (AVR), AF, deep venous thrombosis (DVT), and pulmonary thromboembolism (PTE) and 3.0 ± 0.5 for mitral valve replacement (MVR) and double valve replacement (AVR-MVR).^[11,12]

The costs were considered in two main categories: clinical costs and social costs. Clinical costs included

the registration fee to the hospital, costs associated with the interventional treatment of complications, and the cost of blood and blood product replacement. These costs were recorded according to the invoice prepared by the financial unit of the hospital. For social costs, the daily wage loss was calculated based on the daily income of the employed patients and accompanying persons. Information provided by the patient were used to calculate the costs associated with transportation and accommodation. For the study period, an exchange rate of 1 United States Dollar = 2.66 Turkish Lira was used as the current currency rate of the start date of the study.

Statistical analysis

Statistical analysis was performed using the SPSS for Windows version 11.5 software (SPSS Inc., Chicago, IL, USA). The normal distribution of continuous numerical variables was tested using the Kolmogorov-Smirnov test. Continuous data were expressed in mean \pm standard deviation (SD) and median (interquartile range [IQR]: 25th-75th percentile), while categorical data were expressed in number and frequency. The significance of the difference in median values between the groups was tested using the Mann-Whitney U test. Categorical variables were assessed using the Pearson chi-square, Fisher's exact, or probability ratio test. A p value of <0.05 was considered statistically significant.

RESULTS

A total of 415 patients included in the study were followed for three months, during which a total of 1,259 attendances to the CVS outpatient unit were recorded. The median number of visits per patient to the outpatient unit during this period was 3.0 (IQR: 2.0 to 4.0). Of the patients, 88 (21.2%) received no formal education, while 27 (6.5%) had a university or higher degree. The most common reason for warfarin treatment was cardiac valvular surgery (72.8%, $n=302$) (Table 1). No significant associations between the number of visits and indication of warfarin use were detected ($p=0.86$).

The complication most frequently associated with the need for invasive treatment was gastrointestinal tract (GI) bleeding in 2.1% of the patients (Table 2). Fifty-six patients who had an INR over the target therapeutic range (TTR) had blood and blood product replacement. Also, 14.5% of the patients reported at

Table 1 Sociodemographic and clinical characteristics of the patients (n=415)				
Variables	n	%	Mean±SD	Range
Age (year)			54.1±12.7	14-84
Sex				
Male	198	47.7		
Female	217	52.3		
Educational status				
No formal education	88	21.2		
Primary School	198	47.7		
Secondary School	52	12.5		
High School	50	12.0		
University or higher	27	6.5		
Place of residency				
Ankara province	376	90.6		
Outside Ankara province	39	9.4		
Indications for warfarin use				
Cardiac valve replacement or repair	302	72.8		
Atrial fibrillation	12	2.9		
Intracardiac thrombus	1	0.2		
Pulmonary thromboembolism	2	0.5		
Deep venous thrombosis	97	23.4		
Ventricular support device	1	0.2		
Distribution of patients who had cardiac valve replacement or repair (n=302)				
AVR	89	29.4		
MVR	150	49.5		
AVR-MVR	56	18.5		
Valve repair	4	1.3		
Bio-prosthesis valve replacement	1	0.3		
MVR-TVR	1	0.3		
AVR-TVR	1	0.3		
AVR	89	29.4		
MVR	150	49.5		

SD: Standard deviation; AVR: Aortic valve replacement; MVR: Mitral valve replacement; TVR: Tricuspid valve replacement.

Table 2 Distribution of complications				
Complications	Total		Requiring intervention or hospitalization	
	n	%	n	%
Gingival bleeding	51	12.2	0	0.0
Epistaxis	55	13.2	1	0.2
Hematuria	13	3.1	0	0.0
Menstrual bleeding	16	3.8	1	0.2
Hemorrhagic cerebrovascular accident	0	0.0	0	0.0
Gastrointestinal bleeding	13	3.1	9	2.1
Mechanical valve thrombosis	0	0.0	0	0.0
Total	148	35.6	11	2.6

least one occasion where they altered warfarin dosage without asking for a specialist's opinion.

For clinical cost estimation, invoices sent to the social security institution were examined. Invoices prepared by different healthcare facilities were compared for the treatment of similar complications. Of the complications that were intervened, the highest costs were associated with GI bleeding. Of note, for outpatient services, an invoice of \$18.79 is issued for each outpatient visit due to a contract with the social insurance institution.

The median monthly income of the employed patients was \$714.28 (range: \$187.96 to \$1,879.69) of the overall patient group attending to a control visit, 42.7% were attended by an accompanying person. Of these accompanying persons, 28.8% were actively employed with a monthly median income level of \$563.9 (range: \$338.34 to \$1,879.69). The total loss of wages per visit was \$5.33.

The patients used the following means of transportation at least once for attending to the hospital: 316 patients with mass transportation (range, 1 to 7), 99 patients with a private car (range, 1 to 4), 26 patients with a cab (range, 1 to 4), and three patients on foot (range, 1 to 1). The median distance covered by patients coming from locations other than Ankara province was 250 (range, 80 to 1,398) km. The duration and cost of transportation were 45 (IQR: 30 to 80) min and \$1.12 (IQR: \$0.62 to 2.19) and 240 (IQR: 120 to 240) min and \$5.01 (IQR: \$0 to 8.77) for patients attending from Ankara and outside Ankara, respectively (Table 3). The median

Variables	Median	IQR
Transportation fee (\$)		
Ankara	1.12	0.62-2.19
Other	5.01	0-8.77
Transportation time (min)		
Ankara	45	30-80
Other	240	120-240
Accommodation and food fee (\$)		
Ankara	0	0-0
Other	6.26	2.5-10.02

IQR: Interquartile range.

duration for having an INR measurement within the healthcare facility was 1.0 (range, 1 to 5) days.

The total cost was the sum of the social and clinical costs and the mean total cost was \$31.91±24.7 per patient (Table 4).

Quality of life measurements usually showed a good level of quality of life, as documented by the responses to the questionnaire administered, while less than 2% of the patients were found to have a significantly impaired quality of life (Table 5).

Cost (\$)	Mean±SD
Clinical costs	22.14±14.99
Gastrointestinal bleeding	1.33±6.3
Blood products	1.69±4.28
Outpatient clinic registration	19.12±11.39
Social costs	9.77±29.23
Transport	3.05±6.7
Accommodation, food	1.2±6.12
Loss of wages, patient	3.75±11.48
Loss of wages, accompanying person	1.77±6.93
Total	31.91±24.7

SD: Standard deviation.

Variables	n	%
Mobility problems		
None	312	75.2
Partial	103	24.8
Severe	-	-
Problems of self-care		
None	393	94.7
Partial	18	4.3
Severe	4	1.0
Problems in daily chores		
None	348	83.9
Partial	59	14.2
Severe	8	1.9
Pain-discomfort		
None	264	63.6
Partial	143	34.5
Severe	8	1.9
Anxiety/depression		
None	256	61.7
Partial	154	37.1
Severe	5	1.2

Table 6
Demographic and clinical characteristics of patients within and out of the target therapeutic range of INR

Variables	INR in target value (n=223)		INR out of target value (n=192)		p†
	n	%	n	%	
Educational status					0.396
Illiterate	51	22.9	37	19.3	
Primary School	108	48.4	90	46.9	
Secondary School	29	13.0	23	12.0	
High School	25	11.2	25	13.0	
University	10	4.5	17	8.9	
Employment					0.044
Unemployed	195	87.4	154	80.2	
Employed	28	12.6	38	19.8	
Cares about nutrition	173	77.6	156	81.3	0.358
Trained on warfarin use	139	62.3	131	68.2	0.209

INR: International normalized ratio; † Pearson's chi-square test.

Table 7

Clinical, transportation, accommodation, food, and total cost in patients within and out of the target therapeutic range of INR

Cost (\$)	Mean±SD	p†
Clinical cost		0.005
INR out of TTR	24.02±15.98	
INR in TTR	11.24±13.47	
Social cost		0.894
INR out of TTR	11.24±20.27	
INR in TTR	8.06±11.43	
Total cost		0.044
INR out of TTR	35.26±28.69	
INR in TTR	28.08±18.37	

SD: Standard deviation; INR: International normalized ratio; TTR: Therapeutic target range; † Mann Whitney U test.

Of the overall patient group, 53.7% had INR values outside the TTR. The TTR of INR did not exhibit any associations with the educational status ($p=0.39$) or monthly income ($p=0.096$). On the other hand, actively employed patients had a significantly better TTR of INR ($p=0.04$) (Table 6).

The cost comparison between the patients with the inside TTR or out of the TTR showed a significantly higher clinical and total cost for those out of the TTR, while the difference in social costs was not statistically significant (Table 7).

DISCUSSION

The estimated number of individuals with paroxysmal or persistent AF is around 2.2 million in the United States.^[13] In a study by Uyarel et al.,^[14] each year 35,000 new cases of AF are diagnosed in Turkey, and the annual number of cardiac valve surgeries is approximately 10,000 as reported by Kervan et al.^[15] Another patient group requiring tight monitoring of warfarin therapy consists of those with MCS implantation. Considering the cost of artificial cardiac devices implanted, as well as the fact that cardiac transplantation represents the only therapeutic option in these patients, one may readily acknowledge the significance of INR monitoring in these individuals. In a study by Sharma et al.,^[16] 2% of the general population was found to be on long-term OAT, corresponding to a population segment of 1.6 million subjects in Turkey. As these figures suggest, a continuous increase occurs in the number of individuals on warfarin therapy both globally and also in our country. Regular INR monitoring in patients on warfarin therapy helps to prevent simple, but potentially life-threatening complications. From an economic perspective, regular visits to a healthcare facility for INR control are associated with a certain amount of costs, while treatment of complications arising from inappropriate use may lead to even larger costs and loss of productivity.

Our study population attended to our hospital on an average of 3.0 (IQR: 2.0 to 4.0) occasions within three months. There were some interesting results

observed in this study. As such, 2.6% of the patients had a delay of approximately one year for their initial follow-up laboratory assessment, either since these patients preferred not to spend a considerable amount of time in waiting queues or due to transportation difficulty.

A total of 99.4% of 1,259 outpatient visits were performed only for INR monitoring. Data acquired from hospital management revealed that the total number of outpatient visits to the CVS unit were 5,440 during the study period, implying that 23% of all outpatient visits were performed for INR measurement alone, leading to a serious workload for the outpatient setting. When the presence of an only-INR measurement outpatient clinic (conducted by the cardiology department) is taken into consideration, this workload becomes more serious and overwhelming for clinicians.

According to the data obtained from the Turkish Statistical Institution (TUIK) as of May 2015, the rate of employment in individuals between 15 and 64 years of age is 90.5% in the general Turkish population, compared to an employment rate of only 20.2% for the same age group in our study.^[17] These data suggest that majority of the employed individuals requiring INR monitoring actually do not attend for INR measurements, probably due to the difficulties such as time constraints or getting permission from the workplace or, in other point of view, these patients are not able to secure a job due to their conditions.

Since our clinic represents one of the referral centers in Turkey, individuals residing in locations other than Ankara province represented 9.4% of the total study population. Although initially it was assumed that the majority of these patients had their follow-up examination in our center due to a previous surgical intervention performed here, 97.4% were found to pay a visit to the outpatient facility only for INR measurements. Contrary to our expectations, only 2.6% had attended for routine follow-up of the disease.

A detailed examination of the patients' history revealed that after initiation of warfarin treatment, 4.6% of the patients had at least one complication such as a hemorrhagic cerebrovascular accident or MCV thrombosis requiring an intervention. Although no such complications were observed during the study period, their occurrence would certainly be associated with the significantly increased costs.

Attendance of patients on warfarin therapy to a healthcare center for each INR measurement is associated with a financial and workload burden. Until now, no studies in Turkey have been conducted to assess the financial and workload burden on the National Social Insurance Organization arising from the care of these patients. In our study, the total, clinical, and social costs per attendance to our unit were \$31.91, \$22.14, and \$9.77, respectively. These figures include complications that can be prevented with a better regulation of INR. In a study by Chen et al.^[18] from China, the approximate cost of each INR measurement was found to vary between \$9.8 and \$150.5, depending on the distance between the place of the residency and hospital. In the aforementioned study, such a wide range of costs could be accounted for by the higher level of expenses for transportation and accommodation for patients coming from peripheral areas, compared to those coming from the urban locations. However, the cost of the management of associated complications was not taken into consideration.

Although conventional INR tests are considered the gold-standard approach for evaluating the efficacy of warfarin therapy, technological advances allow the introduction of more practical and more rapid measurement devices targeting better monitoring rates. Such devices enable patients to measure their INR measurements at home and take more active responsibility in their treatment, ultimately leading to improved treatment compliance based on a more individualized strategy. This, in turn, may result in a better regulation of the anticoagulant therapies and decrease the dependency of the patients on healthcare centers. Comparative studies on such novel devices versus conventional INR measurements also showed the reliability of this new-generation POCDs.^[19,20] However, two major questions remain on the use of POCDs. The first question refers to the provider and content of the professional assistance, and the second refers to the possibility that INR measurements with POCDs may actually be costlier. Wells et al.^[20] found an increased monitoring frequency of INR in patients using POCDs, while this increase was also associated with a decreased complication rate. On the other hand, Sharma et al.^[16] found similar average costs with standard monitoring or home monitoring systems, while the latter was associated with a reduced likelihood of thrombotic events and all-cause mortality. Considering the cost of the acute treatment

of the reduced complication, it may be assumed that POCDs may prove to be increasingly more advantageous over time in terms of cost, compared to standard monitoring procedures. The POCDs may allow a decreased need for outpatient visits to the hospital and permit more frequent and regular INR measurements. In our study, only 7.5% of the patients had some information on POCDs. Such a few number of patients who are familiar with POCDs is another obstacle to home-based measurement of INR by patients and consequent dissemination of POCDs. We believe that patients should be informed more about this alternative measurement tool.

The fact that almost half of the patients visiting outpatient clinics come to the clinics with attendants causes an increased cost and loss of labor force, although 53.7% of the patients were detected to be outside the TTR values. Besides, 19.7% of them were not informed about nutrition and complications, and the way of administration of warfarin were not explained to 32.8% of the patients. This necessitates an urgent action plan. We believe that the number of patients within the TTR values would increase with a consequent reduction in complications through patient education about warfarin use and nutrition, enhanced availability and accessibility to informative brochures, and clarification of the importance of regular INR measurements.

Nonetheless, there are several limitations to this study. Some complications associated with warfarin due to a short period were unable to be monitored. Patients who failed to attend to their follow-up visits for any reasons could not be included and their social and medical conditions still remain unclear. Prescription costs were not able to be considered in this study, as the patients were not willing to wait for submitting these data after receiving their results and prescriptions. Economic and social burden analyses could not be performed for patients requiring home care. Also, patients using POCSs were unable to be followed, as they did not attend to the outpatient clinic.

In conclusion, conventional INR measurements have a significant social and economic impact on patients, while they are associated with a significant increase in workload and loss of productivity from the perspective of the healthcare provider. We believe that increased availability of POCDs may play a role in reducing costs associated with laboratory

measurements and complications, and also improve patient compliance with the treatment. However, further studies are warranted to elucidate this issue.

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The effect of cardiopulmonary bypass time on renal function after coronary artery bypass grafting

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ABSTRACT

Objectives: In this study, we aimed to evaluate the effect of duration of cardiopulmonary bypass (CPB) on postoperative acute kidney injury (AKI) in patients who underwent coronary artery bypass grafting (CABG).

Patients and methods: A total of 251 patients (222 males, 29 females; mean age: 61±9.4 years; range, 37 to 88 years) who underwent elective CABG operation between January 2014 and January 2018 were retrospectively analyzed. The patients were divided into three groups by considering the duration of CPB as 0 to 60 min (Group 1), 60 to 120 min (Group 2), and ≥120 min (Group 3). Preoperative, operative, and postoperative data and renal functions of the patients were evaluated using the Acute Kidney Injury Network (AKIN) criteria.

Results: In all three groups, a statistically significant decrease in hemoglobin and estimated glomerular filtration rate (eGFR) values and a statistically significant increase in blood urea nitrogen (BUN) and creatinine values were found (p<0.05). In Group 2 and Group 3, postoperative BUN and creatinine value were significantly higher and eGFR value was significantly lower than Group 1 (p<0.05). In terms of postoperative data, the rate of acute renal failure (ARF) requiring dialysis was significantly higher in Group 2 and Group 3 than Group 1 (p<0.05). The postoperative mortality rate was significantly higher in Group 3 than Group 1 (p<0.05).

Conclusion: In terms of postoperative mortality and morbidity, it is important to identify the risk factors for AKI and to take appropriate precautions for the risk factors. Minimizing perfusion time in patients undergoing CPB may help to decrease the incidence of CPB-induced AKI.

Keywords: Acute kidney injury, cardiopulmonary bypass time, coronary artery bypass grafting.

Heart diseases are still the leading causes of death worldwide. The main reason is the mortality related to course of the diseases and surgical practice of these diseases. Cardiovascular surgery has the risk of lung damage, infection, neurological problems, and renal disease. These complications may cause high mortality and morbidity.^[1]

The kidneys are the most vulnerable organs for cardiopulmonary bypass (CPB). Renal failure, which is a common disease for elderly, is associated with a high mortality rate. Nephrotoxic drugs, cardiogenic shock, major surgical procedures, and intensive care unit (ICU) stay are the main causes of renal failure.^[2-4] The most common and important form of renal failure after cardiac surgery is acute kidney injury (AKI). Cardiopulmonary bypass-related non-pulsatile and hypothermic perfusion, and low blood pressure cause hemodilution, decreased renal perfusion, decreased

estimated glomerular filtration rate (eGFR), and increased renal vascular resistance. The increase of renal vascular resistance causes the increase of angiotensin II secretion and, consequently, renal blood perfusion decreases. Decreased renal perfusion also increases the release of oxygen radicals. Embolic materials related to aggregated platelets and damaged erythrocyte cells cause the occlusion of renal tubules. All these problems increase the risk of postoperative

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AKI.^[5] It is important to investigate the negative effects of CPB, which is essential for cardiac surgery practice, for renal functions.

In the present study, we aimed to investigate the effect of duration of CPB on postoperative AKI in patients who underwent coronary artery bypass grafting (CABG).

PATIENTS AND METHODS

This single-center, retrospective study was conducted at Izmir Katip Celebi University, Faculty of Medicine, Department of Cardiovascular Surgery between January 2014 and January 2018. A total of 251 patients (222 males, 29 females; mean age: 61±9.4 years; range, 37 to 88 years) who underwent elective CABG operation were included. The patients who had preoperative renal diseases and patients who were scheduled for cardiac surgery combined with CABG were excluded. The patients were divided into three groups according to CPB times as follows: 0 to 60 min (Group 1), 60 to 120 min (Group 2), and >120 min (Group 3). Patient's pre-, intra-, and postoperative data were recorded. Renal status of the patients was evaluated according to creatinine and eGFR levels. Acute kidney injury was defined according to the Acute Kidney Injury Network (AKIN) criteria^[6] as follows: Stage 1, an increased postoperative creatinine level of ≥1.5, but <2 times, compared to baseline; Stage 2, an increased postoperative creatinine level of ≥2, but <3 times, compared to baseline; and Stage 3, an increased postoperative creatinine level of ≥3 times, compared to baseline. All groups were compared according to creatinine levels. A written informed consent was obtained from each patient. The study protocol was approved by the Izmir Katip Celebi University, Faculty of Medicine Ethics Committee (date/no: 25.04.2019/188). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Baseline demographic and clinical characteristics including age, sex, body surface area, redo surgery, diabetes mellitus, hypertension, chronic obstructive lung disease, smoking, neurological dysfunction, ejection fraction, pre- and postoperative hemoglobin, white blood cell (WBC), blood urea nitrogen (BUN), creatinine, and eGFR levels were recorded. Intraoperative data including coronary bypass graft counts, CPB time, aortic cross-clamp time, transfusion rate, and postoperative data including mechanical

ventilation time, revision, neurological complication, hemodialysis, ICU stay, in-hospital stay, and mortality rate were noted. Patient's preoperative creatinine levels were the baseline values for the calculation of eGFR. The Cockcroft-Gault formula was used to calculate eGFR (Figure 1).

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed in mean ± standard deviation (SD), while categorical variables were expressed in number and frequency. The Kolmogorov-Smirnov test was used to analyze the distribution of the variables. Due to the unbalanced distribution, the non-parametric tests were used. The Kruskal-Wallis and Mann-Whitney U test were used to analyze quantitative independent data. The Wilcoxon test was used to analyze dependent quantitative data. The chi-square test or Fisher's exact test were used to analyze qualitative independent data. A *p* value of <0.05 was considered statistically significant.

RESULTS

Baseline demographic and clinical characteristics of the patients are shown in Table 1. There was no statistically significant difference among the groups in terms of age, sex, diabetes mellitus, chronic obstructive lung disease, smoking status, renal failure, hypertension, and redo surgery (*p*>0.05). However, preoperative ejection fraction was significantly lower in Group 3 compared to Groups 1 and 2 (*p*<0.05).

There was no statistically significant difference among the groups in terms of WBC and hemoglobin levels in the pre- and postoperative period. However, the WBC value increased in the postoperative period compared to the preoperative period and hemoglobin levels decreased in the postoperative period compared to baseline (*p*<0.05) (Table 2).

There was no significant difference among the groups in terms of preoperative BUN values (*p*>0.05). However, the postoperative BUN values increased in

$$eGFR = \frac{(140 - \text{Age [year]} \times \text{weight [kg]})}{(72)^* \times (\text{serumcreatinine [mg/dL]})}$$

Figure 1. Cockcroft-Gault formula for eGFR calculation.
eGFR: Estimated glomerular filtration rate.

Table 1 Preoperative data													
	Group 1 (n=100)			Group 2 (n=100)			Group 3 (n=51)			p			
	n	%	Mean±SD	Median	n	%	Mean±SD	Median	n		%	Mean±SD	Median
Age (year)			60.2±9.7	61.5			61.9±8.5	63.0			60.7±10.7	60.0	0.382*
Sex													0.015†
Male	92	92.0			89	89.0			41	76.5			
Female	8	8.0			11	11.0			10	23.5			
Diabetes mellitus													0.198†
(-)	65	65.0			53	53.0			28	54.9			
(+)	35	35.0			47	47.0			23	45.1			
Hypertension													0.488†
(-)	42	42.0			50	50.0			25	49.0			
(+)	58	58.0			50	50.0			23	45.1			
Smoking													0.147†
(-)	46	46.0			57	57.0			31	60.8			
(+)	54	54.0			43	43.0			20	39.2			
COPD													0.999†
(-)	88	88.0			88	88.0			45	88.2			
(+)	12	12.0			12	12.0			6	11.8			
Chronic renal failure													1.000†
(-)	100	100.0			100	100.0			51	100.0			
(+)	0	0.0			0	0.0			0	0.0			
Redo surgery													1.000†
(-)	98	98.0			100	100.0			51	100			
(+)	1	1.0			0	0.0			0	0.0			
Preoperative EF (%)			55.3±7.3	60.0			53.2±7.8	55.0			49.6±9.4	50.0	0.000*
Body surface area			1.9±0.1	1.9			1.9±0.2	1.9			1.9±0.3	1.9	0.585*
EuroSCORE			3.1±2.3	3.0			2.6±1.9	2.0			3.5±1.8	3.0	0.014*

SD: Standard deviation; COPD: Chronic obstructive pulmonary disease; EF: Ejection fraction; * Kruskal-Wallis test; † Chi-square test.

Table 2
Laboratory data

	Group 1 (n=100)		Group 2 (n=100)		Group 3 (n=51)		p*
	Mean±SD	Median	Mean±SD	Median	Mean±SD	Median	
Preoperative WBC ($\times 10^3$)	8.2±2.2	8.0	7.9±2.0	7.8	8.2±2.0	7.7	0.506
Postoperative WBC ($\times 10^3$)	13.1±3.6	12.8	13.5±4.2	12.8	14.4±4.0	13.6	0.149
p†	0.000		0.000		0.000		
Preoperative hemoglobin ($\times 10^3$)	13.2±1.4	13.1	13.1±1.5	13.2	12.7±1.6	12.9	0.172
Postoperative hemoglobin ($\times 10^3$)	9.6±1.3	9.4	9.5±1.3	9.5	9.2±1.2	9.1	0.118
p†	0.000		0.000		0.000		
Preoperative BUN	16.3±5.3	15.0	17.6±4.5	17.0	17.0±6.1	16.0	0.052
Postoperative BUN	18.0±5.3	17.5	19.9±6.7	18.5	20.1±5.8	20.0	0.015
p†	0.000		0.000		0.000		
Preoperative creatinine (mg/dL)	0.9±0.1	0.82	0.9±0.2	0.89	0.9±0.2	0.84	0.057
Postoperative creatinine (mg/dL)	1.0±1.0	0.86	1.1±0.3	0.97	1.11±0.36	1.04	0.001
p†	0.003		0.000		0.000		
Preoperative eGFR	114.8±19.8	118.9	108.2±21.1	107.7	111.1±22.2	115.5	0.057
Postoperative eGFR	109±25.9	113.1	96.4±33.1	97.1	92.6±30.8	89.2	0.001
p†	0.000		0.000		0.000		

SD: Standard deviation; WBC: White Blood cells; BUN: Blood urea nitrogen; eGFR: Estimated glomerular filtration rate; * Kruskal-Wallis test (Mann-Whitney U Test); † Wilcoxon Signed Rank test.

all groups compared to baseline ($p < 0.05$). Postoperative BUN levels in Groups 2 and 3 were higher compared to Group 1 ($p < 0.05$). There was no significant difference in postoperative BUN levels between Groups 2 and 3 ($p > 0.05$).

Preoperative creatinine levels did not significantly differ among the groups ($p > 0.05$). However, postoperative creatinine levels increased in all

groups compared to baseline ($p < 0.05$). Postoperative creatinine levels were significantly higher in Groups 2 and 3, compared to Group 1 ($p < 0.05$). There was no significant difference in postoperative creatinine levels between Groups 2 and 3 ($p > 0.05$).

Preoperative eGFR levels did not significantly differ among the groups ($p > 0.05$). However, postoperative eGFR levels decreased in all groups compared to

Table 3
Postoperative AKI rate

	Group 1 (n=100)				Group 2 (n=100)				Group 3 (n=51)				p
	n	%	Mean±SD	Median	n	%	Mean±SD	Median	n	%	Mean±SD	Median	
AKI													0.021†
(+)	4	4.0			10	10.0			9	17.6			
(-)	96	96.0			90	90.0			42	82.4			
AKI Stage													
I	3	3.0			8	8.0			5	9.8			
II	0	0.0			2	2.0			4	7.8			
III	1	1.0			0	0.0			0	0.0			
AKI rate			1.2±1.3	1.06			1.2±0.3	1.09			1.2±0.3	1.15	0.006*

AKI: Acute kidney injury; SD: Standard deviation; * Kruskal-Wallis test (Mann-Whitney U Test); † Chi-square test.

	Table 4 Postoperative data												p
	Group 1 (n=100)				Group 2 (n=100)				Group 3 (n=51)				
	n	%	Mean±SD	Median	n	%	Mean±SD	Median	n	%	Mean±SD	Median	
CPB time (min)			52.5±7.3	54.5			90.2±15.9	89.5			136.0±17.0	130.0	0.000*
Cross-clamp time (min)			27.0±5.3	26.0			49.1±12.4	47.5			67.7±17.7	66.0	0.000*
Postoperative hemodialysis													0.001
(-)	100	100.0			92	92.0			43	84.3			
(+)	0	0.0			8	8.0			8	15.7			
IABP													0.022†
(-)	97	97.0			91	91.0			43	43.0			
(+)	3	3.0			9	9.0			8	15.7			
Extubation time (h)			8.5±3.9	7.0			12.7±12.1	8.5			33.4±91.8	15.0	0.000*
ICU stay (day)			2.7±1.2	2.0			3.1±2.8	2.0			4.8±4.0	4.0	0.000*
Drainage (mL)			825±345	750			980±583	800			1163±927	950	0.018*
Used blood products			3.1±2.5	2.0			3.7±2.7	3.0			5.2±2.6	5.0	0.00*
Revision													0.869†
(-)	96	96			96	96			47	92.2			
(+)	4	4.0			5	5.0			3	5.9			
Neurologic problem													0.668†
(-)	98	98.0			94	94.0			48	94.1			
(+)	2	2.0			4	4.0			2	3.9			
Hospital stay (day)			7.7±3.3	7.0			8.0±4.3	7.0			11.5±8.0	8.0	0.000*
Mortality													0.005†
(-)	100	100.0			100	100.0			49	96.1			
(+)	0	0.0			3	3.0			5	9.8			

SD: Standard deviation; CPB: Cardiopulmonary bypass; IABP: Intra-aortic balloon pump; ICU: Intensive care unit; * Kruskal-Wallis test (Mann-Whitney U Test); † Chi-square test.

preoperative levels ($p < 0.05$). Postoperative eGFR levels were significantly lower in Groups 2 and 3, compared to Group 1 ($p < 0.05$). There was no significant difference in postoperative eGFR levels between Groups 2 and 3 ($p > 0.05$). Laboratory data are shown in Table 2.

The AKIN scores were significantly higher in Groups 2 and 3, compared to Group 1 ($p < 0.05$). However, there was no significant difference between Groups 2 and 3 in terms of the AKIN scores ($p > 0.05$) (Table 3).

The cross-clamp time and CPB time were significantly longer in Group 3 compared to Groups 1 and 2, and they were also significantly higher in Group 2 compared to Group 1 ($p < 0.05$) (Table 4).

The number of patients requiring dialysis was higher in Groups 2 and 3, compared to Group 1 ($p < 0.05$). There was no significant difference between Groups 2 and 3 ($p > 0.05$). Intra-aortic balloon pump (IABP) use and mechanical ventilation time were statistically higher in Group 3, compared to Groups 1 and 2 ($p < 0.05$). Transfusion rate, ICU stay, and in-hospital stay were also higher in Group 3, compared to Group 1 ($p < 0.05$). There was no statistically significant difference between Groups 1 and 2 in terms of these parameters.

The need for drainage and revision was statistically significantly higher in Group 3, compared to Group 1; however, there was no significant difference between Groups 1 and 2. There was no significant difference among the groups in terms of neurological complications ($p > 0.05$). However, the mortality rate was higher in Group 3, compared to Group 1 ($p < 0.05$), although there was no significant difference between Groups 1 and 2 (Table 4).

DISCUSSION

With the aging population, the prevalence of coronary artery disease has been increasing all around the world recently. As the aging population increases, the number of CABG operations also increases.^[7] The CABG is still the gold-standard technique for the treatment of coronary artery disease. Mortality rate varies between 2.5 and 26%.^[7] Renal damage is a frequent complication after CABG and is usually seen as a mild creatinine increase. However, in some cases, creatinine increase may be high or AKI may complicate

prognosis in patients with high comorbidities, leading to the increased mortality.^[8]

Hemodialysis need after cardiac surgery ranges between 1 and 7%. Mortality rate in patients with renal failure is 60%.^[9,10] There is also the increased rate of infection and prolonged hospital stay in patients who have CPB-related AKI.^[11] Therefore, postoperative renal dysfunction is an important complication due to its relation with postoperative mortality and morbidity.^[12,13] The main causes of CPB-related AKI are decreased perfusion pressure, nephrotoxic agents, and CPB-related inflammatory response.^[14-16] The main goal of CPB is to maintain tissue perfusion. Perfusionist regulates this process by coordinating the mean arterial pressure and CPB flow rate.

Extracorporeal circulation with CPB produces systemic inflammatory response. As the CPB time increases, the risk of systemic inflammatory response syndrome (SIRS) also increases.^[17] There are many studies showing that a CPB time longer than 80 min poses a significant risk for SIRS.^[18] Review of the literature also reveals that there is a relation between AKI and CPB, as described previously before a relation between CPB and SIRS. Zhiwei et al.^[19] concluded that prolonged perfusion time was related to AKIN Stage ≥ 2 renal damage and it was a major risk factor for postoperative AKI. In our study, we analyzed patients according to CPB time. We showed that the increased CPB time was strongly related to AKI as follows: Group 1, 4% ($n=4$); Group 2, 10% ($n=10$), and Group 3, 17.6% ($n=9$). The AKIN scores were higher in Groups 2 and 3, compared to Group 1 ($p < 0.05$). We found that one (1%) patient in Group 1, two (2%) patients in Group 2, and four (7.8%) patients in Group 3 had AKIN \geq Stage 2, respectively.

In another study including acute renal failure patients after cardiac surgery, Bove et al.^[12] included 5,068 patients and they found that 171 patients had AKI after cardiac surgery. In addition, 94 patients needed renal replacement therapy and patients who needed renal replacement therapy had a longer mean CPB time (116 ± 51.2 min) compared to those who did not (82 ± 31.7). They concluded that decreased CPB time also decreased the CPB-related AKI. In our study, 16 patients needed postoperative hemodialysis (Group 2, $n=8$, 8%; Group 3, $n=8$, 15.7%). The need for hemodialysis was significantly higher in Groups 2 and 3, compared to Group 1; however, there was no statistically significant difference between

Groups 2 and 3. The main goal of the intraoperative patient management in terms of CPB is to manage optimal perfusion pressure, flow rate, hemodilution, and CPB time. Therefore, managing CPB time in an appropriate level would reduce the AKI risk, postoperative morbidity, and mortality.^[20]

In a study by Elmanday et al.,^[21] CPB time had a statistically significant importance for the development of postoperative AKI. They found that postoperative creatinine and BUN levels were significantly higher and eGFR levels were significantly lower in the AKI group, compared to non-AKI group. In our study, there was no significant difference in the preoperative creatinine, BUN, and eGFR values. However, postoperative creatinine and BUN levels were higher in Groups 2 and 3, compared to Group 1. Also, the eGFR levels were significantly lower in Groups 2 and 3, compared to Group 1. Perioperative anemia is another important indicator of postoperative AKI.^[22,23] In our study, we showed that there was no statistically significant difference in the hemoglobin levels among the groups.

Patients with left ventricular dysfunction have an increased AKI risk.^[22] Low cardiac output and the need for inotropic or mechanical support after cardiac surgery are also major risk factors for AKI.^[22] In our study, three (3%) patients in Group 1, nine (9%) patients in Group 2, and eight (15.7%) patients in Group 3 needed IABP. The need for IABP in Group 3 was significantly higher, compared to Group 1. Ortega-Loubon et al.^[24] performed a study about AKI-related ICU stay and mortality after CABG in 435 patients. The mean ICU stay for their patients with and without AKI was 7.4 ± 9.3 days and 2.7 ± 2.2 days, respectively. The 30-day mortality rate was 18.5% and 3.1% in patients with and without AKI, respectively. In our study, we found that the ICU stay and in-hospital stay were higher in Group 3, compared to the other groups. There was no significant difference between Groups 1 and 2. The mortality rate in Group 3 was significantly higher compared to Group 1. In the literature, there is a limited number of studies regarding AKI and neurological complications after cardiac surgery. A study by Ryden et al.^[25] showed that postoperative neurological complication in patients with AKI were higher compared to those without postoperative AKI. In our study, there was no significant difference among the groups ($p > 0.05$).

The main limitations of this study include its single-center, retrospective design with a relatively small sample size. In addition, only creatinine and eGFR values were used for the AKIN classification; however, there are many other sensitive parameters such as renal-specific proteins to calculate renal function and eGFR. Screening of the risk factors along with the measurement of novel biomarkers may enable early diagnosis of patients who are susceptible to AKI and may be helpful to tailor the appropriate treatment protocol.

In conclusion, the incidence of CPB-related AKI is still high in our surgical practice. The most important way to reduce the risk of CPB-related AKI is to manage the modifiable risk factors for patients and extracorporeal circulation technique. It is a good option to prefer off-pump techniques for patients who have a high postoperative AKI risk. Furthermore, decreasing the inflammatory response and CPB time for on-pump procedures may also contribute to prevent AKI.

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Assessment of quality of life and psychosocial status of mothers whose children underwent congenital heart surgery

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ABSTRACT

Objectives: The aim of this study was to assess the quality of life of mothers whose children underwent cardiac surgery.

Patients and methods: This prospective, case-control study included a total of 103 children (52 males, 51 females; mean age: 59.1±56.1 months; range, 1 month-18 years) who underwent congenital heart surgery and their mothers between September 2019 and April 2020. The children who underwent cardiac surgery and their mothers were included as the study group (n=48). The control group (n=55) included healthy children and their mothers. Sociodemographic data of the children and their mothers were recorded. The World Health Organization Quality of Life-BREF (WHOQOL-BREF) questionnaire was administered to the mothers.

Results: Both groups were similar in terms of age, sex, height, and birth weight, maternal age, education and marital status, and presence of comorbidities (p>0.05). The scores in a 0-100 scale of physical health, psychological health, social relationships and environment domains of the WHOQOL-BREF were statistically lower in the study group (p<0.05). Intensive care duration was negatively correlated with all domains of the WHOQOL-BREF (p<0.05). The domains except for the environment were negatively correlated with the hospital stay (p<0.05).

Conclusion: Lower scores of WHOQOL-BREF were achieved in mothers whose children underwent congenital cardiac surgery. Length of intensive care and hospital stay was negatively correlated with the WHOQOL-BREF. Routine screening and counseling may be valuable in this patient population.

Keywords: Congenital heart disease, quality of life, surgery.

Congenital heart diseases are major health problems that can affect approximately 0.6 to 1 per 100 live births in the Turkish population.^[1] However, there are many different heart diseases in this group, about 50 to 60% of these patients require surgical treatment.^[2] Although pediatric cardiac surgery currently has a highly developed technical and technological infrastructure, operations still have serious morbidity and mortality risks.^[3] The parents, particularly mothers, face serious psychosocial problems regarding the risks of the operation and the difficulties of postoperative care.^[4] Therefore, the anxiety level of the patients and, particularly, their mothers is critical.

Recognizing the differences in the quality of life (QoL) of the mothers of children undergoing heart surgery compared to mothers of healthy children prepares the ground for screening and supportive treatments in this regard. Determining the psychological and social assessment of these mothers

and identifying those who need professional support may explain the source of a social problem.^[5] In the present study, we aimed to evaluate the level of QoL of mothers of children undergoing cardiac surgery.

PATIENTS AND METHODS

This prospective, case-control study was conducted at Dr. Sami Ulus Maternity and Child Health Education and Research Hospital between September 1st, 2019 and April 30th, 2020. A total of 103 children (52 males, 51 females; mean age:

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Table 1
Demographic and clinical characteristics of the children included in the study

	All (n=103)			Study group (n=48)			Control group (n=55)			p			
	n	%	Mean±SD	Min-Max	n	%	Mean±SD	Min-Max	n		%	Mean±SD	Min-Max
Age (month)			59.1±56.1				55.5±63.9				62.2±48.7		0.554*
Sex													0.999†
Male	52	50.5		24	50.0				28	50.9			
Female	51	49.5		24	50.0				27	49.1			
Height (cm)			98.2±35.6				91.4±38.8				104.1±31.8		0.073*
Weight (kg)			20.4±16.4				17.4±16.8				22.9±15.7		0.091*
Intensive care stay (day)			-	-			2.0	1.0-6.0			-	-	
Hospital stay (day)			-	-			7.0	3.0-16.0			-	-	

SD: Standard deviation; * T test was used for independent groups. Descriptive statistics; † Fisher's exact test and Fisher's exact test were used. Descriptive statistics were given as n (%).

59.1±56.1 months; range, 1 month-18 years) aged between one month and 18 years who underwent congenital heart surgery were included. The children who underwent cardiac surgery and their mothers were included as the study group (n=48). The control group (n=55) included healthy children who were admitted to Ankara Training and Research Hospital during the study period and their mothers. A written informed consent was obtained from each parent. The study protocol was approved by the Ankara Training and Research Hospital, Ethics Committee (date, no: 15.01.2021, E-93471371-514.10). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Socio-demographic data of the children and their mothers were recorded. The World Health Organization Quality of Life-BREF (WHOQOL-BREF) questionnaire was administered to all mothers who participated in the study. The results were compared between the groups. Data including health status, physical health, psychological health, social relations, and environmental status were evaluated.

Statistical analysis

Statistical analysis was performed using the Microsoft Office Excel, Jamoviproject (2020), Jamovi (version 1.6.1) and JASP (version 0.13.1). Descriptive data were expressed in mean±standard deviation (SD), median (min-max) or number and frequency, where applicable. Normality test of numerical variables was checked using the Kolmogorov-Smirnov and Shapiro-Wilk tests. The independent t-test was used to compare two independent groups, while the Mann-Whitney U test was used when normal distribution

Table 2 Distribution of diseases in children in the study group		
Disease	n	%
Ventricular septal defect	22	45.80
Atrial septal defect	15	31.30
Others		
Aortic coarctation	11	22.9
Tetralogy of Fallot	4	8.30
Totally anomalous pulmonary venous connection	2	4.20
Single ventricular heart	1	2.10
Valvular disease	1	2.10
Patent ductus arteriosus	1	2.10

Table 3
Demographic and clinical characteristics of the mothers included in the study

	All (n=103)			Study group (n=48)			Control group (n=55)			<i>p</i>
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	
Maternal age (year)			35.0±7.8			34.3±8.6			35.5±7.1	0.445*
Education level (%)										0.552†
None	8	7.8		5	10.4		3	5.5		
Primary-secondary school	57	55.3		24	50.0		33	60.0		
High school	32	31.1		17	35.4		15	27.3		
University	6	5.8		2	4.2		4	7.3		
Marital status (%)										0.105†
Married	95	92.2		47	97.9		48	87.3		
Divorced	7	6.8		1	2.1		6	10.9		
Widow	1	1.0		0	0.0		1	1.8		
Additional disease (%)										0.057†
Yes	17	16.5		12	25.0		5	9.1		
No	866	83.5		36	75.0		50	90.9		

SD: Standard deviation; * T test was used for independent groups. Descriptive statistics; It was given as mean SD; † Pearson chi-square test and Fisher's exact test were used. Descriptive statistics were given as n (%).

assumption was unmet. For multiple comparisons, the Kruskal-Wallis test was used. The Pearson chi-square test was performed to examine the relationship between variables. A *p* value of <0.05 was considered statistically significant.

RESULTS

There were 48 patients in the study group with a mean age of 55.5±63.9 months and 55 healthy

children with a mean age of 62.2±48.7 months in the control group. There was no significant difference in the age, height, and weight values between the two groups (*p*=0.554, *p*=0.073, and *p*=0.091). The median length of intensive care unit (ICU) and hospital stay after surgical treatment was 2 (range, 1 to 6) and 7 (range, 3 to 16) days (Table 1).

In the study group, the most common diagnoses were ventricular septal defect in 22 (45.8%) patients

Table 4
Comparison of WHOQOL-BREF raw score and percentage score between groups

	All (n=103)	Study group (n=48)	Control group (n=55)	<i>p</i>
	Mean±SD	Mean±SD	Mean±SD	
Raw score				
Health status	6.3±1.8	5.7±2.0	6.8±1.5	0.004
Physical health	20.9±4.6	18.2±3.6	23.3±4.1	<0.001
Psychological health	19.6±3.7	18.0±3.5	21.1±3.2	<0.001
Social relations	9.4±3.1	8.0±3.3	10.6±2.5	<0.001
Environment	25.7±5.6	23.3±5.0	27.8±5.4	<0.001
Percentage point (%)				
Health status	53.6±22.7	46.6±24.7	59.8±19.0	0.004
Physical health	49.6±16.5	40.0±13.0	58.1±14.5	<0.001
Psychological health	56.8±15.2	49.9±14.5	62.7±13.3	<0.001
Social relations	53.9±25.5	42.9±26.5	63.3±20.5	<0.001
Environment	55.3±17.6	47.9±15.5	61.8±16.8	<0.001

SD: Standard deviation; WHOQOL-BREF: World Health Organization Quality of Life Scale Short Form T test was used for independent groups. Descriptive statistics; It was given as mean standard ± deviation. P values indicated in bold were considered statistically significant (*p*<0.05).

Table 5
Correlation of WHOQOL-BREF raw score and percentage scores with age, intensive care and length of stay in the study group

	Age		Intensive care stay		Hospital stay	
	Spearman Rho	<i>p</i>	Spearman Rho	<i>p</i>	Spearman Rho	<i>p</i>
Health status	0.156	0.290	-0.466	<0.001	-0.304	0.035
Physical health	0.239	0.102	-0.351	0.014	-0.380	0.008
Psychological health	0.089	0.547	-0.530	<0.001	-0.330	0.022
Social relations	0.134	0.364	-0.339	0.019	-0.385	0.007
Environment	0.062	0.675	-0.315	0.029	-0.279	0.055
Health status (%)	0.156	0.290	-0.466	<0.001	-0.304	0.035
Physical health (%)	0.239	0.102	-0.351	0.014	-0.380	0.008
Psychological health (%)	0.089	0.547	-0.530	<0.001	-0.330	0.022
Social relations (%)	0.124	0.408	-0.317	0.030	-0.362	0.012
Environment (%)	0.062	0.675	-0.315	0.029	-0.279	0.055

WHOQOL-BREF: World Health Organization Quality of Life Scale Short Form T test was used for independent groups. Spearman Rho correlation coefficient was used. The *p* values indicated in bold were statistically significant (*p*<0.05).

and atrial septal defect in 15 (31.3%) patients. Among the diseases in the other group, aortic coarctation was observed in four (8.3%) patients (Table 2).

The mean age of the mothers was 35.0±7.8 years. Primary-secondary school graduation was the most common (55.3%) educational status. Maternal age and education status were similar between the groups (*p*=0.445 and *p*=0.552). Ninety-five of the mothers (92.2%) were married. The number of mothers with a coexisting disease was 17 (16.5%). The most common comorbidity requiring drug therapy was hypothyroidism/hyperthyroidism (*n*=8). Four mothers (3.88%) used antidepressant drugs and two of them (1.94%) started using drugs due to poor health status of their children. There was no significant difference between the groups in terms of marital status and having comorbidities (*p*=0.105 and *p*=0.057) (Table 3).

According to the WHOQOL-BREF, the raw score and percentage point percentages of the fields (health status, physical health, psychological health, social relations and environment status) in the study group were significantly lower than the control group (*p*<0.05 for all) (Table 4).

There were significant negative correlations between the length of stay in the ICU and hospital, and the raw score and percentage scores of all WHOQOL-BREF subdomains (*p*<0.05 for all) (Table 5).

DISCUSSION

In Turkey, nearly 5,000 to 6,000 children need surgical treatment every year for congenital heart diseases.^[1] There are hundreds of very different and complex pathologies in this group. Due to the physiological process of the diseases and the complex nature of surgical applications, the level of anxiety in the mothers of these patients is high at every stage of surgical treatment, which may negatively affect the QoL.^[6]

Changes in the psychological status and QoL of sick children and their families affect many stages of treatment, but should also be considered as a social problem. Statistical findings and quality scales are used to improve the QoL of the mothers of these children.^[7]

Cardiac surgery procedures can be fearful for pediatric patients and their families. The individual who needs the most support at this stage is the mother. The mother must be supported psychologically and mentally at every stage of the treatment. The key is that clinicians have emphasized physical and psychological health, social relationships, and environment domains of mothers. Assessment of QoL by using specific tests can be a guide for determining the need for support and therapy. Also, these tests are useful in evaluating the treatment plan and effectiveness.

In our study, four mothers used antidepressant drugs and only two of them were related to their children's cardiac diseases. However, awareness of mothers about their psychological status is significantly low, leading to poor QoL. Providing professional psychological counseling can be beneficial both in terms of increasing awareness and identifying patients who would be given advanced treatment such as drug therapy or psychiatric support. By increasing the awareness, it may be possible to draw the attention of physicians, nurses, and other health personnel who provide health services to this issue.

However, all QoL scores were significantly lower in the study group, length of stay in the ICU and hospital were related to poor QoL scores. We believe that these mothers deserve to be taken into account specifically.

Quality of life should be improved by recognizing and supporting mothers who are in a difficult process by determining what the changes in QoL are and their severity.^[8] In this way, both the psychological development of sick children and their mothers is supported and social psychological recovery is contributed. For this purpose, in our study, we evaluated the QoL with a questionnaire study among mothers of children with heart disease who underwent surgery.

The data in this study are based on the responses of the voluntary participating mothers to the questionnaires. As the results were subjective, they may have been affected by ethnic changes. The statistical significance between changes could have been increased with a higher number of participants.

In conclusion, the physical health, psychological health, social relations and environmental status of the mothers of children undergoing cardiac surgery seem to be significantly lower compared to healthy mothers.

We believe that it is important to increase the QoL of these mothers with psychological support.

Declaration of conflicting interests

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Does Shamblin classification affect the clinical outcomes following carotid body tumor excision?

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ABSTRACT

Objectives: In this study, we present the late results of patients who underwent carotid body tumor (CBT) resection and compared postoperative complication rates according to the Shamblin classification.

Patients and methods: Between April 2012 and April 2019, a total of 55 consecutive patients (20 males, 35 females; mean age: 56.2±1.8 years; range, 38 to 62 years) who were operated for CBTs were retrospectively analyzed. The patients were classified according to the Shamblin classification. Demographic and clinical characteristics of the patients, postoperative complications, total amount of drainage, and length of hospital and intensive care unit stay were recorded.

Results: Carotid body tumors were bilateral in five patients, while they involved only the right side in 23 and left side in 27 patients. The CBTs were Shamblin type 1 in 16, type 2 in 31, and type 3 in eight patients. Intraoperative vascular reconstruction was required in eight patients. Early postoperative morbidities were transient ischemic attack (TIA) in three, cranial involvement in nine, middle cerebral artery occlusion in one, dysphonia in six, dysphagia in six, and hemiparesis in one patient. Permanent neurological damage (hoarseness 10.9%, ptosis 45%, internal carotid artery 1.81%) was seen in 18.2% of the cases. The length of stay in the hospital and intensive care unit, total amount of drainage, rates of postoperative cranial nerve involvement, permanent neurological damage, disease recurrence, postoperative TIA, and dysphagia were found to be significantly increased in patients in the Shamblin type 3 ($p<0.005$).

Conclusion: Surgery can be performed safely in Shamblin type 1 and 2 tumors, while surgery requires a more meticulous manipulation for type 3 tumors, as these tumors are associated with high cranial nerve damage and complication rates.

Keywords: Carotid body tumors, neurological deficit, Shamblin classification.

Carotid body tumors (CBTs) are rarely vascular neoplasms arising from paraganglionic cells (precursors of neural crest tissues) of the carotid bifurcation. The incidence of CBT is about 1/30,000.^[1] These tumors are bilateral in 10% and familial in 10% of the cases.^[2] Compared to all head and neck tumors, its overall incidence is less than 0.5% and its annual incidence is 0.001%.^[3] Clinically, CBTs are palpable on physical examination as insensitive rubbery pulsatile masses.^[4] These masses can be displaced both horizontally and vertically due to their adhesion to the carotid artery.^[5] Although these tumors are histopathologically benign, they can be considered clinically malignant due to their involvement in neurovascular structures and intracranial invasion. The disease is thought to develop secondary to chronic hypoxia at higher altitudes.^[2]

Surgical excision of CBTs is the gold standard for curative treatment of CBTs.^[6] In 1971, Shamblin et al.^[7] divided them into three categories according to the tumoral invasion of the carotid artery (Table 1).

Surgical removal of CBTs is challenging due to their close proximity to the vital structures (Figure 1).^[8]

Asymptomatic patients usually present to the outpatient clinic with complaints of swelling on the neck. The diagnosis is often confirmed by Duplex ultrasound, computed tomography (CT), magnetic resonance imaging (MRI) and, rarely, conventional angiography.^[9]

In this study, we present the surgical results of CBT resection and long-term outcomes of patients who underwent glomus tumor resection in our clinic.

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Type 1	Tumor minimally invades the carotid artery. It is easy to excise
Type 2	Tumor partially invades the carotid artery. It is adhered to adventitia.
Type 3	Tumor completely surrounded the carotid arteries. Carotid revascularization is required.

Additionally, the necessity and complication rates of vascular reconstruction without embolization and devascularization of the external carotid artery (ECA) in surgically resected CBTs were discussed.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at University of Health Sciences, Koşuyolu High Specialty Education and Research Hospital, Cardiovascular Surgery between April 2012 and April 2019. A total of 55 consecutive patients (20 males, 35 females; mean age: 56.2±1.8 years; range, 38 to 62 years) who were operated for CBTs were included. Duplex ultrasonography, CT, and MRI were used for diagnostic purposes. Tumors were classified according to the Shamblin classification. Diagnostic angiography was performed for tumors

larger than 4 cm. The purpose of performing angiography in these patients was to identify intracerebral circulation and determine the possible indication of carotid artery clamping. Preoperative embolization was not performed in any patient.

Demographic data, clinical presentations, bilaterality, family history, and tumor size were recorded. Postoperative complications (neurological events, cranial nerve injury), total amount of drainage, stay in intensive care unit, and hospital stay were evaluated. Early mortality was defined as hospital mortality within 30 days. Follow-up data were obtained from the outpatient records of the hospital registry. The patients who were followed outside the reference hospital were contacted by telephone and the assessment was performed based on their medical records.

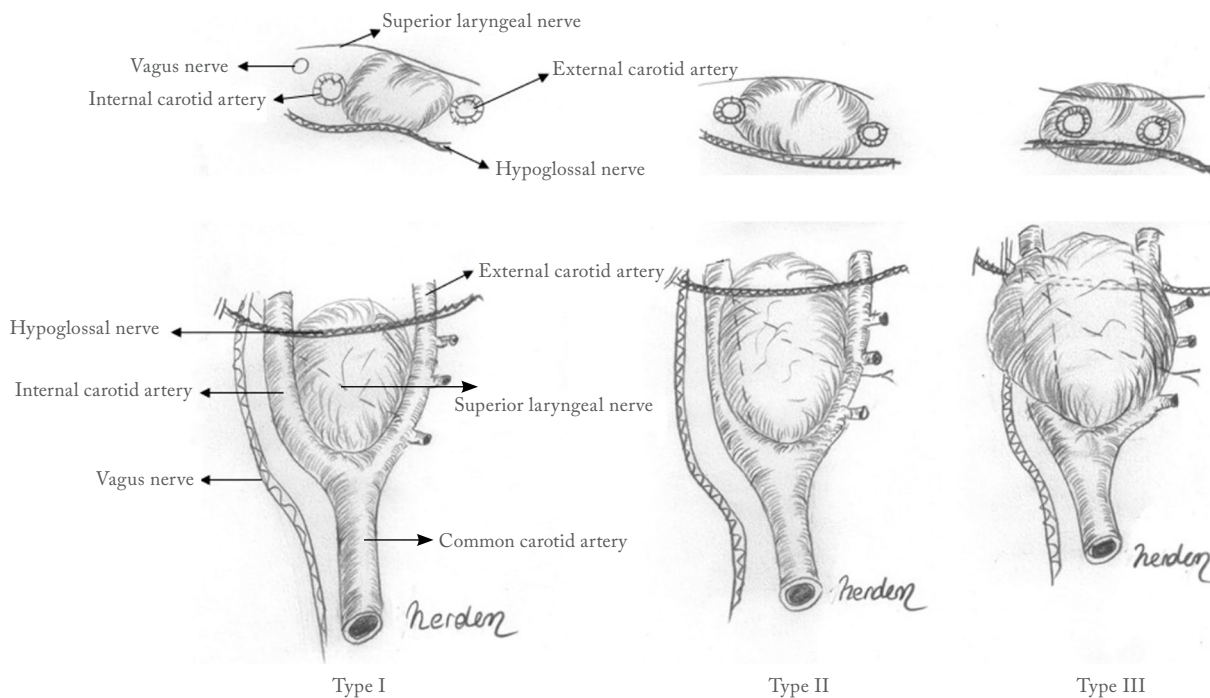


Figure 1. Shamblin classification.

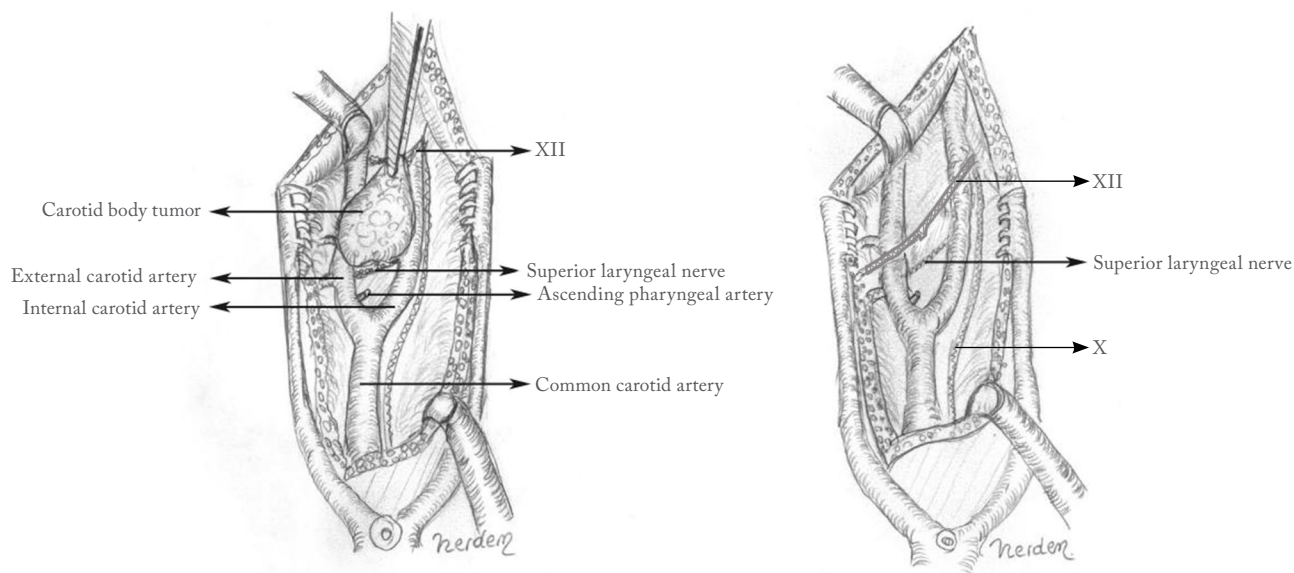


Figure 2. Illustration for carotid body tumor resection.

Surgical technique

Under general anesthesia, all patients were placed in supine position on the operating table with their necks in hyperextension. After the head was brought to extension, it was turned away from the side to be

operated. The area with the lesion was positioned on the upper side. The surgical intervention was initiated with a vertical 5 to 8-cm incision extended vertically along the anterior edge of the sternocleidomastoid muscle toward the earlobe and sternal (notch) jugulum.

Table 2 Baseline characteristics of study population			
	n	%	Mean±SD
Age (year)			56.2±1.79
Sex			
Male	20	35.7	
Female	35	62.5	
Symptoms			
Swelling in the neck	37	67.3	
Dizziness	11	20	
Others	7	12.7	
Laterality			
Right	23	41.1	
Left	27	48.2	
Bilateral	5	9.1	
Shamblin types			
1	16	28.6	
2	31	55.4	
3	8	14.3	
Tumor size (on longitudinal axis)			
<4 cm	30	3.6	
>4 cm	25	44.6	
SD: Standard deviation.			

Table 3
Postoperative complications

Complications	n	%
TIA	3	5.4
Cranial nerve involvement	8	14.5
5	1	1.8
7	4	7.2
9	1	1.8
10	1	1.8
12	1	1.8
MCA occlusion	1	1.8
Dysphonia	6	10.9
Dysphagia	6	10.9
Horner syndrome	2	3.6
Permanent neurological damage	10	18.2
Inadequate resection	7	12.7

TIA: Transient ischemic attack; MCA: Middle cerebral artery.

Common carotid artery, internal carotid artery (ICA), ECA, and superior thyroid artery were wrapped, retracted with a tape, and kept under control.

During the operation, arterial blood flow was not interrupted by clamping, any shunt was not used and, therefore, heparinization was not performed. Before resection of the tumor, vagus and hypoglossal nerves were identified. Bipolar cautery was used to reduce bleeding and minimize nerve damage. The necessary areas were dissected bluntly with cautery. The cleavage between the carotid artery

and the tumor was identified under adventitia, and the dissection was initiated from the appropriate place. Thanks to the appropriate surgical maneuvers performed, the tumors were often resected almost completely (Figure 2).

Since Shamblin type 3 tumors with a greater diameter progressed toward the skull base and surrounded vascular structures more closely, surgery was terminated in a certain area. Blood pressure was followed with arterial monitoring, and cerebral oxygenation was monitored with cerebral near-infrared spectroscopy. For monitoring, arterial blood pressure were attempted to be kept at normotensive levels.

All patients were scheduled for follow-up using Doppler ultrasound at one and six months and annually thereafter. In patients with a positive family history or tumor recurrence history, annual controls were performed with MRI.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 23.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean \pm standard deviation (SD), median (min-max) or number and frequency. The Kolmogorov-Smirnov normality test was used to examine the distribution of variables. One-way analysis of variance (ANOVA) was used to compare variables showing normal distribution among multiple groups, while the Tukey test and Bonferroni correction analyses were used in the comparison of subgroups. In a comparison of more

Table 4
Postoperative outcomes according to Shamblin classification

Postoperative complications	Shamblin 1		Shamblin 2		Shamblin 3		<i>p</i>
	n	Mean \pm SD	n	Mean \pm SD	n	Mean \pm SD	
ICU stay		1.9 \pm 0.1		1.9 \pm 0.1		5.4 \pm 2.4	0.003
Hospital stay		7.9 \pm 0.6		9.3 \pm 0.7		17.9 \pm 6.6	0.248
Drainage (mL)		48.4 \pm 6.3		68.8 \pm 12.8		118.8 \pm 26.6	0.004
Permanent neurological damage	1		2		7		0
TIA	0		0		3		0.01
Dysphagia	0		2		4		0.003
Dysphonia	0		3		3		0.055
Cranial nerve involvement	1		2		6		0.013
Recurrence	0		2		5		0.013

SD: Standard deviation; ICU: Intensive care unit; TIA: Transient ischemic attack.

than two independent samples that were not normally distributed, the Kruskal-Wallis test was employed. A p value of <0.05 was considered statistically significant.

RESULTS

The patients presented to the outpatient clinic for isolated swelling on the neck ($n=37$, 67.3%), dizziness ($n=11$, 20%), and other indications ($n=7$, 12.7%). Preoperative neurological findings were normal in all patients. All patients were evaluated by CT preoperatively. The MRI was performed in 33 patients and preoperative angiography in six patients. Baseline characteristics of the patients are presented in Table 2. The largest and the smallest CBTs were $7.7 \times 5.5 \times 5.4$ cm in diameter and $1.13 \times 0.77 \times 1.3$ cm in diameter, respectively. In four patients with Shamblin type 3 CBTs, ICA was repaired with grafts ($n=4$, 7.2%). A saphenous patch was used in one (1.81%) patient, and the polytetrafluoroethylene (PTFE) patch in three (5.4%) patients. The ECA was ligated in three (5.4%) patients.

The median follow-up was five (range, 2 to 9) years. There was no disease-specific mortality during the follow-up period. One ($n=1$, 1.81%) patient died of coronary artery disease five months after surgery. Disease recurrence ($n=4$) or insufficient resection ($n=3$) was seen in seven ($n=7$, 12.72%) Patients. These patients received postoperative radiotherapy. Postoperative neurological complications were shown in Table 3.

The length of stay in the intensive care unit, duration of hospital, total amount of drainage, rates of postoperative cranial nerve involvement, permanent neurological damage, disease recurrence, postoperative transient ischemic attack, and dysphagia were found to be increased significantly in patients in the Shamblin type 3 subgroup, compared to the other groups ($p<0.05$). Table 4 shows the comparison of postoperative results according to by Shamblin type.

DISCUSSION

Total resection is recommended due to the rare malignant potential of CBTs. Resection can be technically difficult in patients with a larger tumor size and, particularly, in cases with Shamblin type 3. Detection of the tumor when it is of small size results in favorable surgical outcomes, whereas a scarce

number of clinical symptoms in the early period may lead to the establishment of the diagnosis of these tumors in the long-term when they reach larger sizes. In this study, almost half of the patients had tumors larger than 4 cm. Surgical risk is higher in patients with Shamblin type 3 CBTs and, particularly, in cases with large tumoral masses. We believe that the major challenge in CBT management is the late referral of patients to surgery due to the difficulties in diagnosis.

Histopathological analysis of the tumor reveals a weak malignant potential in 5% of glomus tumors. Therefore, malignancy is defined only by the presence of distant metastases.^[10] In this study, any evidence of malignancy was not found in the follow-up period of patients. There is a familial predisposition in 7 to 9% of the cases.^[2] In this study, family history was obtained in only four (7.27%) patients. In this series, 35 women (63.6%) and 20 men (36.6%) were included. Bilateral CBTs were seen in 10% of the cases. In this report, these rates are consistent with the literature (9.1%) (Figure 3).^[2]

The risk of cranial nerve paralysis has been reported at a rate of 10 to 40% in surgical resection of CBTs.^[11,12] Therefore, the risk of serious complications after surgical treatment appears to be an important factor in decision-making for each individual patient. In our study, this rate was 18.2%.



Figure 3. Computed tomography image showing bilateral carotid body tumors.

Surgery is the definitive treatment method in the management of CBTs, but conservative approaches or radiotherapy can be also used in these patients.^[13] Despite the satisfactory results of the early grade of tumors, Shamblin type 3 tumors and tumors larger than 4 cm remain challenging cases for surgeons. Some attempts have been considered to facilitate surgery and reduce the associated complications. In the 1980s, considering the tumor receiving the blood supply from the ECA, devascularization of the ECA was suggested.^[14,15] Contrary to this assumption, in our experience, ligation of the ECA does not often reduce blood loss and does not facilitate dissection of the bifurcation.

Preoperative embolization before CBT surgery has become to be a current trend to reduce tumor size, surgical bleeding, and resection related complications.^[16] However, the effectiveness of embolization is still controversial.^[17] With the advances in endovascular surgery and prevalent use of coated stents, the collaterals of the tumor fed from the ECA have been bypassed, leaving the tumor to shrink or even disappear. These limited case reports suggest that without the use of intra-arterial gel foams, the risk of peri-procedural stroke may be reduced.^[14] However, these techniques are rarely used. In our study, we did not use any of the aforementioned techniques.

Although external radiotherapy is still a controversial treatment option, it can be used in patients in whom CBTs cannot be surgically removed.^[18,19] It has been demonstrated that radiotherapy slows down or temporarily stops tumor growth, but it is not a curative approach.^[19] In addition, in inoperable elderly patients and patients with multisystemic disease, considering the slow growth rates of their CBTs, watchful waiting or external radiotherapy may be a more appropriate treatment method.^[20,21] The long-term results of this treatment have not been shown, yet. Although radiotherapy is an appropriate approach for elderly patients, it is not a sufficient treatment for the young age group.^[22,23] In our seven patients, radiotherapy was used due to inadequate resection or disease recurrence.

In the treatment of Shamblin type 1 and 2 CBTs, removal of the tumor with careful subadventitial dissection is preferred. In type 3 tumors, reconstruction of the ECA or ICA may be required.

If massive bleeding occurs in type 3 tumors, the mass can be removed by clamping the arteries and, in the event of further damage occurring during the procedure, vascular reconstruction may be indicated. While eight of our patients required reconstruction, in three cases, ECA was ligated due to bleeding. Surgical removal of the tumor should be definitely preferred in patients with Shamblin type 3 tumors, and in patients under 50 years of age with long life expectancy.^[4,24]

This study has several limitations that are inherent due to the retrospective design. We were unable to perform preoperative embolization to any patient during our study period. In particular, the high complication rates in Shamblin type 3 class patients may indicate the need for pre- or intraoperative devascularization strategies in this patient group. In addition, the low number of Shamblin type 3 patients in the study period may have caused the complication rates in this patient group to be overestimated.

In conclusion, we believe that Shamblin type 1 and type 2 tumors can be treated safely with surgery and, since type 3 tumors are associated with high cranial nerve damage and high complication rates, a special attention is required during surgery, and radiotherapy would be a treatment alternative in cases with recurrent tumors and metastases.

Declaration of conflicting interests

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Comparison of electrocautery and LigaSure™ vessel sealing system in radial artery harvesting as coronary artery bypass surgery conduit: A prospective, randomized study

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ABSTRACT

Objectives: In this study, we aimed to compare the efficiency of electrocautery with the LigaSure™ vessel sealing system.

Patients and methods: This randomized study included a total of 53 patients (44 males, 9 females; mean age: 63.7±8.4 years; range, 39 to 83 years) who underwent coronary artery bypass grafting (CABG) for radial artery (RA) harvesting with electrocautery or LigaSure™ vessel sealing system between January 2019 and September 2019. The patients were randomly assigned into two groups. Group 1 consisted of 27 patients operated with the LigaSure™ small jaw sealer/divider and Group 2 consisted of 26 patients operated with electrocautery. The length of the conduit, the amount of intraoperative blood loss, the number of hemostatic clips before and after the anastomosis, the amount of postoperative blood loss, the number of ecchymoses, hematoma and infection are compared.

Results: The amount of blood loss from the beginning of harvesting to the end of the closure of the skin of left arm was significantly lower in Group 1 ($p=0.004$). The difference in the number of hemostatic clips before and after the anastomosis of RA to coronary artery was statistically significantly lower in Group 1 ($p<0.001$ and $p<0.001$, respectively). There was no statistically significant difference in the amount of blood loss postoperatively ($p>0.6$), number of ecchymoses ($p>0.1$), and postoperative hematoma ($p>0.1$) and infection ($p>0.03$) between the groups.

Conclusion: Our study results suggest that the LigaSure™ vessel sealing system is a better option of RA harvesting, particularly in patients who are prone to bleed.

Keywords: Cardiovascular pathology, coronary arteries, coronary circulation.

The radial artery (RA) is an excellent and a widely used conduit in coronary artery bypass grafting (CABG) owing to its own anatomical advantages for coronary revascularization. It is the most commonly used conduit after left internal mammary artery.^[1] The major advantages are its muscular wall adapting to the arterial blood pressures, the luminal diameter that is 1.8 to 2.7 mm in local populations which is similar to that of the coronary arteries,^[2] and the length that is >20 cm.^[3] Also, as an arterial conduit lacks valves on the contrary of venous conduits, the luminal diameter usually remains unchanged throughout the length of the vessel.

The increasing usage of RA as a coronary artery conduit demands clinicians to improve the techniques of harvesting for greater clinical outcomes. The RA can be harvested endoscopically or by open techniques. In the open setting, harvesting can be done by sharp dissection, electrocautery, harmonic scalpel or vessels sealing device.

In the literature, there is no study comparing different open surgery techniques in RA harvesting. In the present study, we aimed to investigate the intra- and postoperative variables between RA harvesting with electrocautery and LigaSure™ small jaw device in open CABG.

PATIENTS AND METHODS

This prospective, randomized study was carried out in the Department of Cardiovascular Surgery, Acibadem Altunizade Hospital between January

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2019 and September 2019. Patients with more than 90% stenosis of the coronary artery and those who were scheduled for CABG were screened. A total of 53 patients (44 males, 9 females; mean age: 63.7±8.4 years; range, 39 to 83 years) who underwent CABG for RA harvesting with electrocautery or LigaSure™ vessel sealing system were included. Both techniques were described in detail to all participants before the operation. A written informed consent was obtained from each patient. The study protocol was approved by the Acibadem Mehmet Ali Aydınlar University, Ethics Committee (Date: 21/03/2019; No: 2019/6-30). The study was conducted in accordance with the principles of the Declaration of Helsinki. The Allen test was performed to all patients. The patient's left arm was supinated and pulse oximeter was placed on the index finger of the left hand. Radial and ulnar arteries were palpated, and both were compressed until the pulse oximeter trace was present. Afterwards, the ulnar artery was released, and seconds were counted until the trace was fully returned. A positive result was considered between 3 and 5 sec, indicating a patent ulnar artery. The patients with a positive Allen test result were enrolled. By using a computer-generated random list, all patients were randomized into two groups. Group 1 consisted of 26 patients operated with the LigaSure™ (Medtronic, Minneapolis, MN, USA) small jaw sealer/divider (LF1212A) for RA harvesting during open CABG surgery and Group 2 consisted of 27 patients operated with low-energy electrocautery (Erbe Elektromedizin GmbH, Tübingen, Germany). Electrocautery is a device used for hemostasis and tissue dissection using direct or alternative current to generate heat. The LigaSure™ small jaw is a vessel-sealing device that uses both electrothermal energy and pressure.^[4]

The lengths of the harvested RAs, duration of the harvest, amount of blood loss from the beginning of harvesting to the end of the closure of the skin of the left arm, number of hemostatic clips before and after the anastomosis of RA to coronary artery, amount of blood loss postoperatively, presence of ecchymoses, hematoma and infection were compared. The length of the RA was measured in cm. The amount of blood loss per operatively was measured by the number of gauzes used for left arm, and one gauze was estimated to absorb 10 mL. The amount of blood loss postoperatively was evaluated by the mL of blood collected in the drainage bag. Ecchymoses,

hematoma, and paresthesia were documented as the absence or presence, 1 and 0, respectively. The length of the conduits was measured in cm. The duration of the harvest of the left RA was considered to be from the first incision of the left forearm to the freeing of the conduit. Data including age, sex, and body surface area (BSA) were recorded.

Subcutaneous tissue and fascia were dissected with the LigaSure™ curved, small jaw, open sealer /divider after the cutaneous incision in Group 1. Although the dissections were done mainly with the LigaSure™, some of the thin branches were dissected with scissors. The branches were freed from the RA at the distance of 2 mm with the LigaSure™. After the dissection was done, RA was ligated distally. Branches were clamped with bulldog clamps and the bleeding was checked. Branches larger than 5 mm were clipped. After the proximal and distal anastomosis were done, the branches were controlled and bleeding branches were clipped.

Once the incision was done along the length of the RA, subcutaneous tissue and fascia were dissected with electrocautery in Group 2. The branches of RA were dissected with scissors along the length. All branches were clipped with small titanium hemoclips (Horizon™ ligating clips; Weck-Teleflex, North Carolina, USA), and tissue side was tied with 4.0 silk. After the dissection was done, the RA was cut distally and clamped with bulldog clamps. The branches were checked by the antegrade flow. Leaking branches were clipped. After the proximal and distal anastomosis were done, the branches of the artery were controlled and clipped.

Statistical analysis

Statistical analysis was performed using the SPSS version 9 software (SPSS Inc., Chicago, IL, USA).

Table 1
Demographic characteristics of patients

Parameters	Group 1		Group 2	
	%	Mean	%	Mean
Age (year)		64.2±6.7		63.3±9.8
Sex				
Male	81.4		84.6	
Female	18.6		15.4	
BSA (m ²)		1.4±0.2		1.31±0.2
BSA: Body surface area.				

Parameters	Group 1	Group 2	<i>p</i>
	Mean	Mean	
Amount of bleeding (mL)	47.0±24.3	102.3±65.4	0.004
Number of hemostatic clips used before harvest	0.1±0.3	0.8±1.1	0
Number of hemostatic clips used after harvest	0.3±0.6	1.7±1.8	0

Parameters	Group 1		Group 2		<i>p</i>
	n	Mean	n	Mean	
Amount of blood loss postoperatively (mL)		19.2±15.1		19.8±16.8	0.682
Number of patients with ecchymoses	8		6		0.104
Number of patients with hematoma	2		4		0.171
Number of patients with surgical site infection	1		0		0.039

Continuous variables were expressed in mean ± standard deviation (SD) or median (interquartile range [IQR]), while categorical variables were expressed in number and frequency. Continuous variables were compared using the Student's unpaired t-test. Categorical variables were compared using the chi-square test. A *p* value of <0.05 was considered statistically significant.

RESULTS

Baseline demographic characteristics of the patients are shown in Table 1. During the study, 53 patients were operated. There were no significant differences in age and BSA between the groups.

The mean length of the RAs was 12.4±1.2 cm in Group 1 and 13.0±1.9 cm in Group 2. The difference in duration of the harvest between the groups was statistically non-significant (*p*=0.804). The amount of blood loss from the beginning of harvesting to the end of the closure of the skin of the left arm was

significantly less in Group 1 (*p*=0.004). The difference in the number of hemostatic clips before and after the anastomosis of RA to coronary artery was also statistically significantly less in Group 1 (*p*<0.001 and *p*<0.001, respectively) (Table 2).

The amount of postoperative blood loss (*p*>0.6), number of ecchymoses (*p*>0.1), and postoperative hematoma (*p*>0.1) and infection (*p*>0.03) were comparable, indicating no statistically significant difference (Table 3).

The duration of the harvest and the length of the conduits are given in Table 4. The one-year survival rate of the patients was 100%. The patency rates of the conduits was planned to be determined after the control coronary angiography of the patients at the end of the 5th and 10th years. No control coronary angiography at the end of the first year was planned, due to the cost of angiographic procedures at the hospital setting.

Parameters	Group 1	Group 2
	Mean	Mean
Duration of harvest (min)	41.8±8.3	38.6±8.3
Length of the conduit (cm)	12.4±1.2	13.0±1.9

DISCUSSION

The LigaSure™ sealing systems use bipolar radiofrequency and pressure to merge the collagen and elastin within the walls of vessels.^[5] The effects of the LigaSure™ sealing systems have been a subject of studies, particularly in colorectal, urological, and gynecological surgeries. Nevertheless, the number of

studies using this device in CABG surgeries is still limited. In our study, the use of this device in RA harvesting was described.

Although electrocautery is a widely used instrument in various surgeries for tissue dissection, there are several undesired effects in graft harvesting for CABG surgeries. In a study, electrocautery was found to induce more spasms and intimal injuries, compared to harmonic scalpel.^[6] It was also reported in another study that preparation for harvesting the RA using electrocautery took more time than using ultrasonic cautery during CABG and the amount of postoperative drainage was significantly lower in the later technique.^[7]

The LigaSure™ is a relatively new device in CABG surgeries. Although more studies are needed in this context, a study showed lower mean operative time in patients who underwent thyroidectomy using the LigaSure™ rather than conventional clamp tie and electrocautery technique.^[8] In a retrospective, observational study, the LigaSure™ usage resulted in lower blood loss and fewer blood transfusions and perioperative complications than suturing in the peripartum hysterectomy.^[9] In another study, the LigaSure™ system reduced the volume of blood transfusions and intraoperative blood loss.^[10] In CABG, blood flow through the internal thoracic artery was found to be sufficient in a study to be used as a conduit.^[11]

Harmonic scalpel is a device that dissects and cauterizes the tissue simultaneously.^[12] In a retrospective study, the use of a harmonic scalpel was associated with shorter dissection time with similar risks to conventional internal mammary artery harvesting.^[13] Compared to blunt and sharp dissection, harmonic scalpel resulted in less spasm of the RA during CABG.^[14] Nevertheless, harmonic scalpel resulted in more graft edema and longer operation duration than electrocautery in RA harvesting.^[15] In our study, the amount of intraoperative blood loss was less during the use of LigaSure™ compared to electrocautery.

In conclusion, the significant difference in the amount of blood loss from the beginning of harvesting to the end of the closure of the skin shows a promising use of the LigaSure™ in patients who are prone to bleed. Although further large-scale studies are needed to show the differences in variables studied in this study and others, the outcomes of this study

are encouraging for the LigaSure™ to be used in the CABG.

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Mid- and long-term results in patients with thoracic endovascular aortic repair

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ABSTRACT

Objectives: In this study, we aimed to examine the mid- and long-term results of the patients undergoing thoracic endovascular aortic repair (TEVAR) in our clinic.

Patients and methods: Between June 2006 and October 2018, a total of 71 patients (59 males, 12 females; mean age: 60.9±13.3 years; range, 17 to 79 years) who underwent TEVAR electively or urgently were retrospectively analyzed. Data including demographic and clinical characteristics of the patients and operative data were recorded.

Results: Of the patients, 22 (31%) were urgently operated and 49 (69%) were electively operated. Cerebrovascular disease (CVD) developed in three (4.2%) patients. Thirty-day overall survival of patients who were operated on emergency was found to be 72.7%, and this rate was 98% in elective patients (p=0.001). One-year overall survival of our patient series was 76.1%. One-year survival rate of emergency patients was 54.5%, and this rate was 85.7% in elective patients (p=0.002). Two-year overall survival of emergency patients was 45.5% and it was 79.6% in elective patients (p=0.002). While the survival rate of preoperative smokers after two years was 60.8%, it was calculated as 90% of preoperatively non-smokers (p=0.022).

Conclusion: Thoracic endovascular aortic repair treatment seems to show similar results to open surgery in terms of mortality and other complications in the mid- and long-term. With the developing stent-graft technology, TEVAR results can be even better in the future.

Keywords: Mortality, thoracic aortic aneurysm, thoracic endovascular aortic repair.

Standard conventional surgical treatment of thoracic aortic aneurysms (TAAs) is still associated with high mortality and morbidity. The risks of open surgical methods are quite high due to factors such as long clamping times, cardiac stress during clamping, protection of the medulla spinalis, and the use of extra-corporeal circulation. Alternative methods have been sought in the treatment of aortic aneurysms to minimize these risks. For the first time in 1991, Parodi et al.^[1] reported successful endovascular treatment in patients with abdominal aortic aneurysms. Over time, endovascular stent grafts have started to be used in patients with TAA, and very good results have been reported, particularly in the early period.^[2,3] One of the most important disadvantages in the applicability of endovascular treatment is that the patient requires anatomical compatibility. The scope of anatomical suitability criteria has expanded due to the recent advances in technology and increasing surgical experience. In addition, thoracic endovascular aortic repair (TEVAR) has been applied to some patients who are anatomically unsuitable with hybrid procedures.

The main disadvantages of TEVAR are endoleaks and graft migration. Currently, endovascular methods are widely used as an alternative to classical surgical treatment thanks to the developing technology, increasing surgical experience, the introduction of hybrid procedures, and the advantages it provides in the early period. However, in the long term, TEVAR seems to lose its advantages due to endoleak in the early and mid-term due to problems such as graft migration and the growth of aneurysm sac.

In this study, we aimed to examine the mid- and long-term results of patients undergoing TEVAR in our clinic.

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PATIENTS AND METHODS

This single-center, retrospective study was conducted at Izmir Atatürk Training and Research Hospital, Cardiovascular Surgery Clinic between June 2006 and October 2018. A total of 83 patients who underwent TEVAR electively or urgently were screened. Of these patients, 12 were excluded from the study due to missing data. No other exclusion criteria were applied. Finally, a total of 71 patients (59 males, 12 females; mean age: 60.9 ± 13.3 years; range, 17 to 79 years) were included in the study. A written informed consent was obtained from each patient. The study protocol was approved by the Izmir Katip Celebi University, Faculty of Medicine, Clinical Research Ethics Committee (date, no 18.06.2020, 0228). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Data including age, sex, smoking history, hypertension, diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), previous cerebrovascular disease (CVD) and prior cardiovascular disease were recorded. On preoperative computed tomography (CT), the aneurysm and normal aortic diameters, pre- and postoperative laboratory blood values, transthoracic echocardiography findings, proximal and distal landing zone and diameters, oversize percentages, extubation, intensive care unit (ICU) stay and discharge times, endoleak development, and type and use of additional stent graft, the need for additional surgical interventions, need for debranching, blood product requirement and amount, stent graft diameters, and mortality rates were evaluated. All data were collected using the file archive of our clinic and the computer records of the patients. The patients who were asymptomatic and had degenerative or traumatic aneurysms exceeding 5.5 cm, the patients who had saccular aneurysms, and all symptomatic TAAs were managed by endovascular techniques.

General anesthesia was administered to the majority of the patients. The patients with comorbidities underwent local anesthesia + sedation. Following proper site cleaning, all patients were covered using sterile drapes. In the surgical method we used, the access route was preferred as the femoral region in all our patients. Common femoral artery, superficial femoral artery, and profunda femoris artery were rotated one by one with nylon tape through a femoral incision from the side with suitable iliac anatomy. After the femoral arteriotomy, the hydrophilic guidewire

was advanced over the catheter from the ascending to the aorta. In most cases, the Medtronic® (Medtronic Inc., Minneapolis, MN, USA) graft brand was used, as it was easier to reach these grafts in emergency cases. In 18 cases, the left subclavian artery was closed in our endovascular graft application and three cases required left subclavian bypass. No fenestrated graft was used in any of the cases.

Statistical analysis

Statistical analysis was performed using the IBM SPSS for Windows version 22.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean \pm standard deviation (SD) for normally distributed variables and in median (min-max) for non-normally distributed variables. Categorical variables were expressed in number and frequency. The Pearson chi-square and Fisher's exact tests were used to analyze categorical variables. The compliance of continuous variables to normal distribution was examined using visual (histogram) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). The t-test was used for the comparison of normally distributed variables between two groups, and the Mann-Whitney U test was used for the comparison of variables that did not show normal distribution between the two groups. The survival rates were calculated using the Kaplan-Meier survival analysis. The effects of variables on survival were analyzed using the log-rank test. Possible factors whose effects on survival were analyzed in the univariate analysis were included in the Cox regression analysis with backward and enter selection methods. A p value of <0.05 was considered statistically significant.

RESULTS

Baseline demographic and clinical characteristics of the patients are shown in Table 1. Of the patients, 22 (31%) were urgently operated and 49 (69%) were electively operated. Of the patients, four (5.6%) had a saccular aneurysm and 67 (94.4%) had a fusiform aneurysm.

The median follow-up was 51.3 (range, 17 to 78 years) months. Of the patients included in the study, 53 (74.6%) were smoking and 25 (35.2%) had a history of COPD. Nineteen (26.8%) of the patients had DM, 25 (35.2%) had hyperlipidemia, 15 (21.1%) had a history of chronic renal failure, 14 (19.7%) had coronary artery disease,

16 (22.5%) had peripheral artery disease, and six (8.5%) had a history of previous CVD (Table 1). Blood product was used in seven patients. A total of 28 units of blood products were used. The median length of stay in the ICU was 3.4 (range, 1 to 28) days. While general anesthesia was applied to 64 of the patients, TEVAR operation was performed under local anesthesia and sedation for seven of them. Proximal landing zone was 0 in one patient (1.4%), 1 in four patients (5.6%), 2 in 13 patients (18.3%), 3 in 36 patients (50.7%), 4 in 17 patients (24%) according to the Ishimaru classification. The mean proximal landing zone diameter was 31.1±5.5 mm, while the mean distal landing zone diameter was 30.8±7.3 mm.

No additional surgical intervention was performed in 63 (88.7%) of the patients. Carotico-subclavian bypass was performed in five (7%) patients, and subclavian-subclavian bypass was performed in three (4.2%) patients. Celiac artery was closed in only two (2.8%) of the cases (Table 2).

Table 1		
Demographic and clinical characteristics of patients (n=71)		
Variables	n	%
Age (year)		
17-40	6	8.4
41-75	61	86
>75	4	5.6
Sex		
Male	59	83.1
Smoking history	53	74.6
Associated diseases		
Hypertension	58	81.7
COPD	25	35.2
Diabetes mellitus	19	26.8
Hyperlipidemia	25	35.2
Chronic renal failure	15	21.1
Coronary artery disease	14	19.7
Peripheral artery disease	16	22.5
Previous CVD	6	8.5
Previous cardiac operations	13	18.3
Etiology in cases		
Degenerative aneurysm	53	74.6
Dissecting aneurysm	7	9.9
Dissection	1	1.4
Trauma	5	7
Connective tissue disease	5	7
COPD: Chronic obstructive pulmonary disease; CVD: Cerebrovascular disease.		

Additional balloons were required in 32 (45.1%) of the patients. While no endoleak developed in 52 (73.2%) patients on angiography performed after the procedure, 19 patients (26.8%) developed endoleaks.

Table 2		
Operative data (n=71)		
Variables	n	%
Emergency	22	31
Elective	49	69
Anesthesia		
General	64	90.1
Local + sedation	7	9.9
Graft brand		
Medtronic	49	69
Jotec	2	2.8
GORE	16	22.5
Cook	1	1.4
Relay	3	4.2
Proximal lengthening	3	4.2
Distal lengthening	8	11.3
Additional balloon	32	45.1
Debranching	5	7
Frozen elephant trunk	4	5.6
LSA closure	18	25.4
Celiac artery closure	2	2.8
Proximal landing zone		
0	1	1.4
1	4	5.6
2	13	18.3
3	36	50.7
4	17	24
LSA: Left subclavian artery.		

Table 3		
Postoperative data (n=71)		
Variables	n	%
Postoperative complications		
Acute renal failure	7	9.9
Wound infection	9	12.7
Cerebrovascular diseases	7	9.9
Pneumonia	9	12.7
Additional surgical intervention		
Carotico-subclavian bypass	5	7
Subclavian-subclavian bypass	3	4.2
Open surgery	1	1.4
Endoleak type		
1	16	22.5
2	3	4.2

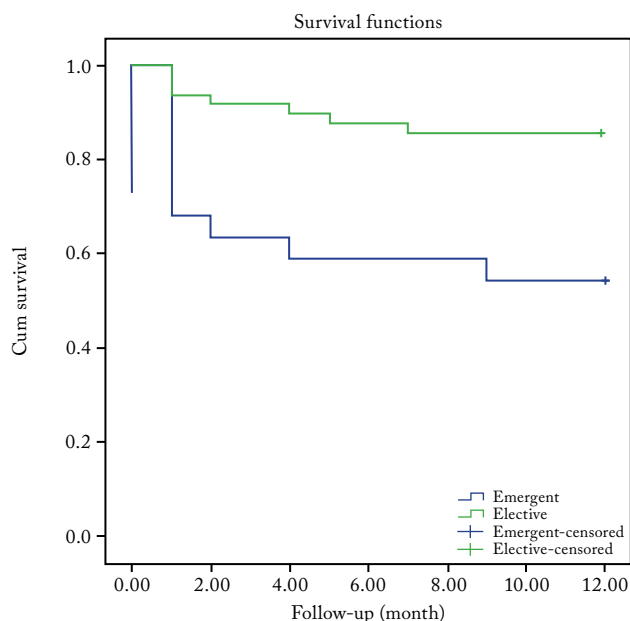


Figure 1. Kaplan-Meier survival analysis comparing elective and emergent cases in one year.

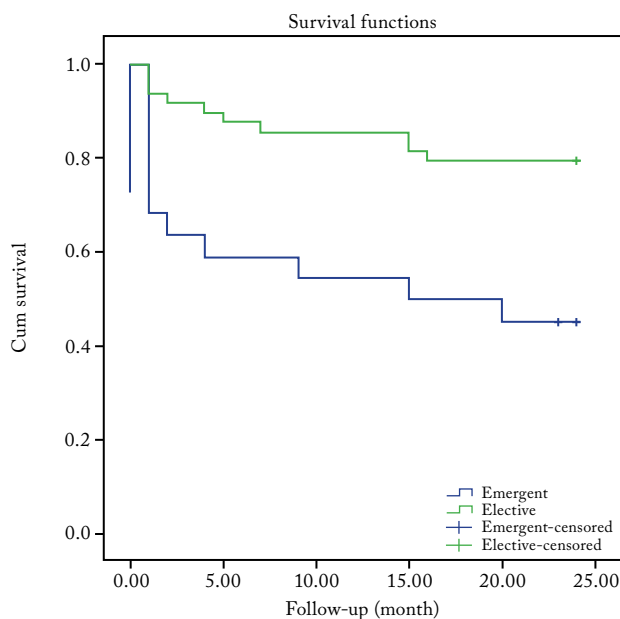


Figure 2. Kaplan-Meier survival analysis comparing elective and emergent cases in two years.

Type 1 endoleak developed in 16 patients and type 2 endoleak in three patients.

There were seven (9.9%) patients who developed acute renal failure, nine (12.7%) patients developed wound infection, seven (9.9%) patients developed CVD, and nine (12.7%) patients developed pneumonia at the postoperative first month (Table 3). In the postoperative follow-up, a total of three patients had permanent paresis and/or plegia.

The 30-day survival of the patients who were operated urgently was 72.7%, and this rate was 98% in elective patients ($p=0.001$). The one-year survival of our patient series was 76.1%. The two-year survival was 69.5% and the overall survival was 42.4%. The one-year survival rate of emergency patients was 54.5%, and this rate was 85.7% for elective patients ($p=0.002$). Emergency operation increases the one-year mortality risk by 5.6 times (Figure 1), COPD by 6.4 times, hyperlipidemia by 3.3 times. The two-year survival of emergency patients was 45.5%, and this rate was 79.6% in elective patients ($p=0.002$) (Figure 2). The two-year survival of smokers was 60.8%, while it was 90% for non-smokers ($p=0.022$). The two-year survival of patients with and without COPD was 40% and 84.8%, respectively ($p<0.001$). According

to the analysis, emergency operation increased the two-year mortality risk by 3.9 times compared to elective operations ($p=0.002$), and COPD increased by 6.2 times in the same way. Each unit increase in age at five-year survival increased the risk of mortality by 4% (odds ratio [OR]: 1.04). While the five-year survival rate of male patients was found to be 33.9%, this rate was 83.3% in females ($p=0.008$). Five-year survival rate of smokers and non-smokers was 28.6% and 78.7%, respectively ($p=0.001$). The five-year survival of patients with and without DM was 14% and 51.8%, respectively ($p<0.001$). The five-year survival of patients with and without hyperlipidemia was 25.7% and 51.6% ($p=0.017$). The five-year survival of the patients with and without COPD was 8.9% and 61.3%, respectively ($p<0.001$).

DISCUSSION

The primary objective of this study is to investigate the effect of TEVAR on mortality, particularly in the mid- and long-term. In our study, one-year survival was 76.1%, two-year survival was 69%, and five-year survival was 42.4%. In our study, mortality in the emergency TEVAR procedure was 17.1 times higher than in the elective TEVAR.

In a systematic review and meta-analysis on TEVAR treatment in degenerative aneurysms, Biancari et al.^[4] found 30-day mortality to be 4% and one-year mortality to be 19.7%. In a meta-analysis, 30-day mortality was found to be 19% in patients who underwent TEVAR with a ruptured TAA.^[5] In our study, the 30-day mortality was 2% (n=1) in patients who underwent elective TEVAR, indicating a lower rate than reported in the literature. This patient, who had exitus, died from acute renal failure on the postoperative fifth day. In a multi-center study, 30-day mortality was found to be 27.9% in patients with a ruptured TAA who underwent emergency TEVAR.^[6] In our study, the 30-day mortality was 27.3% (n=6/22) in patients who underwent emergency TEVAR, consistent with the literature data. The median time to death for our patients who were taken to emergency TEVAR and died was six (range, 0 to 10) days. We believe that, in the cox regression analysis performed with five parameters affecting 30-day mortality, emergency TEVAR application increased the mortality by 17.1 times compared to elective TEVAR procedure. In the aforementioned meta-analysis, the first 30-day mortality in emergency patients who underwent open surgery reached up to 33%.^[5] In our study, although there were patients with severe hypotensive shock in the emergency TEVAR group, the mortality rate was lower than the first 30-day open surgery mortality rate reported in this meta-analysis. In our study, one-year survival rate was 76.1%. In the cox regression analysis of one-year survival; the emergency TEVAR procedure increased the one-year mortality by 5.6 times. In addition, unlike 30-day mortality, COPD increased one-year mortality by 6.4 times and hyperlipidemia by 3.3 times. In our study, two-year survival rate was 69% (45.5% of emergency patients and 79.6% of elective patients). When the factors affecting two-year survival were analyzed, COPD increased two-year mortality by 6.2 times and emergency TEVAR by 3.9 times.

In a study conducted by Schaffer et al.,^[7] 11,996 patients who underwent TEVAR for various reasons were evaluated. The five-year survival rate was calculated as 60% in patients treated with TEVAR. In our study, the five-year survival rate was 42.4%. When one-year and five-year causes of death were examined in our study, none of the causes of death were the aneurysms or events related to the TEVAR procedure. While the most common cause of death at one year was myocardial infarction, malignancy was the most common cause of death at five years. In our

study, since there was no aneurysm-related death in the mid- and late periods; our five-year survival rate is lower than the literature, suggesting that the causes of comorbidities may be higher in patients included in the study. When the factors affecting five-year mortality were examined in our study, the most important factors were advanced age and male sex. Other factors were DM (increased mortality by 2.8 times) and smoking (increased mortality by 3.1 times).

Another focus of the discussions in the literature is whether sex has an effect on mortality. Deery et al.^[8] reported 12% mortality in female patients and 8% in male patients during one-year follow-up of patients who underwent TEVAR. They found a statistically significantly higher mortality rates among female patients. In our study, there was no significant difference in terms of 30-day mortality, and one- and two-year mortality between male and female patients. However, when the five-year mortality was examined using the Cox regression analysis, male sex increased the five-year mortality by 4.3 times compared to female sex. Considering the causes of death of our patients, the atherosclerotic process stands out which may explain the higher frequency of mortality in men, particularly in the long-term.

There are different findings in the literature when other factors affecting mortality in patients treated with TEVAR are examined. In a study conducted by Geisbüsch et al.,^[9] risk factors for mortality after TEVAR were reported as renal failure, over 75 years of age, and emergency operations as independent risk factors. Chung et al.^[10] defined the presence of preoperative leukocytosis and aneurysm diameter as independent risk factors for late mortality. Wang et al.^[11] reported the results of TEVAR in patients with impaired renal function and that emergency patients with a creatinine value of >2 mg/dL had a poor prognosis. Dillavou and Makaroun^[12] also reported that increased preoperative creatinine levels had a predictive value for mortality or morbidity endpoints. Salihi et al.^[13] showed that early mortality developed due to low cardiac output syndrome. In a meta-analysis by Harky et al.,^[14] when the patients who underwent TEVAR and those who underwent open surgery were compared, the one-year mortality rate was 22.19% and the five-year mortality rate was 44.26% in 3,908 patients who underwent TEVAR. In 10,672 patients who underwent open surgery, the one-year mortality rate was 24.04%, and the five-year mortality rate was 37.37%. When these results were compared, no

significant difference was found between one-year and five-year mortality rates. In our study, one-year mortality in patients who underwent TEVAR was found to be 23.9%. The five-year survival rate was found to be 42.4%. Considering five-year mortality rates in our study versus the literature data, the deaths at five years were not associated with an aneurysm. We believe that TEVAR would not lose its advantage in the mid- and long-term in the near future. The secondary objective of our study was to evaluate mid- and long-term complications of the TEVAR procedure. In particular, the patients who required paresis, plegia, endoleaks, and aneurysm-related reintervention after discharge. In the meta-analysis by Biancari et al.,^[4] the rate of postoperative paraplegia was found to be 3.2% and the rate of permanent paraplegia was found to be 1.4% in patients who received TEVAR due to TAA. The formation rate of CVD was calculated 2.7%. In our study, plegia/paresis occurred in seven patients in the postoperative period (9.9%). In one of these patients, plegia was permanent (1.40%). Three patients developed CVD, and the rate of CVD occurrence was calculated as 4.2%.

There are several limitations to this study. First, since the tomography data of some postoperative patients could not be accessed, these patients were excluded from the study. Second, the postoperative opaque nephropathy relationship could not be established, as the data on how much opaque material were used during the operation could not be reached in most patients. Since it is a retrospective study, we could not reach some patients such as tomography, blood results, and postoperative follow-up and, therefore, we had to reduce the number of patients in the study.

In conclusion, TEVAR treatment seems to show similar results to open surgery in terms of mortality and other complications in the mid- and long-term. It seems that TEVAR treatment does not lose its obvious advantage in the early period and, also, in the mid- and long-term. With the developing stent-graft technology, TEVAR results can be even better in the future.

Declaration of conflicting interests

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Esophagitis and gastritis are associated with premature atrial contractions in patients with gastroesophageal reflux disease

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ABSTRACT

Objectives: This study aims to investigate the association between premature atrial contractions (PACs) and esophagitis and/or gastritis in patients with gastroesophageal reflux disease (GERD) symptoms.

Patients and methods: A total of 108 patients (58 males, 50 females; mean age: 46.1±13.1 years; range, 37 to 63 years) who underwent gastroduodenal endoscopy to evaluate the presence of esophagitis and/or gastritis between February 2017 and September 2018. The patients underwent 24-h electrocardiographic monitoring for PACs. Esophagitis and/or gastritis rate was compared between PACs (+) and PACs (-) groups.

Results: The PACs (+) patients were older with a male preponderance. The PACs (+) patients were also more likely to have esophagitis and/or erosive gastritis ($p<0.001$), higher serum creatinine ($p=0.015$), and larger left atrial diameter ($p=0.049$) compared to PACs (-) group. The PAC count was higher in patients with esophagitis and/or gastritis. Multivariate analyses showed that male sex ($p=0.033$) and presence of esophagitis and/or gastritis ($p<0.001$) were independent predictors of PACs.

Conclusion: Esophagitis and/or gastritis in patients with GERD symptoms are independently associated with both the increased prevalence and number of PACs. Treatment of GERD may reduce PACs and subsequent further atrial arrhythmias, such as atrial fibrillation.

Keywords: Esophagitis, gastritis, gastroesophageal reflux disease, rhythm holter, premature atrial contraction.

Premature atrial contractions (PACs), also known as atrial premature complexes (APCs) or atrial premature beats (APB) which originate from the ectopic pacemaker tissue within the atria, are commonly encountered arrhythmias in clinical practice.^[1] Although PACs were considered to be benign electrophysiological phenomena initially, it was later found to be associated with the development of atrial fibrillation (AF). Moreover, AF burden was demonstrated to decrease by ablation of PACs.^[2] Thus, it has seen a growing interest in PACs by considering it to be a mediator between normal sinus rhythm and AF, in recent years. In addition to AF, it is associated with stroke, death, cardiovascular events, and coronary artery disease (CAD).^[3] Therefore, it is essential to evaluate preventable risk factors related to PACs.

In recent decades, it has renewed interest in the association between the gastrointestinal tract, particularly esophageal, and the cardiovascular system. Gastroesophageal reflux disease (GERD) is the most

common gastrointestinal diagnosis during daily practice.^[4] It is defined as the reflux of gastric contents caused epigastric symptoms such as heartburn and/or complications. When the esophagus is exposed to gastric acid and pepsin, erosive or non-erosive inflammation may occur in its mucosal surface layer. In this respect, esophagitis is well-recognized complication of GERD. Besides, gastritis is inflammation of the stomach and usually accompanies reflux disease. It is diagnosed with gastric endoscopy performed to reveal GERD-related disorders.^[5] Although both gastritis and esophagitis were shown to be related to cardiac symptoms and

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arrhythmias –predominantly AF- in previous studies, the underlying mechanisms are still needed to be elucidated.^[6] In this study, we aimed to investigate the association between PACs and esophagitis and/or gastritis in patients with GERD symptoms and to fill the gap in the existing literature on this topic.

PATIENTS AND METHODS

This cross-sectional, observational study was conducted at Recep Tayyip Erdoğan University Faculty of Medicine, Department of Gastroenterology between February 2017 and September 2018. A total of 108 patients (58 males, 50 females; mean age: 46.1±13.1 years; range, 37 to 63 years) who underwent gastroduodenal endoscopy with the complaints of GERD such as heart burn and regurgitation were included. All patients underwent 24-h Holter electrocardiographic (ECG) monitoring for PACs following gastroduodenal endoscopy with the preliminary diagnosis of GERD. Those were diagnosed with esophagitis and gastritis were retrieved from the hospital database. Exclusion criteria were as follows: pregnancy, congenital and structural heart disease, acute or chronic kidney failure (estimated glomerular filtration rate <60 mL/min/1.73 m²), CAD, heart failure, previous cerebrovascular disease, malignancy, presence of any end-stage disease, any type of malignancy, basal rhythm of other than sinus rhythm, history of cardiac radiofrequency ablation or cryoablation, chronic obstructive pulmonary disease, use of any drug with arrhythmia stimulant feature (theophylline, beta-agonist, etc.) or antiarrhythmics (beta-blockers, calcium channel blockers, and amiodarone), endocrine disorders, history of gastric and or esophageal surgery, and acute or chronic inflammatory diseases. In addition, patients with >30 sec of atrial tachycardias such as supraventricular tachycardia or AF were excluded from the study. A written informed consent was obtained from each patient. The study protocol was approved by the Recep Tayyip Erdogan University, Faculty of Medicine, Ethics Committee (date, no: 02.06.2019, 40465587-12). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Demographical and laboratory data

Clinical characteristics including a detailed medical history and physical examination were obtained from each patient by experienced cardiologists and gastroenterologists. All data were stored in the database

of our institution. Routine biochemistry including creatinine, glucose, aspartate aminotransferase (AST), and alanine aminotransferase (ALT), low-density lipoprotein, high-density lipoprotein, total cholesterol, triglyceride levels and complete blood count were measured at the time of hospital admission. Glomerular filtration rate values were calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Systolic and diastolic arterial pressure, previous history of CAD, hypertension (HT), diabetes mellitus (DM), hyperlipidemia (HL), and smoking status were evaluated. The diagnoses of HT and DM were made according to current guidelines.^[7] The presence of HL was defined according to age and sex-adjusted percentiles from the National Health and Nutrition Examination Survey (NHANES) III data. The height and weight data of the patients were recorded, and body mass index (BMI) was calculated according to the weight (kg)/height (m²) formula.

Endoscopy and identification of esophagitis and gastritis

An experienced gastroenterologist performed endoscopy using an Olympus-brand endoscopy device (SBE, Olympus Medical Systems Corporation, Tokyo, Japan). The entire stomach and esophagus, including the duodenum, were visualized and obtained images were recorded. Adequate biopsy specimens were taken from duodenum, antrum, and corpus respectively and referred to the pathological examination. The classification of esophagitis was reported according to the Los Angeles classification of GERD, whereas gastritis was evaluated according to the Sydney classification system.^[8,9]

Rhythm Holter monitoring

A DMS 300-3A-brand Holter device (DMS 300-3A; Bravo, Huntington Beach, CA, USA) was used for 24-h of heart rhythm monitoring. At the beginning of the rhythm monitoring, the patients were informed about possible problems that may arise and management. The patients were asked to press the event-recording button, when any sensation of palpitations occurred. After the 24-h monitoring of cardiac rhythm, the records were transferred to the software for analysis. A preliminary evaluation was made, and all parasitic records were deleted. We evaluated records and analyzed the presence of PACs and other possible arrhythmias, and improper PAC recordings were excluded. As a result, premature atrial beat or complexes, and

Table 1
Demographic and clinical characteristics of study population

Variables	PACs (-) (n=35)			PACs (+) (n=73)			p				
	n	%	Mean±SD	Median	Min-Max	n		%	Mean±SD	Median	Min-Max
Age (year)	11	30.6	43.9±12.1			47	64.4	47.2±12.8			0.019
Sex											0.001
Male											
BMI (kg/m ²)	11	30.6	30.1±4.6			23	31.5	29.1±4.2			0.849
Hypertension	1	2.8				9	12.3				0.373
Diabetes mellitus	8	22.2				22	30.1				0.472
Hyperlipidemia	11	30.6				69	94.5				<0.001
Esophagitis and/or gastritis											0.251
Systolic blood pressure (mmHg)			121.4±9.3					123.4±8.1			0.334
Diastolic blood pressure (mmHg)			76.3±5.2					75.1±6.8			0.293
Left ventricular EF			62.7±2.6					61.9±3.6			0.510
PW thickness (mm)			9.5±0.1.2					9.7±1.4			0.207
IVS thickness (mm)			9.8±1.2					10.1±1.3			0.049
Left atrial diameter (mm)			34.2±4.1					36.1±4.3			0.128
Leukocytes (10 ³ /mm ³)			6.9±1.5					6.4±1.5			0.088
Hemoglobin (g/dL)			14.2±1.2					13.7±1.6			0.023
Glucose (mg/dL)			93.3±12.1					97.1±12.5			0.015
Creatinine (mg/dL)			0.78±0.12					0.84±0.12			0.675
Total cholesterol (mg/dL)			195±45					199±48			0.709
LDL cholesterol (mg/dL)			113.5±32.9					116.1±30.6			0.365
HDL cholesterol (mg/dL)			47.5±9.5					45.7±9.5			0.090
Triglycerides (mg/dL)			99.4±42.1					119.3±49.2			0.399
TSH*				1.4	1.01-1.8				1.6	1.01-2.0	0.391
Free T4			0.97±0.19					1.02±0.17			0.760
Free T3			2.91±0.48					2.98±0.37			0.144
ACE inhibitor use	5	14.7				18	24.7				0.402
Angiotensin receptor blocker use	2	5.6				2	2.7				0.377
Statin usage	2	5.6				7	9.6				

PAC: Premature atrial contraction; SD: Standard deviation; BMI: Body mass index; EF: Ejection fraction; PW: Posterior wall; IVS: Interventricular septum; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; TSH: Thyroid stimulating hormone; ACE: Angiotensin-converting enzyme; * Mann-Whitney U test was used.

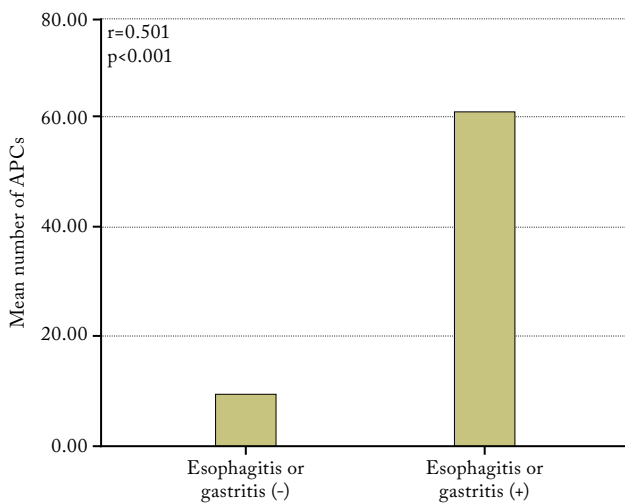


Figure 1. Comparison characteristics of patients according to number of PACs.

PACs: Premature atrial contractions.

premature supraventricular beat or complexes in 24-h Holter recordings were considered the presence of PACs. In the presence of PACs, we calculated and recorded their count. The Minnesota code criteria (Minnesota codes 8.1.1 and 8.1.2) were used to identify PACs.

Echocardiographic evaluation

Transthoracic echocardiography was performed in all patients using a General Electric Vivid S3 device (GE Vingmed Ultrasound AS, Horten, Norway). Left atrial diameter, septum, and posterior wall thicknesses were obtained at the parasternal long-axis image. Left ventricular ejection fraction

was calculated from the apical four and two-chamber views using the modified Simpson's method.

Statistical analysis

Statistical analysis was performed using the PASW version 18.0 software (SPSS Inc., Chicago, IL, USA). Continuous variables were presented in mean \pm standard deviation (SD) or median (interquartile range [IQR]), while the categorical variables were presented in number and frequency. The normality of the data was tested using the Kolmogorov-Smirnov test. Normally distributed continuous variables were compared using the Student t-test, while the non-normally distributed variables were compared using the Mann-Whitney U test. The chi-square test was used for the categorical variables between two groups. Analysis of variance (ANOVA) was used to compare the mean values for normally distributed variables and the Kruskal-Wallis test for non-normally distributed variables among different groups. Linear and logistic regression analyses were used for the multivariate analysis of independent variables, which were included if they were significantly different in the univariate analysis. A p value of <0.05 was considered statistically significant.

RESULTS

Of the patients, 28 (25.9%) had neither esophagitis nor gastritis and were diagnosed with non-erosive reflux disease. The remaining 80 (74.1%) patients had esophagitis and/or erosive gastritis at gastroduodenal endoscopy. Occurrence of at least 10 premature atrial extrasystoles through the entire monitoring period was

Table 2
Multivariate regression analysis for PAC prediction

Variables	Univariate			Multivariate		
	OR	95% CI	p	OR	95% CI	p
Age (year)	1.048	1.007-1.091	0.023	1.060	0.994-1.131	0.075
Sex, male	4.108	1.746-9.668	0.001	5.547	1.150-26.755	0.033
Creatinine	40.8	2.12-783	0.014	0.008	0.999-2.861	0.107
Esophagitis and/or gastritis	39.2	11.4-134.4	<0.001	43.25	10.315-181.36	<0.001
Diabetes mellitus			0.138			
Left atrial diameter			0.057			

OR: Odds ratio; CI: Confidence interval; Multivariate analysis with enter method was performed including all parameters with a p value of <0.1 in the univariate analysis.

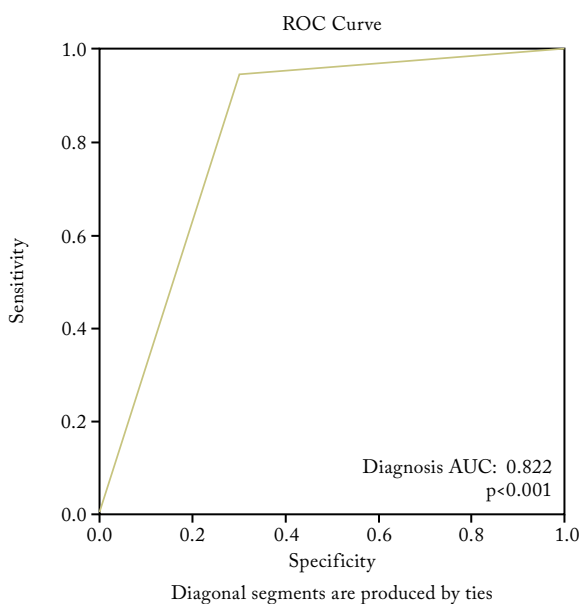


Figure 2. ROC curves of esophagitis and/or gastritis in determination of presence of PACs.

ROC: Receiver operating characteristic; AUC: Area under the curve; PACs: Premature atrial contractions.

accepted as PACs (+) and the patients were divided into two groups according to the PACs presence. The PACs (+) group was older (47.2 ± 12.8 vs. 43.9 ± 12.1 , respectively; $p=0.019$) and more likely to be male (47% vs. 11%, respectively; $p=0.001$). In addition, PACs (+) patients predominantly had esophagitis and/or erosive gastritis (94.5% vs. 30.6%, respectively; $p<0.001$), higher serum creatinine concentrations (0.8 ± 0.1 vs. 0.8 ± 0.1 mg/dL, respectively; $p=0.015$), and larger left atrial diameters (36.1 ± 4.3 vs. 34.2 ± 4.1 mm, respectively; $p=0.049$) compared to PACs (-) group. Other parameters were similar between the groups (Table 1).

The mean PAC count was significantly higher in patients with esophagitis and/or erosive gastritis (42.6 ± 32.8 vs. 5.8 ± 15.6 , respectively; $p<0.001$) (Figure 1). Similarly, the rate of patients with PACs was significantly higher in patients with esophagitis and/or erosive gastritis, compared to those with non-erosive reflux disease (86.3% vs. 13.8%, respectively; $p<0.001$).

Multivariate analyses showed that male sex (odds ratio [OR]=5.547, 95% confidence interval [CI]: 1.150-26.755, $p=0.033$) and the presence of esophagitis and/or erosive gastritis (OR=43.25, 95% CI: 10.315-181.36, $p<0.001$) were independent predictors of PACs (Table 2).

The receiver operating characteristic (ROC) analysis demonstrated that the presence of esophagitis and/or erosive gastritis was associated with PACs with a sensitivity of 94.5% and a specificity of 69.4% (area under curve= 0.811, $p<0.001$) (Figure 2).

DISCUSSION

In the present study, we found that the presence of esophagitis and/or gastritis were independently and strongly associated with both the prevalence and number of PACs in patients with GERD symptoms. To the best of our knowledge, this is the first study evaluating the contribution of esophagitis and/or gastritis to PACs in the literature.

In routine daily practice, GERD is one of the most common symptoms. However, the prevalence of GERD varies between populations, it has been reported to be between 10 and 20%.^[10] The association between the upper gastrointestinal system and cardiovascular diseases was paid more attention after firstly described as gastrocardiac syndrome by Roemheld^[10] in which patients with cardiac symptoms did not have cardiac examination findings. Moreover, cardiac and upper gastrointestinal complaints were mimicking each other and gastroesophageal reflux-stimulated dysrhythmia was identified in subsequent studies.^[6,11-13] Although the possible mechanisms between esophagitis and gastritis and cardiac arrhythmia are speculative, inflammation and sympathovagal imbalance were postulated to be cornerstone etiologies causing dysrhythmia.^[14]

Acid reflux reflexively causes an increase in vagal stimulation in patients with GERD. Furthermore, mucosal acid damage, particularly in esophagitis, allows the access of acid content to deeper layers of the esophagus where the vagal nerve endings are located, which culminates in vagal stimulation.^[10] A similar process also occurs in patients with gastritis. Damage to the gastric mucosa due to *Helicobacter pylori* and other provocative factors facilitate the contact of gastric acid content with the vagal nerve endings.^[11] The clinical study by Wang et al.^[12] is an important guide in determining the correlation between vagal tone increase and cardiac arrhythmias. The withdrawal of acetylcholine causes cyclic adenosine monophosphate-mediated stimulation of calcium and, then, excessive intracellular calcium causes the initiation of late afterdepolarizations. Subsequently, triggered and/or spontaneous atrial depolarizations are generated.^[12] Karaman et al.^[13]

conducted another study supporting this result and demonstrated that afterdepolarization may enhance the development of ventricular extrasystole beats.^[13] Considering the association of late afterdepolarization with atrial arrhythmias, rebound afterdepolarization due to adenosine withdrawal during enhanced vagal tone may be another possible mechanism playing a role in the development of PACs in patients with gastritis and esophagitis.

On the other hand, the association between sympathovagal imbalance and AF was identified previously.^[14,15] Rieder et al.^[16] showed that stimulation of the esophagus by gastric acidic content could cause arrhythmia by altering the vagal and sympathetic balance. Moreover, vagal stimulation was demonstrated to shorten the atrial refractory period, thus facilitating the intra-atrial reentry circuit. David and Johnson^[17] simultaneously monitored 24 h of cardiac rhythm and intra-esophageal pH and revealed that esophageal acid stimulation provoked cardiac autonomic reflex. Furthermore, acid suppression relieved cardiac symptoms in these patients. In addition, it was also shown that esophageal acid stimulation reduced coronary blood flow and caused anginal symptoms in patients with CAD. Reduced coronary flow may cause ischemia which creates a substrate for the development of atrial arrhythmias. Another finding of the relevant study was that, as the heart transplant recipients had complete heart denervation, coronary blood flow was not reduced in response to neural reflexes.^[18]

Chronic inflammation plays a critical role in the development of esophagitis and gastritis.^[11] Thus, the inflammation could play a substantial role in the development of PACs. Recurrent acid secretions increase mucosal inflammation and the secretion of interleukin (IL)- 1β , IL-6, and other inflammatory cytokines. These cytokines were also shown to have a robust role in the pathogenesis of AF.^[6,19] On the other hand, a recent experimental study showed that inflammatory cytokines might even cause the development of ventricular arrhythmias by triggering fibrosis in cardiac tissues.^[20,21] As a result, inflammation and ongoing fibrosis may also form the basis for arrhythmia formation in the atrial myocardium and may be postulated to be another mechanism associated with the development of PACs in patients with esophagitis and gastritis.

The close anatomic vicinity of the left atrium and esophagus should be considered in these clinical

settings. The thickness of the tissue layer between the posterior wall of the left atrium and the esophagus is about 5 mm. This tissue layer includes esophageal vessels, lymph nodes, as well as the paraesophageal nerve plexus which regulate the motility of the upper gastrointestinal tract. This creates mechanical pressure on the atrium and that mechanical pressure can cause local ischemia in the myocardial wall.^[6,22] Moreover, there is a paracrine interaction between the left atrium and esophagus. In this way, esophagitis may cause changes in action potential characteristics and heterogeneous conduction distribution in the atrial myocardium which is the substrate for PACs. In addition, atrial tachycardia was stimulated through the esophagus in pediatric patients which could not be stimulated even from intracardiac tissues. Besides, some atrial arrhythmias were found to be triggered by certain meals, indicating that the esophagus has also an unknown relationship with atrial arrhythmias.^[23] Also, hiatal hernia was found to be closely associated with persistent AF.^[24] Thus, anatomic proximity may be another possible mechanism underlying PACs in patients with GERD symptoms.

It was also reported in previous studies that PACs had an AF-triggering effect, and the elimination of PACs resulted in a decrease in AF recurrence.^[2,13] Thus, PACs generation functions as a bridge between GERD and AF development.^[22] Considering the AF is one of the major cardiovascular risk factors for morbidity and mortality worldwide, preventable risk factors such as PACs should be detailed examined in patients with GERD. Hence, the treatment of esophagitis and gastritis may decrease the burden of PACs and subsequently of AF, without any medical and/or invasive cardiovascular treatment. Indeed, proton pump inhibitors were shown to decrease AF symptoms and frequency of AF episodes in some studies. These findings were also confirmed with 24-h Holter ECG monitoring.^[10,14,15]

The small sample size is the main limitation of the present study. In addition, inflammatory markers were unable to be evaluated. Finally, our study has an observational design, which does not implicate causality.

In conclusion, esophagitis and/or gastritis are strongly and independently associated with the presence of PACs. Detecting atrial arrhythmias in routine examination including ECG is difficult. Therefore, patients with GERD symptoms may be

assessed further for PAC presence, the preceding findings of AF. Atrial fibrillation is the most common sustained arrhythmia and is associated with significant morbidity and mortality. It is possible to reduce the rates of AF and other atrial arrhythmias with the treatment of esophagitis and gastritis.

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A mitral blood cyst causing stenosis in the left ventricular outflow tract: A case report

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ABSTRACT

Intracardiac blood cysts are commonly observed in the autopsies of fetuses and infants. Most patients are below six months of age, and most cysts spontaneously regress with aging. Intracardiac blood cysts are rarely described in children and adults. A nine-year-old girl was admitted to our clinic with atypical chest pain. Echocardiography revealed a cystic formation on the anterior mitral leaflet. The cyst caused the obstruction of the left ventricular outflow tract. The patient was evaluated by a multidisciplinary team, and surgical intervention was decided. After cyst resection, the mitral valve did not require further intervention. Histopathological examination confirmed that the cyst was a mitral blood cyst. The patient was discharged without any postoperative complications.

Keywords: Cardiac tumor, left ventricular outflow tract stenosis, mitral blood cyst.

First reported by Elässer^[1] in 1844, intracardiac blood cysts are rare lesions. As detailed by Khan et al.,^[2] blood cysts are thin-walled cysts filled with non-organized thrombi. In 1983, Hausser et al.^[3] used echocardiography to demonstrate the movement of the hypoechoic structure and the site of attachment.

Blood cysts are most commonly seen in the mitral and tricuspid valves, and rarely affect the pulmonary or aortic valve. Until 2009, mitral blood cysts were seen in eleven patients and 81.8 of these mitral cysts caused from anterior leaflet. Intracardiac cysts are associated with a variety of symptoms, including shortness of breath, chest pain at rest and during exertion, and even syncope; however, neurological deficits are less common and are associated with embolic stroke or transient ischemic attack following cyst rupture.^[4] In this article, we report a case of a mitral blood cyst causing stenosis in the left ventricular outflow tract.

or T wave changes. Echocardiography revealed a 25×20-mm blood cyst attached to the ventricular side of the anterior mitral leaflet that protruded toward the left ventricular outflow tract during each systole and led to an increased mean mitral valve gradient of 25 mmHg (Figure 1). The findings were confirmed by transesophageal echocardiography. During surgery, aortotomy revealed a thin-walled lobular cystic formation attached to the anterior mitral leaflet. The cyst was excised (Figure 2). Surgical inspection did not reveal any mitral valve defects. Postoperative transesophageal echocardiography did not reveal mitral regurgitation or a pressure gradient in the left ventricular outflow tract. The patient was discharged without any complications. The pathological examination confirmed that the mass was a blood cyst. A written informed consent was obtained from the parents and/or legal guardians of the patient.

CASE REPORT

A nine-year-old girl was referred to our clinic from an external center, after a blood cyst was detected in the mitral valve following atypical chest pain. There were no signs of previous disease. Electrocardiogram did not reveal arrhythmia or significant ST-segment

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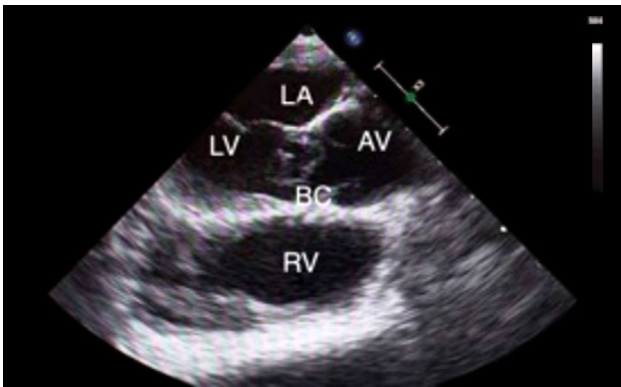


Figure 1. Preoperative echocardiography showing cystic appearance.

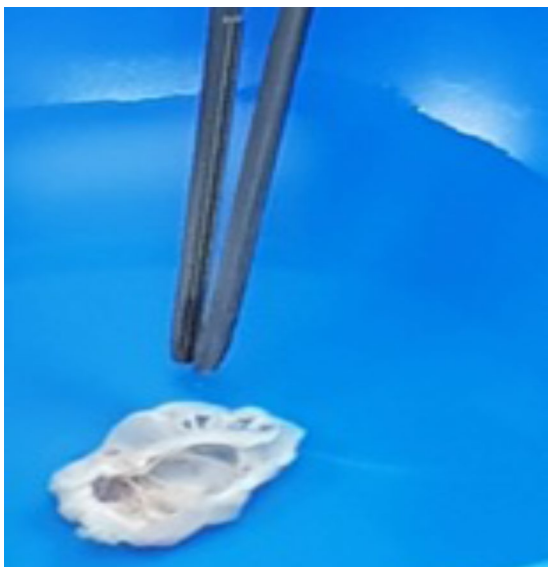


Figure 2. An intraoperative view after cyst excision.

DISCUSSION

Most intracardiac masses are tumors, and 90% are benign. Myxoma is the most common intracardiac tumor in 70% of cases.^[5] Other possible causes of intracardiac tumors include endocarditis, fibroelastoma, cardiac metastasis, or vegetation in the mitral valve.^[6]

Echocardiography is a reliable method for the diagnosis of blood cysts. The appearance of a hypoechoic cyst in the absence of signs of systemic disease should raise suspicion for a blood cyst. Transesophageal echocardiography is critical in the differential diagnosis between cysts and

thrombus. The demonstration of the intramural contrast in contrast-enhanced echocardiography is a pathognomonic sign of blood cysts.^[7] Magnetic resonance imaging has been shown to be superior in the assessment of intracardiac masses and their differential diagnosis, although histopathological examination is currently the gold standard.^[8]

Several theories have been proposed regarding the formation of intracardiac blood cysts. These include dilation of the vascular space, heteroplastic tissue changes, inflammation, anoxia, and hemorrhagic diathesis. The underlying mechanism of the formation of intracardiac blood cysts is still unclear.^[8] In rare cases, a causal relationship cannot be established between cyst formation and a known factor; however, blood cyst formation secondary to a hematoma has been reported in several cases with a history of cardiac surgery.^[9]

There is no consensus or any guidelines on the optimal management of blood cysts. The vast majority of patients with mitral blood cysts require surgical resection.^[10] Pelikan et al.^[11] reported that asymptomatic cysts could be monitored by echocardiography due to their benign nature and that resection should be reserved for patients with impaired cardiac functions. Paşaoğlu et al.^[12] recommended the resection of cystic tumors of the heart, particularly valvular cysts. However, surgical resection is usually recommended for symptomatic patients,^[1,13] large tumors, valvular dysfunction,^[14] or patients who are asymptomatic, but would undergo open heart surgery for other reasons.^[15]

Khan et al.^[2] also reported that as blood cysts were associated with the intracardiac cavity, and their rupture might cause systemic and coronary embolization. They recommended that asymptomatic small cysts should be monitored, while patients should be administered anticoagulant therapy due to the risk of thromboembolism.

In our patient, there were no other etiologies to explain chest pain, and the cyst was associated with the anterior mitral leaflet and protruded into the left ventricular outflow tract in each systole, thereby, creating a pressure gradient. Therefore, surgical resection was decided. Surgery allows confirmation of the diagnosis through the pathological examination, and the elimination of malignancy. However, follow-up with serial echocardiographic imaging may be a viable option for asymptomatic or inoperable patients.

In conclusion, although rare, blood cysts should be considered in the differential diagnosis of hypoechoic masses as evidenced by echocardiography. There are no available data on the long-term follow-up of patients with intracardiac blood cysts. The cysts can be fully surgically resected. If a valvular defect or a disruption of valvular coaptation occur after surgical excision, it should be corrected simultaneously.

Declaration of conflicting interests

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Asymptomatic double aortic arch diagnosed incidentally in an adult patient

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ABSTRACT

Vascular rings are rare major congenital vascular anomalies characterized by a complex anatomical anomaly of the aortic arch and associated with the vascular structures surrounding the trachea and esophagus like a ring. Symptoms usually occur in infancy or early childhood. Diagnosis in adult age is extremely rare. In this article, we present a rare adult case of double aortic arch diagnosed incidentally.

Keywords: Adult, asymptomatic, double aortic arch, vascular ring.

Vascular rings, which account for less than 1% of congenital heart diseases,^[1] were first described by Gross^[2] in 1945. In double aortic arch (DAA), due to errors in the regression of the right aortic arch, both aortic arches form a vascular ring that completely surrounds the trachea and esophagus. Each aortic arch passes superior to the main bronchus on the same side and enters the descending aorta, often localized on the left with respect to the right side of the spine. In most cases, this anomaly is diagnosed in infancy or childhood, depending on the symptoms caused by esophagus and tracheal obstruction. Diagnosis in adults, particularly in asymptomatic cases, is extremely rare.^[3] Herein, we present a rare adult case of DAA diagnosed incidentally.

CASE REPORT

A 42-year-old male patient with a diagnosis of schizophrenia was admitted to our clinic with non-specific chest and back pain. Physical examination and laboratory tests were normal. Chest radiography showed bilateral aortic notches at the level of aortic arch (Figure 1). Three-dimensional (3D) computed tomography (CT) angiography, a non-invasive test that provides high-quality 3D imaging, revealed nearly same sized DAA. Brachiocephalic truncus was not seen. The right common carotid artery and the right subclavian artery were originating from separate roots from the right aortic arch. The left common carotid artery and left subclavian artery were originating from separate roots from the left aortic arch (Figure 2). At the

junction of the arches on the posterior, the esophagus was minimally compressed between the trachea and the arch (Figure 3). However, since our patient did not have respiratory and nutritional disorders due to

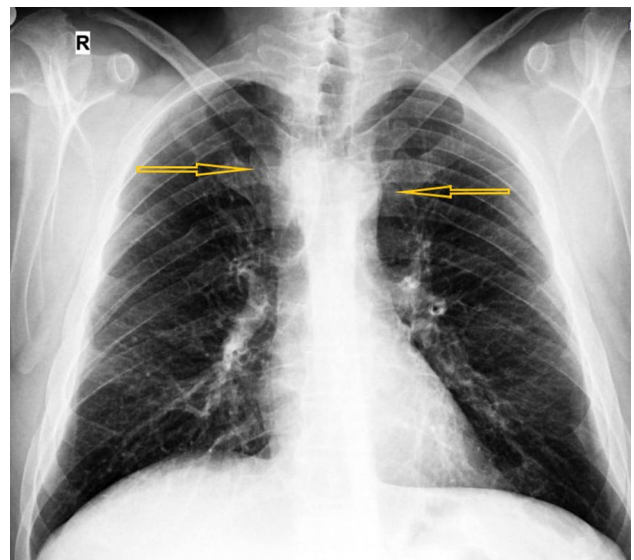


Figure 1. Chest radiography showing bilateral aortic notches.

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Figure 2. Multislice computed tomography showing a vascular ring; anterior, anterolateral and lateral view.

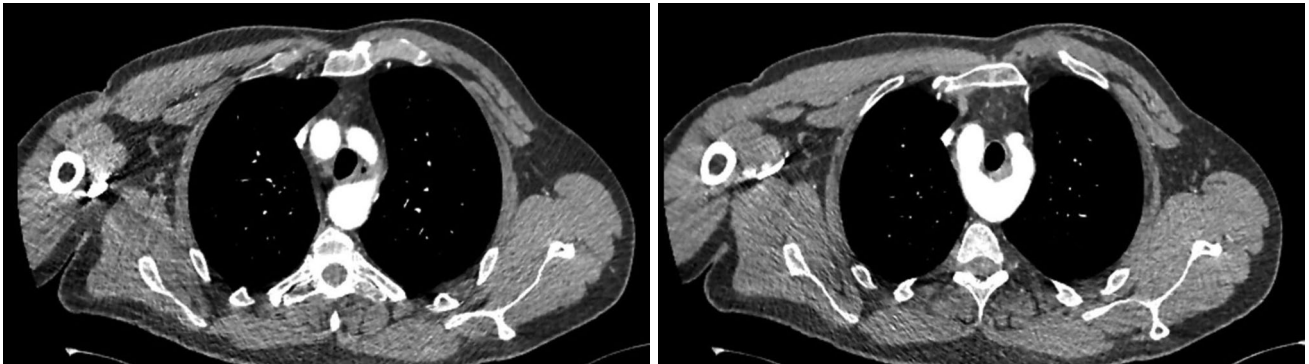


Figure 3. The esophagus is minimally compressed between trachea and arch.

DAA, the cause of his complaints was investigated, and he was also evaluated by the cardiology and chest diseases departments. However, no organic reason was able to be found. Considering that he had non-specific complaints related to schizoaffective disease, he was referred to the psychiatry clinic. He was also regularly scheduled for follow-up in the cardiovascular surgery outpatient clinic. A written informed consent was obtained from the patient.

DISCUSSION

Double aortic arch, the most common form of vascular rings, is a congenital anomaly that occurs, when the ascending aorta is divided into two parts and

passes around the trachea and esophagus and, then, turns into a single pattern aorta.^[4]

The embryological development of the vascular ring has been described in detail in the literature. In the embryonic arch system, there are six parts of the aortic arch originating from the ventral aortic root. The first, second, and fifth arches regress and a DAA is formed. In general, the left fourth arch forms the aortic arch. If the left fourth arch regresses and the right arch remains, this results in a right-sided aortic arch.^[4] In DAA, due to errors in the regression of the right aortic arch, both aortic arches form a vascular ring that completely surrounds the trachea and esophagus. Classically,

there are three types of DAA: right dominant aortic arch, left dominant aortic arch, and balanced-type aortic arch. In 75% of cases, the right arch is dominant and, in about 20% of cases, the left arch is dominant. In 5% of the cases, both arch dominance is equal.^[5] In our case, the patient had a balanced-type aortic arch.

Double aortic arch may cause compression of these structures by surrounding the trachea and esophagus. Symptoms such as respiratory distress, feeding difficulties, recurrent pneumonia, stridor and dysphagia may occur as a result of tracheal and/or esophageal compression at birth and in early infancy.^[6] However, partial compression may show an asymptomatic course, as in our patient.

Chest X-ray may be normal and diagnosis may be missed. Various imaging methods, such as magnetic resonance imaging (MRI), CT scanning, and aortography, can be used to reveal DAA and determine the most optimal surgical approach for surgical candidates.^[7]

The presence of symptoms for vascular rings is a surgical indication at all ages. In particular, adults without symptoms may not need surgery. Nevertheless, we argue that, cases similar to our patient may need a close follow-up with regular laboratory studies and proper physical examination. Surgical delay may cause serious morbidity and irreversible complications of the respiratory system, leading to death even.^[8] Medical therapy is a choice that can contribute to surgical treatment. Surgery for aortic arch division can be accomplished through a right or left thoracotomy and it can reach out to relieve tracheoesophageal structures. Maximum effort is required to avoid vascular and neighboring structures for acceptable postoperative results. Despite this, long-term surveillance after surgery is 90 to 95% of all cases. Particularly asymptomatic adults may not need surgery.^[8]

In conclusion, although double aortic arch is well described in childhood it is rare in adult patient because of its asymptomatic course. Surgery may be necessary if it causes symptoms due to tracheal and esophageal compression otherwise patients should be followed up under regular medical follow-up.

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Supravalvular mitral ring in a patient with Turner syndrome: A case report

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ABSTRACT

Turner syndrome is a relatively common genetic disorder of female development characterized by partial or complete absence of an X chromosome. Some of the patients may present with cardiovascular abnormalities. However, there is no case with Turner syndrome with a supravalvular mitral ring (SMR) in the literature. Herein, we present a case of SMR accompanied by Turner syndrome who presented with progressive shortness of breath and exertional dyspnea, that was successfully treated.

Keywords: Mitral stenosis, supramitral ring, Turner syndrome.

Supravalvular mitral ring (SMR) is a rare anomaly of the mitral valve. It is a circumferential ridge or membrane that arises from the left atrial wall. The thickness and extent of the SMR may vary from a thin membrane to a thick discrete fibrous ridge.^[1] The mitral valve is often abnormal and may be accompanied by valvular stenosis or fusion of leaflets, a small valve orifice, and abnormal papillary muscle morphology.^[2] Adhesion to the mitral valve can disrupt its function, which is the major mechanism of mitral flow obstruction. It can progress over time and reduce cardiac output.^[1] More than 90% of all SMR cases are associated with other congenital abnormalities,^[1] and the incidence of concomitant SMR in Turner syndrome is unknown. Herein, we report a case of SMR accompanied by Turner syndrome who presented with progressive shortness of breath and exertional dyspnea that was successfully treated.

CASE REPORT

A 15-year-old female who was diagnosed with Turner syndrome presented to our clinic with exertional dyspnea and rapid fatigue (New York Heart Association [NYHA] Class III). The electrocardiogram showed sinus rhythm. The echocardiography revealed severe mitral stenosis due to supramitral ring. The peak and mean mitral valve gradients were 49 and 26 mmHg, respectively (Figure 1). The mitral valve diameter was 12 mm

(Figure 2). The left atrium was dilated, and the interatrial septum was deviated to the right. The echocardiogram also showed a bicuspid aortic valve and a patent foramen ovale. The findings were confirmed by transesophageal echocardiography. There were no other pathologies which required an additional intervention. During surgery, the mitral valve was explored through a transeptal approach. A mitral ring was observed originating from the middle of the anterior mitral leaflet and extending toward the posterior leaflet and, then, to the supravalvular region (Figure 3). The tissue was excised. Any interchordal space obliterations were corrected (Figures 4 and 5). Follow-up surgical inspection revealed a good valve diameter. The postoperative transesophageal echocardiography showed a mean mitral valve gradient of 6 mmHg (Figure 6). The patient was discharged without any complications. A written informed consent was obtained from the parents and/or legal guardians of the patient.

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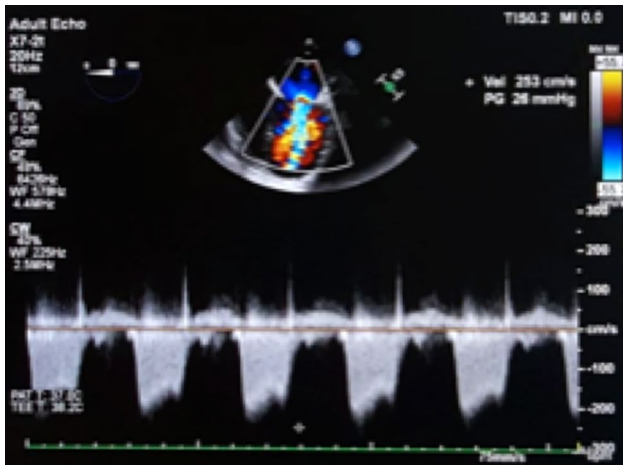


Figure 1. Preoperative mitral stenosis gradient.

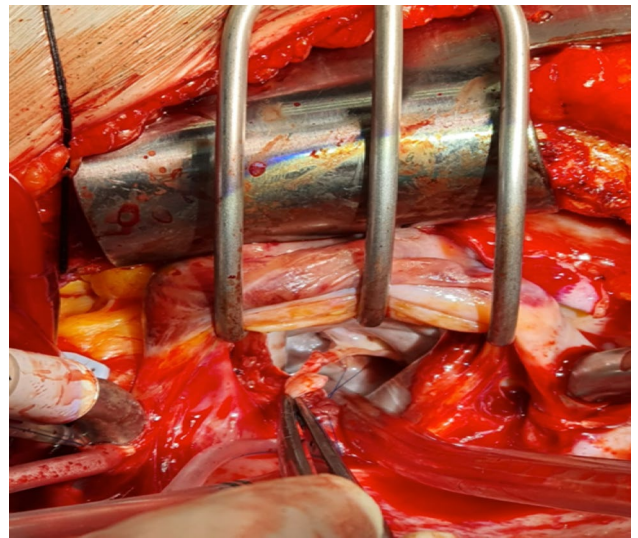


Figure 4. An intraoperative view of supravalvular ring resection.

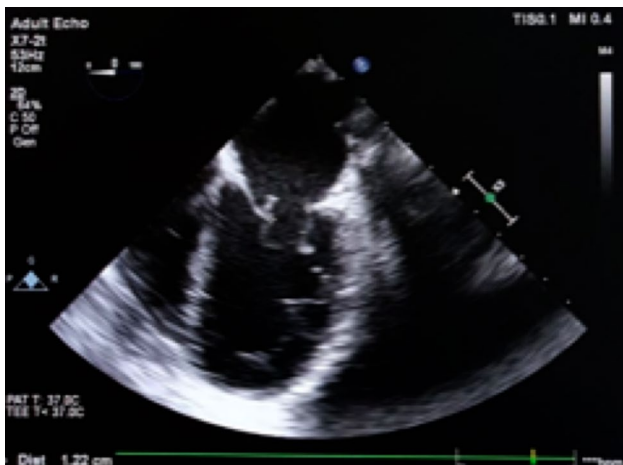


Figure 2. A preoperative view of mitral valve opening and supravalvular ring.



Figure 5. View of the ring after resection.

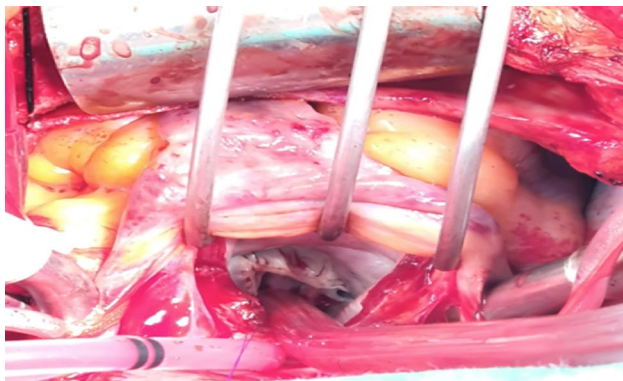


Figure 3. An intraoperative view of supravalvular ring.



Figure 6. Postoperative follow-up echocardiography showing mitral valve patency.

DISCUSSION

Several studies have shown an increased incidence of mitral valve disease in patients with Turner syndrome; however, the study of Bondy et al.^[3] found that the incidence of mitral valve disease was similar in Turner syndrome patients compared to the overall population.

Supravalvular mitral ring has not been described in patients with Turner syndrome. Supramitral ring rarely occurs as an isolated lesion and is often accompanied by other congenital heart diseases, including left-sided obstructive heart lesions, such as the parachute mitral valve, valvular and subvalvular aortic stenosis, bicuspid aortic valve, and coarctation of the aorta. It frequently presents as a part of Shone's complex. Supravalvular mitral ring has been rarely reported as concomitant with the Tetralogy of Fallot,^[4] atrial septal defect, cor triatriatum, left-sided superior vena cava, unroofed coronary sinus, partial anomalous pulmonary venous return, pulmonary venous obstruction, double orifice mitral valve, transposition of the great arteries, atrioventricular discordance, or double outlet right ventricle.^[5] Although cor triatriatum is a rare anomaly, it can be encountered in all age groups and should be considered in the differential diagnosis with supramitral ring, as both anomalies are similar in terms of clinical signs and symptoms.^[6]

First described by Fisher^[7] in 1902, SMR has been the subject of several studies to better understand the associated cardiac abnormalities. Collison et al.^[8] proposed that cardiac anomalies associated with SMR could be classified into two main categories: SMR associated with ventricular septal defect, and SMR associated with left-sided obstructive pathologies, particularly sub-aortic membrane, bicuspid aortic valve, and coarctation of the aorta. In the first scenario, it is important to rule out SMR in the context of patients with ventricular septal defect and turbulence across the mitral valve. In the second scenario, it has been argued that supramitral ring should be excluded in patients with multi-level left heart obstructions to prevent residual defects.^[8] In the light of these findings, the lesions described for the second scenario and the cardiovascular pathologies associated with Turner syndrome show more overlap. The present case had also a bicuspid aortic valve, but there was no obstructive lesion requiring an intervention.

A study by Toscano et al.^[9] described two different variants of mitral ring, namely supramitral and intramitral. It is of surgical significance to differentiate

these two subtypes of mitral pathologies. Supramitral ring is usually associated with a normal mitral valve apparatus and can occur concomitantly with congenital heart defects, as previously mentioned. Intramitral ring is usually a part of the Shone's complex and is associated with a normal subvalvular apparatus. The intramitral ring can, therefore, be considered a subtype of congenital mitral stenosis, characterized by varying degrees of obstruction, both at the level of the ring and the supravalvular apparatus. The supravalvular type is a form of left atrial obstruction, whereas the intravalvular type can be a part of an intrinsic mitral pathology.

Resection of the supramitral ring is simpler and more definitive, whereas intramitral ring resection is more challenging. Although ring resection is necessary, it is rarely sufficient, as the anatomy of the subvalvular apparatus significantly contributes to inflow obstruction. Satisfactory hemodynamic results can be achieved through papillary muscle splitting and correction of the interchordal space obliterations to increase the effective mitral orifice. Commissurotomy may postpone and avoid valve replacement. Ring resection provides excellent long-term results in all cases of supramitral ring and in half of the cases of intramitral obstruction. Residual mitral stenosis is present in the remaining half of patients with intramitral obstruction. This condition is always accompanied by an abnormal supravalvular apparatus or valve hypoplasia, and follow-ups reveal moderate-to-advanced valve deficiencies, despite reoperation. Predictors of poor surgical outcomes include mitral annulus hypoplasia and abnormal supravalvular apparatus. Moreover, being younger than one year of age has been shown to be associated with poor surgical outcomes.^[9] In their study, Yildirim et al.^[10] argued that, even in patients with mitral annulus hypoplasia, the stenosis gradient could be reduced to reasonable values only with effective ring resection. Our case had no major pathology related to the subvalvular apparatus, and the existing interchordal obliterations were corrected.

The morphology and optimal treatment of the SMR are still controversial. Once detected, detailed echocardiography should be performed considering possible concomitant pathologies. In the presence of suspicious findings, the diagnosis should be confirmed with transesophageal echocardiography. A transeptal surgical approach can achieve optimal resection of the ring without causing mitral valve dysfunction, as

was the case with the patient in the present report. A transseptal surgical approach is also favorable, as it facilitates the detection of concomitant pathologies.^[8]

In conclusion, although rare, supramitral ring should be considered in patients with Turner syndrome. Concomitant pathologies must be carefully considered before surgery. A transseptal surgical approach is recommended. Simple resection is sufficient for isolated lesions. Any concomitant mitral inflow obstruction must be corrected simultaneously. Early results are excellent for isolated defects.

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