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C-reactive protein/albumin ratio in predicting atrial fibrillation after coronary artery bypass grafting

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ABSTRACT

Objectives: In the present study, the purpose was to investigate the usability of the preoperative C-reactive protein/albumin ratio as a predictor of the development of postoperative atrial fibrillation in patients who undergo coronary artery bypass grafting.

Patients and methods: A total of 336 patients (228 males, 108 females; mean age: 58.1±8.5 years; range 35 to 88 years) who underwent isolated coronary artery bypass grafting with cardiopulmonary bypass between January 2019 and January 2021 were reviewed in the single-center, retrospective study. Those with postoperative sinus rhythm were considered Group 1 (n=258), and patients with postoperative atrial fibrillation were defined as Group 2 (n=78). Preoperative routine biochemical tests of the patient groups were evaluated.

Results: The incidence of postoperative atrial fibrillation was 23.2%. Statistically significant differences were detected between the two groups in terms of age (p<0.001) and previous percutaneous coronary intervention (p=0.028). In multivariate analysis, age, hemoglobin, mean platelet volume, neutrophil/lymphocyte ratio, and C-reactive protein/albumin ratio variables were found to be independent predictive factors of postoperative atrial fibrillation development (p<0.001, p=0.005, p=0.002, p<0.001, and p<0.001, respectively).

Conclusion: Preoperative hemoglobin, mean platelet volume, calculated neutrophil/lymphocyte ratio, and C-reactive protein/albumin ratio values can be used as predictors of postoperative atrial fibrillation development in patients who will undergo coronary artery bypass grafting.

Keywords: Atrial fibrillation, C-reactive protein, albumin, coronary artery bypass grafting.

One of the most common complications in the postoperative period after coronary artery bypass grafting (CABG) is cardiac arrhythmias, and the most common one is atrial fibrillation, particularly in the first 24 to 72 h.[1] Postoperative atrial fibrillation (PoAF) leads to thromboembolic events and hemodynamic disorders by impairing ventricular functions, and therefore, causes increased morbidity and mortality.[2] Inflammation plays a prominent role in the pathophysiology of PoAF. An acute systemic inflammatory response occurs due to CABG and cardiopulmonary bypass (CPB), and the patient's preoperative inflammatory status significantly affects this inflammatory response.[3,4]

C-reactive protein (CRP)/albumin ratio (CAR) is a new marker that is associated with inflammation. C-reactive protein is a nonspecific inflammation biomarker. Albumin, on the other hand, is an important protein regulating the oncotic pressure in the body with a carrier role in the blood. Low albumin levels are considered an indicator of poor prognosis.[5] Therefore, the CAR value has been associated with many cardiovascular diseases and their prognosis.[6]

In this study, the purpose was to investigate the usability of the CAR value obtained from preoperative routine biochemical tests as a predictor of PoAF development in patients who undergo CABGs.

PATIENTS AND METHODS

Patients who underwent isolated CABG with CPB by the same surgical team in the Adıyaman Training and Research Hospital, Cardiovascular Surgery Clinic

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between January 2019 and January 2021 were included in this single-center, retrospective study. The data on the patients were obtained from the electronic registry system and archive files. Patients who underwent emergency surgery, reoperations, combined cardiac surgeries, off-pump surgery, preoperative rhythm disorders, preoperative amiodarone treatment, or an acute or chronic infection, patients with a systemic inflammatory disease that requires anti-inflammatory treatment, chronic liver or renal disease, or hematological disease, and those who received steroid therapy were excluded from this study. After applying the exclusion criteria, 336 (228 males, 108 females; mean age: 58.1±8.5 years; range 35 to 88 years) patients were included in the study. Patients with postoperative sinus rhythm were considered Group 1 (n=258; mean age: 56.2±9.8 years), and patients with PoAF were defined as Group 2 (n=78; mean age: 64.3±10.3 years). Demographic characteristics of the patients, comorbidities, preoperative echocardiographic findings (left atrium diameter and ejection fraction [EF]), blood parameters, perioperative (number of distal anastomoses, cross-clamp time, CPB time) data, and postoperative (inotropic support need, total drainage amount, intensive care unit [ICU] stay, and hospital stay) data were recorded.

Preoperative routine laboratory analyzes of the patients were checked from blood samples taken from the antecubital vein at the time of admission to the clinic. Automated analyzers were used for complete blood count and biochemical measurements (CELL-DYN Ruby; Abbott Park, IL, USA, and Architect 16000; Abbott Park, IL, USA). Hemoglobin, white blood cell, neutrophil, lymphocyte, mean platelet volume (MPV), platelet, creatinine, blood urea nitrogen, CRP and albumin values were recorded, and also neutrophil/lymphocyte ratio (NLR) and CAR were calculated.

The patients were followed up with continuous electrocardiography (ECG) monitoring in the ICU in the postoperative period. Arterial blood pressure and heart rate measurements were performed routinely every 4 h, with daily 12-lead ECG control

Table 1
Preoperative variables and demographic characteristics of the patients

	Group 1 - PoAF (-) (n=258)			Group 2 - PoAF (+) (n=78)			
Variables	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			56.2±9.8			64.3±10.3	<0.001*
Sex							
Male	173	67.1		55	70.5		0.567†
Hyperlipidemia	88	34.1		23	29.5		0.447†
Hypertension	142	55.0		48	61.5		0.310†
Diabetes mellitus	85	32.9		27	34.6		0.784†
CVA	18	7.0		9	11.5		0.194†
COPD	31	12.0		15	19.2		0.104†
Current smoker	65	25.2		18	23.1		0.704†
BMI (kg/m^2)			27.4±4.6			28.5±5.0	0.071‡
Previous PCI	41	15.9		21	26.9		0.028†
ACE-I/ARB use	59	22.9		21	26.9		0.461†
Beta-blocker use	77	29.8		27	34.6		0.425†
Preoperative HR (bpm)			79.1±10.0			81.0±11.1	0.170‡
Left atrial diameter (cm)			3.6±0.2			3.7±0.3	0.082*
Left ventricle EF (%)			50.5±6.2			49.0±7.1	0.189*

PoAF: Postoperative atrial fibrillation; SD: Standard deviation; CVA: Cerebrovascular accident; COPD: Chronic obstructive pulmonary disease; BMI: Body mass index; PCI: Percutaneus coronary intervention; ACE-I: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin-receptor blocker; HR: Heart rate; EF: Ejection fraction; * Mann-Whitney U test; † Chi-square test; ‡ Student-t test.

in patients transferred to the inpatient clinic after the ICU. If there were no contraindications, beta-blocker (metoprolol) treatment was administered to the patients in the preoperative period and in the postoperative period from the first day to avoid the development of PoAF. Patients with complaints such as palpitations, shortness of breath, or increased heart rate were immediately evaluated with a 12-lead ECG. According to monitor or 12-lead ECG recordings, an episode of atrial fibrillation (irregular RR intervals and distinct P waves) lasting at least 30 sec was defined as PoAF, with reference to the European Society of Cardiology definition of atrial fibrillation.[7]

Statistical analysis

Analyzes were made with the SPSS version 11.5 software (SPSS Inc., Chicago, IL, USA). Quantitative variables were expressed as the mean ± standard deviation, and qualitative variables were presented as numbers and percentages. The normality distribution of the data was evaluated with the Shapiro-Wilk test. The chi-square test was used to evaluate the relationship between qualitative variables. Whether there were differences between the categories of the qualitative variable that had two categories in terms of a quantitative variable was evaluated with Student's t-test if normal distribution assumptions were met and with the Mann-Whitney U test if not. Receiver operating characteristic (ROC) analysis was performed for quantitative variables, and the Youden index was used to calculate the cut-off value for quantitative variables. Logistic regression analyzes were used to determine the risk factors that affected the development of PoAF. A *p* value of <0.05 was considered statistically significant.

Table 2
Preoperative laboratory values and perioperative/postoperative variables of the patients

	Group 1 - PoAF (-) (n=258)			Group 2 - PoAF (+) (n=78)			
Variables	n	%	Mean±SD	n	%	Mean±SD	*p*
Creatinine (mg/dL)			0.9±0.2			0.9±0.3	0.201*
BUN (mg/dL)			22.1±4.1			21.0±3.7	0.081*
Albumin (g/dL)			3.9±0.3			3.7±0.2	<0.001*
CRP (mg/dL)			6.4±2.5			11.5±3.1	<0.001‡
Hemoglobin (g/dL)			13.7±1.5			14.1±2.0	0.070‡
White blood cell (10^3/µL)			7.9±1.2			8.1±1.5	0.533*
Neutrophil (10^3/µL)			4.7±1.0			5.1±1.2	0.019*
Lymphocyte (10^3/µL)			2.2±0.5			1.8±0.6	<0.001*
Mean platelet volume (fL)			8.5±1.0			9.1±0.8	<0.001*
Platelet (10^3/µL)			245.0±40.3			239.0±49.4	0.575*
NLR			2.2±0.7			3.0±1.0	<0.001*
CAR			1.7±0.6			3.1±0.9	<0.001‡
CPB time (min)			90.0±14.9			94.0±27.5	0.252*
Cross-clamp time (min)			45.0±8.3			46.1±10.2	0.539*
Number of distal anastomoses			3.1±1.0			3.2±1.0	0.354*
Inotropic support	39	15.1		15	19.2		0.386†
Total drainage (mL)			610.0±154.7			580.0±168.3	0.310*
ICU stay (days)			1.9±0.6			2.3±0.8	<0.001*
Hospital stay (days)			6.3±1.3			7.9±1.2	<0.001*

PoAF: Postoperative atrial fibrillation; SD: Standard deviation; BUN: Blood urea nitrogen; CRP: C-reactive protein; NLR: Neutrophil/lymphocyte ratio; CAR: C-reactive protein/albumin ratio; CPB: Cardiopulmonary bypass; ICU: Intensive care unit; * Mann-Whitney U test; † Chi-square test; ‡ Student-t test.

Table 3
Logistic regression analysis to identify possible predictors of PoAF

	Univariate analysis			Multivariate analysis		
			95% CI			95% CI
Variables	*p*	OR	Lower-Upper	*p*	OR	Lower-Upper
Age	<0.001	1.083	1.053-1.113	<0.001	1.132	1.076-1.190
Previous PCI	0.030	1.950	1.069-3.558			
Left atrial diameter	0.042	2.874	1.041-7.932			
Preoperative HR	0.170	1.017	0.993-1.043			
CPB time	0.098	1.012	0.998-1.025			
Number of distal anastomoses	0.384	1.120	0.868-1.446			
White blood cell	0.220	1.129	0.930-1.371			
Hemoglobin	0.035	1.184	1.012-1.387	0.005	1.530	1.133-2.064
Mean platelet volume	<0.001	1.949	1.468-2.589	0.002	2.049	1.305-3.216
NLR	<0.001	3.482	2.393-5.066	<0.001	3.383	1.828-6.260
CAR	<0.001	13.394	7.351-24.404	<0.001	19.164	8.281-44.352

CI: Confidence interval; OR: Odds ratio; PCI: Percutaneus coronary intervention; HR: Heart rate; CPB: Cardiopulmonary bypass; NLR: Neutrophil/lymphocyte ratio; CAR: C-reactive protein/albumin ratio.

RESULTS

In the present study, which included 336 patients, PoAF developed in 23.2% (n=78). There was a statistically significant difference between the mean age of the groups (p<0.001). No statistically significant differences were found between the patient groups in terms of sex, hyperlipidemia, diabetes mellitus, hypertension, chronic obstructive pulmonary disease cerebrovascular accident, current smoking habit, body mass index, preoperative medical treatment (beta-blocker and angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker use), and preoperative heart rate. The rate of previous percutaneous coronary intervention (PCI) was significantly higher in Group 2 (p=0.028). There were no significant differences between the groups in terms of left ventricular EF and left atrium diameter parameters, which were evaluated preoperatively (Table 1).

The comparison of the preoperative laboratory values of the patient groups is given in Table 2. Albumin and lymphocyte levels were significantly lower in Group 2 (p<0.001 and p<0.001, respectively), and CRP, neutrophil, and MPV values were significantly higher (p<0.001, p=0.019, and p<0.001, respectively). The mean NLR value was 2.2±0.7 in Group 1 and 3.0±1.0 in Group 2, and the difference was statistically significant (p<0.001). The mean CAR value was 1.7±0.6 in Group 1 and 3.1±0.9 in Group 2, and the difference was statistically significant (p<0.001). Although there were no significant differences between the patient groups in terms of perioperative variables, among the postoperative variables, only ICU and hospital stay were found to be statistically significantly higher in Group 2 (p<0.001 and p<0.001, respectively; Table 2).

Age, previous PCI, left atrial diameter, hemoglobin, MPV, NLR, and CAR variables were found to be statistically significant risk factors in univariate analysis and were included in multivariate analysis to identify possible predictors of PoAF development (Table 3). According to the results of this analysis, age, hemoglobin, MPV, NLR, and CAR variables were found to be independent predictive factors for the development of PoAF (p<0.001, p=0.005, p=0.002, p<0.001, and p<0.001, respectively).

The ROC curve analysis was used to determine the predictive effects of MPV, NLR, and CAR variables on the development of PoAF (Figure 1). The cut-off value was 9.1 for MPV (area under the curve [AUC]: 0.695, 95% confidence interval [CI]: 0.634-0.756, p<0.001) with 61.5% sensitivity and 72.9% specificity. The cut-off value was 2.5 for NLR (AUC: 0.746, 95% CI: 0.679-0.812, p<0.001)

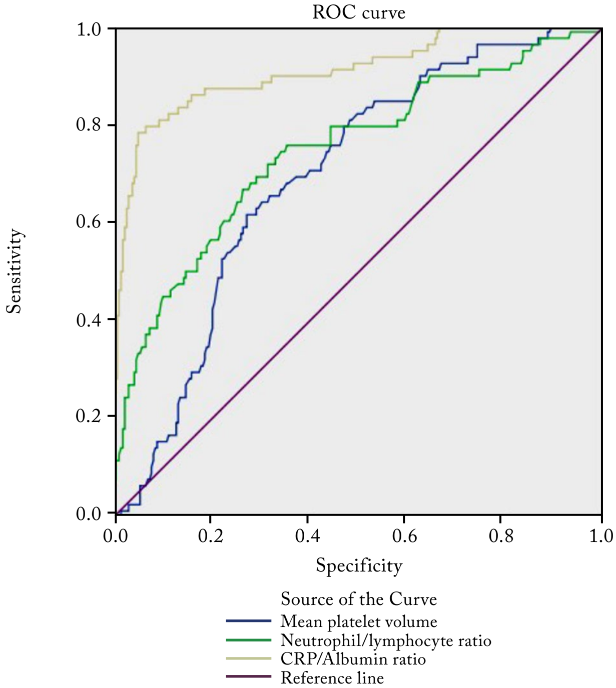

Figure 1. Receiver operation characteristic curve of MPV, NLR, and CAR for predicting PoAF.

ROC: Receiver operating characteristic; CRP: C-reactive protein; MPV: Mean platelet volume; NLR: Neutrophil/lymphocyte ratio; CAR: C-reactive protein/albumin ratio; PoAF: Postoperative atrial fibrillation.

with 71.8% sensitivity and 68.6% specificity. The cut-off value was 2.7 for CAR (AUC: 0.909, 95% CI: 0.867-0.951, p<0.001) with 78.2% sensitivity and 95% specificity (Table 4).

DISCUSSION

In this retrospective study investigating the relation between the development of PoAF and preoperative CAR value in patients who underwent CABG with CPB, it is remarkable that the NLR and CAR values of the patient group that developed PoAF were significantly higher. Additionally, age, hemoglobin, MPV, NLR, and CAR variables were found to be independent predictive factors of PoAF development.

Postoperative atrial fibrillation is a common complication of CABG, and its incidence has been reported between 6 and 40% in patients who undergo isolated CABG.[4] In the present study, the incidence was found to be 23.2%. Inflammation is an important factor in the pathophysiology of many postoperative complications in cardiac surgery. The inflammatory status of the patient in the preoperative period and the inflammatory response due to CPB in the perioperative period affect postoperative morbidity and mortality. It is considered that, in particular, the immune cells and mediators responsible for the inflammatory response affect the atrial tissue in the development of PoAF.[8]

After the role of inflammation in the pathophysiology of diseases and their associated complications were understood, many inflammatory biomarkers were associated with diseases. The NLR is a hematological parameter that is evaluated for this purpose and is also known as an indicator of subclinical inflammation.[9] Neutrophilia suggests nonspecific inflammation and is associated with atherothrombosis owing to platelet activation. Lymphopenia, however, indicates the strength of physiological stress and is considered an indicator of poor prognosis.[10,11] Neutrophilia and lymphopenia cause increased NLR levels, and therefore, high NLR values are associated with poor prognosis. Berkovitch et al.[12] calculated the NLR values at admission in their study, which included 21,118 individuals with the primary endpoint as new-onset atrial fibrillation. The results of this study demonstrate that there is a relation between high NLR and new-onset atrial fibrillation, and it was reported that a one-unit increase in NLR increases the risk of developing atrial fibrillation by 14% (95%

Table 4
Results of the ROC curve analysis

Variables	AUC	SE	*p*	95% CI Lower-Upper	Sensitivity (%)	Specificity (%)	Cut-off value
Mean platelet volume	0.695	0.031	<0.001	0.634-0.756	61.5	72.9	9.1
NLR	0.746	0.034	<0.001	0.679-0.812	71.8	68.6	2.5
CAR	0.909	0.021	<0.001	0.867-0.951	78.2	95.0	2.7

ROC: Receiver operating characteristic; CI: Confidence interval; AUC: Area under the curve; SE: Standard error; NLR: Neutrophil/lymphocyte ratio; CAR: C-reactive protein/albumin ratio.

CI: 1.06-1.23, p<0.001). In our study, it was revealed that the preoperative NLR values of our patient group with PoAF were significantly higher and a one-unit increase in NLR increased the risk of developing PoAF 3.383 times.

It is already known that there is a relation between low preoperative hemoglobin levels and increased postoperative mortality and morbidity in cardiac surgery.[13] In our study, although the preoperative hemoglobin levels were higher in our patient group who developed PoAF, hemoglobin was found to be an independent predictor of PoAF development in multivariate analyzes. Due to the inflammation in the body, the number of young and large-volume platelets increases; consequently, the MPV value, which is the indicator of platelet size, also increases.[2] In a study including 1,138 patients with isolated CABG, it was reported that the preoperative MPV value was significantly higher in the patient group that developed PoAF.[14] Consistent with the literature data, preoperative MPV values were significantly higher in the patient group with PoAF in our study, and MPV was found to be a predictor of PoAF development.

C-reactive protein is the most commonly used nonspecific inflammatory biomarker. Weymann et al.[4] reported in their meta-analysis that there is a significant relationship between the development of PoAF after cardiac surgeries and preoperative high CRP levels. In our study, it was found that there were significantly higher preoperative CRP levels in the patient group who developed PoAF. Albumin is a protein that has colloid osmotic effects, antithrombotic, anti-inflammatory, and antioxidant properties, and based on these characteristics, the decrease in albumin levels is an indicator of poor prognosis.[15,16] It exhibits antioxidant and anti-inflammatory properties by scavenging reactive oxygen species and free radicals that cause inflammation and endothelial dysfunction. It is known that increased reactive oxygen species increase the sensitivity of PoAF by affecting the atrial cells. In a published meta-analysis, it was reported that there is a negative correlation between serum albumin levels and the development of atrial fibrillation.[17] In our study, significantly lower albumin levels were noted in our patient group who developed PoAF.

The CAR is a marker defined as a predictor of the inflammatory status and prognosis and is considered more valuable than albumin or CRP alone.[6,18,19] Karabağ et al.[20] classified 403 stable angina pectoris patients according to the Syntax score and found that CAR was more significant alone than CRP and albumin in determining the severity of the disease. Park et al.[21] retrospectively reviewed 875 medical ICU patients, and found CAR to be an independent predictor of 28-day mortality (OR: 1.01, 95% CI: 1.00-1.02, p=0.001). In their study, which included 830 patients who underwent isolated CABG, Karabacak et al.[6] discovered that the preoperative CAR value was an independent predictor for the development of PoAF. In our study, the patient group that developed PoAF had significantly higher preoperative CAR values compared to the patient group with postoperative sinus rhythm, and preoperative CAR was also determined to be an independent predictor for the development of PoAF.

The main limitations of the study are its retrospective design and relatively low number of patients. Another significant limitation is that the development of PoAF was not evaluated after discharge. In addition, there may have been some patients whose PoAF development could not be evaluated as the patients were not followed up with the telemetry system in the inpatient clinic. The presence of comorbid hyperlipidemia was compared in the patient groups; however, the use of statin group drugs with dose-dependent effects for the treatment of hyperlipidemia was not evaluated, which can be considered a limitation since statins also have pleiotropic effects (antioxidant and anti-inflammatory).

In conclusion, statistically significant relations were detected between PoAF development and CAR values in patients who underwent CABG. Age, hemoglobin, MPV, NLR, and CAR variables were independent predictors for the development of PoAF in the analyzes performed. In addition, the predictive value of CAR value in the development of PoAF was higher than other parameters. Evaluation of hemoglobin, MPV, NLR, and CAR values, which can be easily obtained from preoperative routine biochemical tests, can provide early detection of patients at risk for PoAF, whose diagnosis is crucial due to the risk of increased morbidity and mortality.

Ethics Committee Approval: The study protocol was approved by the Adıyaman University Faculty of Medicine Ethics Committee (Date: 19/01/2021, no: 2021/01-10). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: Due to the retrospective nature of the study, informed consent was not obtained from the patients.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept, design, literature review, writing the article: A.A.P.; Idea/concept, design, writing the article, references and fundings: A.K.A.; Idea/concept, design, references and fundings, materials: Y.S.U.; Data collection and/or processing, analysis and/or interpretation, materials: M.E.; Idea/concept, control/supervision, literature review, critical review: Ş.Y., A.F.Ö.

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Evaluation of mortality scores in patients with adult congenital heart defects

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ABSTRACT

Objectives: Currently, there is no approved risk stratification for adult congenital heart surgery; accordingly, this study aimed to evaluate risk stratification for congenital heart surgery in the pediatric age in terms of its prognostic value in adult patients as well as the effectiveness of the newly developed Adult Congenital Heart Surgery (ACHS) score in this patient group.

Patients and methods: A total of 205 patients (115 males, 90 females; mean age: 25.0±11.4 years; range, 18 to 65 years) operated on due to congenital heart disease between January 1, 2011, and August 1, 2019, were studied retrospectively. Aristotle Basic Complexity (ABC) score, Society of Thoracic Surgery European Association for Cardiothoracic Surgery (STAT) score, and ACHS score were evaluated. Receiver operating characteristic (ROC) curves were created to evaluate the ability of scoring systems to predict mortality.

Results: The mortality rate was 4.4% (n=9). For mortality, areas under the ROC curve were 0.89, 0.89, and 0.70 for ABC, STAT, and ACHS scores, respectively. The mean ACHS score was 0.42±0.34. The cut-off point of the ACHS score was identified as 0.7 and above. The specificity of the cut-off value of 0.7 regarding the ACHS score was 94.39%. Adult Congenital Heart Surgery scores were found to be statistically high in patients with mortality ($p=0.037$; $p<0.05$).

Conclusion: Adult Congenital Heart Surgery scores had higher specificity in determining mortality in cases with an ACHS score of 0.7 and above. The ACHS score could also be used to determine the expected mortality rate, similar to the ABC and STAT scores.

Keywords: Adult congenital heart surgery score; aristotle basic complexity score; mortality; society of thoracic surgery european association for cardiothoracic surgery score.

In congenital heart disease, Aristotle Basic Complexity (ABC) and Society of Thoracic Surgery European Association for Cardiothoracic Surgery (STAT) scores are frequently used to determine mortality. In grown-up congenital heart (GUCH) patients, surgery is complex due to residual lesions, complications, or sequelae after previous palliative surgery or complete correction.[1]

Previous studies reported that GUCH patients had several risk factors for morbidity and mortality after surgery. Mortality rates detected in GUCH patients are low; however, our knowledge about this growing population of patients is still limited.[2] This study aimed to determine the effectiveness of the Adult Congenital Heart Surgery (ACHS) score for early mortality in primary surgery and reoperations and compare it with ABC and STAT scores.

PATIENTS AND METHODS

In this retrospective study, 205 patients (115 males, 90 females; mean age: 25.0±11.4 years; range, 18 to 65 years) operated on due to congenital heart disease at the Kartal Koşuyolu Yüksek Ihtisas Training and Research Hospital between January 1, 2011, and August 1, 2019, were included. The patients were divided into 27 subgroups according to the type of operation. In our study, ABC and STAT mortality scores of each patient were calculated, and an ACHS score was given according to the procedures performed on the patients based on the studies conducted by Fuller et al.[1] in 2015. Patients who underwent multiple procedures during the operation were given an ACHS score with the highest mortality score. Mortality was determined as the hospital mortality.

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Table 1
Distribution of diagnoses, mortality and number of operation

	Mortality				Number of operation									
					1		2		3		4		5	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Aortic valve repair	1	0.5	0	0	1	100	0	0	0	0	0	0	0	0
Aortic aneurysm	2	1.0	0	0	1	50	0	0	1	50	0	0	0	0
Aortic stenosis, subvalvular	1	0.5	0	0	1	100	0	0	0	0	0	0	0	0
Atrial septal defect	28	13.7	0	0	28	100	0	0	0	0	0	0	0	0
Aortic valve replacement	2	0.1	0	0	2	100	0	0	0	0	0	0	0	0
Coronary artery bypass graft	2	1.0	0	0	1	50	1	50	0	0	0	0	0	0
Double chamber right ventricle	9	4.4	0	0	7	77.8	2	22.2	0	0	0	0	0	0
Ebstein anomaly	6	2.9	1	16.7	6	100	0	0	0	0	0	0	0	0
Fontan operation	3	1.5	1	33.4	0	0	2	66.7	0	0	0	0	1	33.4
Fontan revision	1	0.5	1	100	0	0	0	0	0	0	0	0	1	100
Aortic coarctation	2	1.0	0	0	2	100	0	0	0	0	0	0	0	0
Conno procedure	1	0.5	1	100	0	0	0	0	0	0	1	100	0	0
Mitral valve repair	9	4.4	2	22.3	2	22.3	4	44.4	3	33.3	0	0	0	0
Mitral valve replacement	3	1.5	0	0	1	33.3	2	66.7	0	0	0	0	0	0
Partial atrioventricular septal defect	19	9.3	0	0	19	100	0	0	0	0	0	0	0	0
Pulmonary artery reconstruction	7	3.4	1	14.3	5	71.4	2	28.6	0	0	0	0	0	0
Pace implantation	2	1.0	0	0	1	50	1	50	0	0	0	0	0	0
Partial abnormal pulmonary venous return	26	12.7	0	0	26	100	0	0	0	0	0	0	0	0
Patent ductus arteriosus	3	1.5	0	0	3	100	0	0	0	0	0	0	0	0
Pulmonary valvuloplasty	3	1.5	0	0	3	100	0	0	0	0	0	0	0	0
Pulmonary valve replacement	15	7.3	0	0	1	6.7	11	73.3	3	20.0	0	0	0	0
Right ventricle-pulmonary artery conduit	3	1.5	1	33.4	1	33.4	1	33.3	1	33.3	0	0	0	0
Right ventricular outflow tract reconstruction	10	4.9	0	0	3	30.0	6	60.0	0	0	1	10.0	0	0
Aortopulmonary shunt	3	1.5	1	33.4	1	13.3	2	66.7	0	0	0	0	0	0
Scimitar syndrome	3	1.5	0	0	3	100	0	0	0	0	0	0	0	0
Tricuspid valve repair	7	3.4	0	0	4	57.1	3	42.9	0	0	0	0	0	0
Tetralogy of Fallot	5	2.4	0	0	5	100	0	0	0	0	0	0	0	0
Ventricular septal defect	29	14.1	0	0	21	72.4	8	27.6	0	0	0	0	0	0

Statistical analysis

The NCSS (Number Cruncher Statistical System) version 2007 (NCSS LLC., Kaysville, UT, USA) software was used for statistical analyses. Descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum) were used to evaluate the data of the study. The compliance of the quantitative data with the normal distribution was tested via the Kolmogorov-Smirnov test, Shapiro-Wilk test, and graphical assessments. The Mann-Whitney U test was used to compare two groups that did not indicate normal data distribution. In the comparison of qualitative data, the Fisher-Freeman-Halton exact test and Fisher exact test were used. Diagnostic screening tests (sensitivity, specificity, positive predictive value, and negative predictive value) and ROC curve analysis were used to determine the cut-off value of the parameters. A *p* value of <0.05 was considered statistically significant.

RESULTS

The distribution of the patients according to diagnoses, numbers of reoperations, and mortality is presented in Table 1. The most frequent diagnoses were ventricular septal defect with 14.1% (n=29), atrial septal defect with 13.7% (n=28), partial abnormal pulmonary venous return with 12.7% (n=26), partial atrioventricular septal defect with 9.3% (n=19), and pulmonary valve replacement with 7.3% (n=15).

The ABC, STAT, and ACHS score distributions according to mortality are provided in Table 2. Mortality was observed in 4.4% (n=9) of the patients included in the study. In terms of mortality, statistically significant differences were identified for ABC, STAT (p=0.001; p<0.01), and ACHS scores (p=0.037; p>0.05); the scores of patients with mortality were higher. We used the binomial exact test (DeLong test) to compare the areas under the ROC curves. Accordingly, the ABC and STAT mortality scores were not significantly different in predicting mortality (p>0.05), whereas the ABC and ACHS scores were significantly associated (p<0.05). There was also a borderline significance between the STAT mortality score and the ACHS score (p≤0.05; Figure 1). Based on this significance, cut-off points were calculated for the scoring systems. The cut-off values and ROC curve results are given in

Table 2
Evaluation of aristotle basic, STAT and ACHS scores according to mortality

	Mortality										
	(-) (n=196)					(+) (n=9)					
	n	%	Mean±SD	Median	Q1-Q3	n	%	Mean±SD	Median	Q1-Q3	*p*
Aristotle basic complexity score			6.64±2.12	7.0	5-8			10.70±2.36	10.0	9.5-12	0.001*†
Aristotle basic complexity category											0.001*‡
Level 1	59	100				0	0				
Level 2	74	98.7				1	1.3				
Level 3	45	95.7				2	4.3				
Level 4	18	75.0				6	25.0				
STAT mortality score			0.51±0.38	0.5	0.2-0.7			1.58±0.84	1.4	0.8-2.5	0.001*†
STAT mortality category											0.001*‡
Level 1	87	100				0	0				
Level 2	78	98.7				1	1.3				
Level 3	18	85.7				3	14.3				
Level 4	13	72.2				5	27.8				
ACHS score			0.39±0.27	0.4	0.2-0.5			0.92±0.91	0.4	0.4-0.9	0.034**†

STAT: Society of Thoracic Surgery European Association for Cardiothoracic Surgery; ACHS: Adult Congenital Heart Surgery; SD: Standard deviation; Q: Quartile; † Mann Whitney U Test; ‡ Fisher Freman Halton test; * p<0.01; ** p<0.05.

Table 3
Diagnostic screening tests and ROC curve results for ABC, STAT and ACHS score by mortality

	Diagnostic scan						ROC curve	
	Cut off	A	B	PPV	NPV	AUC	95% CI	*p*
ABC score	≥9	88.89	84.69	21.05	99.40	0.899	0.784-1.000	0.001**
STAT score	≥0.8	88.89	84.18	20.51	99.41	0.898	0.790-1.000	0.001**
ACHS score	≥0.7	44.44	94.39	26.67	97.37	0.706	0.538-0.874	0.037*

ROC: Receiver operating characteristic; ABC: Aristotle Basic Complexity score; STAT: Society of Thoracic Surgery European Association for Cardiothoracic Surgery; ACHS: Adult Congenital Heart Surgery; A: Sensitivite; B: Spesifisite; PPV: Positive predictive value; NPV: Negative predictive value; AUC: Area under the curve; CI: Confidence interval; * p<0.05; ** p<0.01.

Table 3 (Figure 2). The cut-off values were ≥9, ≥0.8, and ≥0.7 for the ABC, STAT, and ACHS scores, respectively, and a statistically significant difference was observed between these values (p=0.001; p <0.01). The numbers of reoperations and postoperative complications, the mortality scores of the patients who underwent reoperation, and the relevant ROC curve results are presented in Tables 4, 5, and 6, respectively (Figure 2).

DISCUSSION

Adults with congenital heart disease make up a rapidly growing segment of the cardiovascular patient population.[2] In their study, Gilboa et al.[3] estimated that the number of patients reached 1.4 million. The incidence of congenital heart disease in Türkiye is about 1%, and there are approximately 12,000 new patients each year.[4] Today, more than 85% of children

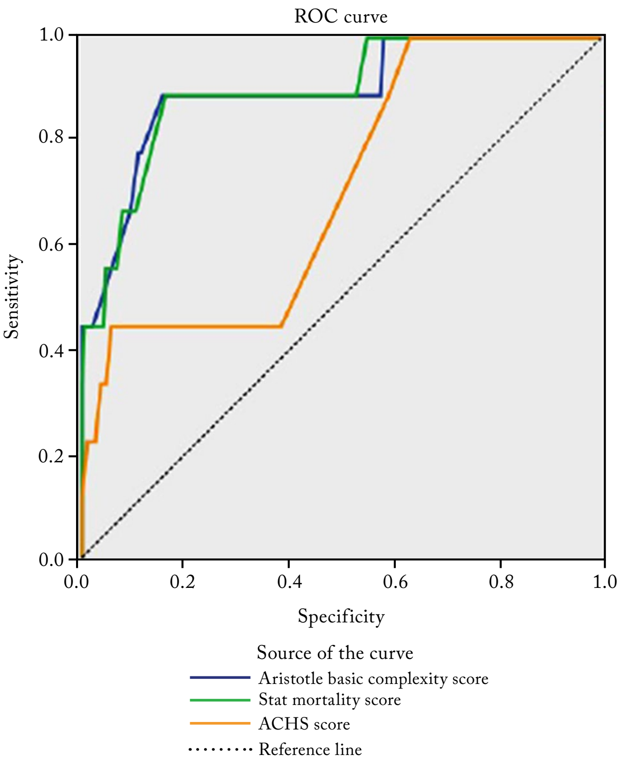

Figure 1. ROC curves for ABC, STAT and ACHS scores by mortality.

ROC: Receiver operating characteristic; ABC: Aristotle Basic Complexity score; STAT: Society of Thoracic Surgery European Association for Cardiothoracic Surgery; ACHS: Adult Congenital Heart Surgery.

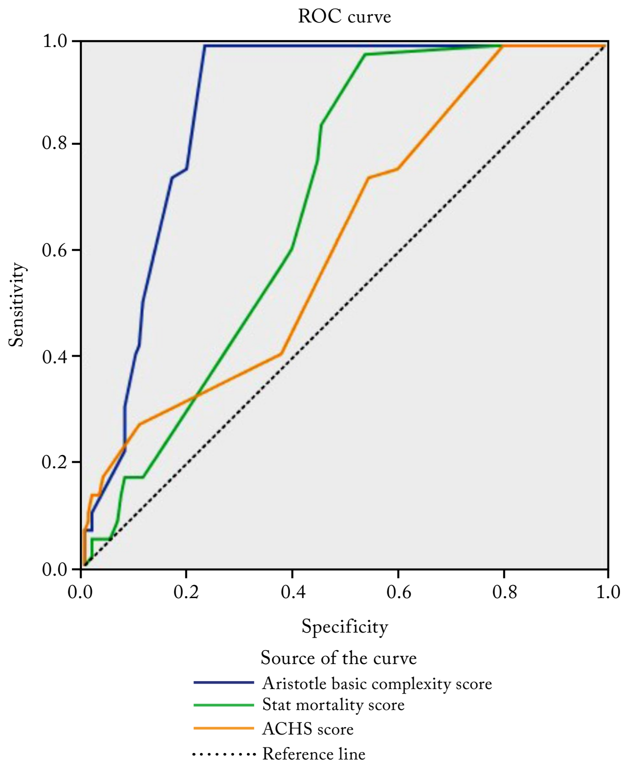

Figure 2. ROC curves for ABC, STAT and ACHS scores according to mortality in reoperated patients.

ROC: Receiver operating characteristic; ABC: Aristotle Basic Complexity score; STAT: Society of Thoracic Surgery European Association for Cardiothoracic Surgery; ACHS: Adult Congenital Heart Surgery.

Table 4
Distribution of reoperation and postoperative complication

	n	%	*p*
Reoperation			
(-)	146	71.2	
(+)	59	28.8	
2nd operation	47	22.9	
3rd operation	7	3.4	
4th operation	3	1.5	
5th operation	2	1.0	
Postoperative complication			0.02*
(-)	177	86.3	
(+)	28	13.7	
Wound infection	2	7.1	
Arrhythmia	5	17.9	
Neurological complication	3	10.7	
Delayed sternal closure	2	7.1	
Low cardiac output	4	14.3	
Postoperative bleeding-induced exploration	7	25.0	
ECMO	3	10.7	
Postoperative early reoperation	7	25.0	
Prolonged ventilation	5	17.9	
Pericardial effusion	3	10.7	
Mortality			
(-)	196	95.6	
(+)	9	4.4	

ECMO: Extracorporeal membrane oxygenation; Fisher Freeman Halton exact test; * $p<0.01$.

with congenital heart disease are expected to reach adulthood.[5,6]

Risk stratification regarding the procedures is important in determining surgical mortality. In 2004, Lacour-Gayet et al.[7] developed the ABC score to assess surgeon performance in congenital heart surgery. In 2006, Kang et al.[8] demonstrated that this score is somewhat useful in determining mortality but cannot be used as a statistically significant tool. In 2007, O'Brien et al.[9] argued that the ABC score is useful for differentiating low-and high-risk patients. A 2011 study by Photiadis et al.[10] supported this opinion but indicated that the ABC score is based on the complexity of surgical procedures and does not take into account patient-related factors. In their 2012 study, Hörer et al.[11] demonstrated that the ABC score is not suitable for predicting mortality in combined surgical procedures.

In 2014, Kogon et al.[12] published a study comparing the STAT and ABC scores. In this retrospective study, they argued that the scoring systems used in pediatric patients were also valuable in the adult group. They suggested that ABC and STAT scores had similar results in determining mortality; however, ABC score was more effective in determining major complications and length of hospitalization.

In 2015, Cavalcanti et al.[13] argued that the ABC and STAT scores were not significantly different in predicting mortality. A 2016 study by Hörer et al.[14] suggested that the ABC score had a low predictive value but outperformed the STAT score. In 2019, Bobillo-Perez et al.[15] indicated that the predictive performance of the STAT score was better than that of the ABC score.[16]

The controversial state of scoring systems in the adult group caused the search for a new scoring system. In their study published in 2015, Fuller et al.[1] suggested that the ACHS mortality score was effective. In this study, they divided the patients into 152 groups and determined an ACHS mortality score

Table 5
Evaluation of ABC, STAT and ACHS scores according to mortality in reoperated patients

	Mortality										
	(-) (n=146)					(+) (n=59)					
	n	%	Mean±SD	Median	Q1-Q3	n	%	Mean±SD	Median	Q1-Q3	*p*
Aristotle basic complexity score			6.64±2.12	7.0	5-8			10.70±2.36	10.0	9.5-12	0.001*†
Aristotle Basic Complexity category											0.001*‡
Level 1	59	100				0	0				
Level 2	60	80.0				15	20.0				
Level 3	16	34.0				31	66.0				
Level 4	11	45.8				13	54.2				
STAT mortality score			0.51±0.38	0.5	0.2-0.7			1.58±0.84	1.4	0.8-2.5	0.001*†
STAT mortality category											0.001*‡
Level 1	78	89.7				9	10.3				
Level 2	44	55.7				35	44.3				
Level 3	14	66.7				7	33.3				
Level 4	10	55.6				8	44.4				
ACHS score			0.39±0.27	0.4	0.2-0.5			0.92±0.91	0.4	0.4-0.9	0.034**†

ABC: Aristotle Basic Complexity score; STAT: Society of Thoracic Surgery European Association for Cardiothoracic Surgery; ACHS: Adult Congenital Heart Surgery; SD: Standard deviation; Q: Quartile; † Mann Whitney U test; ‡ Pearson Chi square test; * $p<0.01$; ** $p<0.05$.

ranging from 0.1 to 3.0 for each. In 2019, Abouelella et al.[17] stated that the ACHS score is currently the best predictor of mortality in GUCH patients and that the mortality rate was 4%.

In our study, we investigated the effectiveness of GUCH using this scoring system. In the present study, hospital mortality was 4.4% (n=9). In terms of mortality, statistically significant differences were identified for ABC, STAT (p=0.001; p<0.01), and ACHS scores (p=0.037; p>0.05); the scores of patients with mortality were higher (Table 3). In our study, we calculated the cut-off values and performed ROC curve analysis for the prediction of mortality. The ROC curve results for ABC, STAT, and ACHS scores for predicting mortality are given in Table 3. Based on this significance, cut-off points were calculated for the scoring systems. The incidence of mortality was 13.455 times higher in patients with a cut-off value of ≥0.7 in their ACHS mortality scores.

Abouelella et al.[17] reported a postoperative complication rate of 18%, similar to the rate of 28% stated by Mascio et al.[18] The reported incidence of neurological complications is 7%.[19] In our study, postoperative complications were detected in 13.7% of the cases (n=28), and it is consistent with the literature (Table 4). In our study, extracorporeal membrane oxygenation was required in 10.7% (n=3) of patients (aortopulmonary shunt, n=1; pulmonary artery reconstruction, n=1; mitral valve repair, n=1) due to low cardiac output. All of these patients died while on support. Neurological complications were observed in 10.7% (n=3) of our patients, including one patient who underwent right ventricle to pulmonary artery conduit replacement and later died due to intracranial bleeding, as well as two patients who underwent pulmonary valve replacement and mitral valve replacement. These patients developed postoperative convulsions, but no pathologies were detected in their examinations; therefore, the condition was attributed to temporary ischemia and completely resolved with medical treatment.

A statistically significant relationship was found between postoperative complication rates according to the occurrence of reoperation (p=0.002; p<0.01); the rate of postoperative complication incidents in those reoperated was higher than in those who were not reoperated. The ABC, STAT, and ACHS results of reoperated patients are demonstrated in Table 5.

Table 6
ROC curve results for ABC, STAT and ACHS scores in reoperated patients

	ROC curve		
	AUC	95% CI	*p*
Aristotle basic complexity score	0.881	0.835-0.927	0.001*
STAT mortality score	0.698	0.628-0.768	0.001*
ACHS score	0.626	0.544-0.707	0.005*

AUC: Area under the curve; ROC: Receiver operating characteristic; CI: Confidence interval; * p<0.01.

The ABC, STAT, and ACHS scores of the patients who underwent reoperation were significantly higher than the scores of those who did not. The areas under the ROC curves were 0.81 (p=0.001, p<0.01), 0.69 (p=0.001, p<0.01), and 0.62 (p=0.034, p<0.05), respectively.

When the areas undser the ROC curve were compared, the ABC score was found to be more effective in predicting mortality than the ACHS score (p=0.001; p<0.01). The STAT mortality score and ACHS score were not significantly different (p=0.626; p>0.05; Table 6).

The small sample size of the study is its main limitation. Some complex surgeries, such as Fontan operation, are rare in adulthood, and therefore the number of patients to be compared is small. Additionally, some data losses are not excluded due to the retrospective design.

In conclusion, for primary operations, all scoring systems could significantly predict mortality; however, the ABC and STAT scores had better predictive value compared to the ACHS score. The predictive value of STAT and ACHS scores was similar in reoperations, whereas the ABC score had a higher predictive value. The ACHS mortality score has good predictive power in adult congenital heart patients. Preoperative risk prediction could be used safely to analyze surgical results.

Ethics Committee Approval: The study protocol was approved by the Koşuyolu High Specialization Education and Research Hospital Ethics Committee (Date: 08.12.2020, no: 2020/13/390). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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The effect of right conventional radial artery access site and left distal radial artery access site on quality of life in coronary angiography: Which route is more appropriate?

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ABSTRACT

Objectives: There are not many studies comparing the right conventional and left distal radial (anatomical snuffbox) access in coronary angiography (CAG) or percutaneous coronary intervention (PCI) in terms of patient satisfaction and complications; therefore, in this study, we planned to compare these two approaches and determine the ideal radial access site for the patients.

Patients and methods: A total of 120 patients (80 males, 40 females; mean age: 59.2±11.7 years; range, 18 to 90 years) who underwent CAG or PCI via the radial artery between February 2022 and April 2022 were included in the prospective observational study. The patients were divided into right conventional radial artery access (Group 1; n=68) and left distal radial artery (access (Group 2; n=52) groups.

Results: The rate of minor bleeding was higher in the right conventional access group compared to the left distal access group (16.2% *vs.* 3.8%; p=0.031). Major bleeding, hand ischemia, and radial artery occlusion were not observed in the study population. The rate of patients who had pain that disrupts daily activities was statistically higher in Group 1 than in Group 2 (17.6% *vs.* 5.8%). The patients in Group 2 were more satisfied with the transradial CAG/PCI compared to Group 1 (94.3% *vs.* 66.2%; p=0.001).

Conclusion: Left distal radial artery access from the anatomic snuffbox was a safer method than right conventional radial artery access for CAG or PCI. Patients were more satisfied with the left distal radial access than the right conventional radial access.

Keywords: Anatomic snuffbox, complication, quality of life, radial access.

Coronary artery disease (CAD) is the leading cause of death worldwide. The development of techniques and devices in percutaneous coronary interventions (PCI) performed by coronary angiography (CAG) for the diagnosis and treatment of CAD has significantly reduced the mortality rate due to CAD.[1]

Coronary angiography and PCI can be performed via the femoral, brachial, and radial arteries. Among them, the most preferred method of access is the femoral artery. However, studies have shown that femoral access is associated with high rates of vascular and bleeding complications.[2-4] The advantages of transradial access include less risk of bleeding, lower morbidity, lower total hospital costs, early discharge, higher patient comfort, and lower risk of ischemia in the hand due to double blood supply.[5]

In one study, a low overall incidence of complications was reported by transradial access, and the recovery times were shorter compared to transfemoral access.[6] In addition, it was determined that most patients (94%) would choose to perform subsequent procedures this way.[6] Transradial access has recently started being widely used by many centers in CAG.

In CAG and PCI procedures, vascular complications can occur in radial access, although the radial access is a safer method compared to the femoral access. Symptomatic radial artery occlusion (RAO), nonocclusive radial artery injury, and radial artery spasms are common complications of the radial access.[7] Pseudoaneurysm formation and radial artery

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perforation have been reported as rare complications.[8] Distal radial access is recommended due to a lower risk of local complications compared to standard radial access, particularly due to the lower incidence of RAO and better comfort for both the patient and the operator.[9]

There are studies that include the safety, effectiveness, and patient satisfaction of the radial and femoral approaches.[10] However, there are not many studies comparing CAG performed with the conventional and left distal radial (anatomical snuffbox) access in terms of patient satisfaction and complications. Therefore, in our study, we planned to compare the radial access sites in terms of patient satisfaction and complications and determine the ideal radial access site in patients who underwent CAG or PCI.

PATIENTS AND METHODS

One hundred and twenty patients (80 males, 40 females; mean age: 59.2±11.7 years; range, 18 to 90 years) who were scheduled for CAG or PCI due to the diagnosis of chronic coronary syndrome at the Department of Cardiology of three institutions between February 2022 and April 2022 were included in the prospective observational study. The patients were divided into right conventional radial artery access (Group 1) and left distal radial artery access (Group 2) groups according to the access site. Patients with palpable conventional or distal radial pulses were included in the study. Patients with a nonpalpable conventional or distal radial pulse, previous history of CAG via radial access, severe forearm artery malformation, history of coronary artery bypass graft or radial artery use, history of infection at the access site, contrast allergy, severe chronic renal failure, severe liver failure, active malignancy were excluded from the study. Age, sex, body mass index (BMI), blood pressure, smoking history, comorbid diseases, and treatments of the patients were recorded in the case report form. Echocardiographic parameters and laboratory results were checked from the system.

Operators had at least two years of experience in both conventional and distal radial intervention. It was left to the discretion of the operator whether the intervention was done by the conventional or distal radial access. Allen's test was not applied to the patients before the procedure to not affect the patient selection and as it is not routinely used in clinical practice.

Questionnaires were conducted to evaluate whether the patients were satisfied with the CAG procedure performed through the radial artery, whether they would recommend this method to their relatives who might need CAG, and whether the patients experienced pain that limited their daily activities after this procedure. Questionnaires were asked to the patients face-to-face or by phone/mail.

Radial intervention procedure

In the case of right conventional radial access, the patient's right arm was placed comfortably on a side panel. In the left distal radial access, the patient's left arm was placed on the abdomen, and the left hand was placed on the right groin with the puncture area. Appropriate sterilization was provided before radial artery puncture. Afterward, local anesthesia with 2-3 mL of 2% lidocaine was applied to the access site. The radial artery was punctured with a 20 G needle at a 45-degree angle. Coronary angiography was performed with a 5F right-left diagnostic catheter. The guiding catheters used in the PCI procedure were 6F for both sides. A 6F sheath was used in all patients. This situation eliminated the effect of the study results depending on the sheath size.

For the prevention of radial artery vasospasm and thrombosis, a mixture of heparin and isosorbide dinitrate was administered through the sheath in a similar account to all patients. Catheter advancement was performed with a standard 0.035 guidewire. After the sheath was removed after the procedure, manual compression was applied to the access site in all patients to ensure hemostasis. During and after the procedure, the patient's complaints and site complications were evaluated.

Statistical analysis

Analyses were performed using the IBM SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). The suitability of numerical variables to normal distribution was examined using the Kolmogorov-Smirnov test. Numerical variables are expressed as the mean and standard deviation. Categorical variables were presented as numbers (n) and percentages (%). To compare the two groups in terms of numerical variables, the independent samples t-test was used if the data were normally distributed, and the

Mann-Whitney U test was used for the nonnormally distributed data. The relationship between categorical variables was examined using the Pearson chi-square test and Fisher exact test. The significance level was accepted as p<0.05.

RESULTS

The mean BMI was 27.48±4.63. No statistically significant difference was found between the groups in mean age (59.3±11.3 *vs.* 59.1±11.7 years; p=0.915), male-to-female ratio (67.6 *vs.* 65.4; p=0.794), and mean BMI (27.28±3.63 *vs.* 27.74±5.70; p=0.592). The demographic data of the patients are presented in Table 1. Twenty-one (30.9%) patients in Group 1 and 14 (26.9%) patients in Group 2 underwent both CAG and PCI (p=0.636).

There were no statistically significant differences between the groups in terms of hypertension (57.4% *vs.* 63.5%; p=0.498), diabetes mellitus (32.4% *vs.* 32.5%; p=0.487), hyperlipidemia (42.6% *vs.* 32.7%; p=0.266), and anemia (7.3 *vs.* 11.5%; p=0.431). The most common comorbid diseases were hypertension (60%) and CAD (47.5%) (Table 2).

The mean hemoglobin value was 13.58±1.92 in Group 1 and 13.55±2.29 in Group 2, while the mean LDL value was 110.98±38.07 in Group 1 and 99.06±37.95 in Group 2. In the echocardiography, the mean left ventricular ejection fraction of the patients was 54.87%. The mean left ventricular ejection fraction was 56.10±7.29 in Group 1 and 53.27±9.54 in Group 2, and there was no statistical difference. No significant difference was found in drug use, particularly in preoperative anticoagulant and antiaggregant use, except for aldosterone antagonists. The laboratory findings of the patients and treatments are summarized in Tables 3 and 4.

According to the access site, minor bleeding was the most common local complication (10.8%). The rate of minor bleeding was higher in patients using the right conventional radial access compared to those using the left distal radial access (16.2% *vs.* 3.8%; p=0.031). No major bleeding was observed in any of the patients. A pseudoaneurysm was observed in two patients in Group 1. Hand ischemia or RAO was not observed in any patient. Although the radial spasm rate was higher in the left distal radial group compared to the right conventional radial group,

Table 1
Demographic and clinical characteristics of the study population

	Right conventional (n=68)			Left distal (n=52)			Total (n=120)			
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			59.31±11.32			59.08±12.37			59.21±11.74	0.915
Sex										
Male	46	67.6		34	65.4		80	66.7		0.794
BMI			27.28±3.63			27.74±5.70			27.48±4.63	0.592
SBP (mmHg)			138.49±18.05			142.19±20.65			140.09±19.23	0.297
DBP (mmHg)			78.99±10.88			80.90±15.28			79.82±12.95	0.423
Heart rate (/min)			75.82±11.78			78.27±18.26			76.88±14.92	0.376
Cigarettes	24	35.3		14	26.9		38	31.7		0.329
Alcohol	18	26.5		12	23.1		30	25		0.671
Chest pain	52	76.5		26	50		78	65.0		**0.003**
Palpitation	10	14.7		5	9.6		15	12.5		0.403
Dyspnea	29	42.6		16	30.8		45	37.5		0.183
Presyncope	7	10.3		2	3.8		9	7.5		0.184
Syncope	3	4.4		0	0		3	2.5		0.125
Type of procedure-PCI	21	30.9		14	26.9		35	29.2		0.636

SD: Standard deviation; BMI: Basal metabolic index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure, PCI: Percutanous coronary intervention.

Table 2
Comorbid diseases in the study population

	Right conventional (n=68)		Left distal (n=52)		Total (n=120)		
	n	%	n	%	n	%	*p*
Hypertension	39	57.4	33	63.5	72	60.0	0.498
Diabetes mellitus	22	32.4	20	38.5	42	35.0	0.487
Previous CAD history	37	54.4	20	38.5	57	47.5	0.083
Hyperlipidemia	29	42.6	17	32.7	46	38.3	0.266
Atrial flutter/fibrillation	6	8.8	5	9.6	11	9.2	0.882
Stroke/TIA	2	2.9	2	3.8	4	3.3	0.784
Peripheral artery disease	6	8.82	4	7.69	10	8.34	0.824
Thyroid disease	7	10.3	1	1.9	8	6.7	0.069
COPD	3	4.4	5	9.6	8	6.7	0.257
CRF	8	11.8	4	7.69	12	10	0.461
Anemia	5	7.3	6	11.5	11	9.2	0.431

CAD: Coronary artery disease; TIA: Transischemic attack; COPD: Chronic obstrcutive pulmonary disease; CRF: Chronic renal failure.

Table 3
Biochemical and imaging findings of the patients

	Right conventional (n=68)	Left distal (n=52)	Total (n=120)	
	Mean±SD	Mean±SD	Mean±SD	*p*
Hemoglobin (g/dL)	13.58±1.92	13.55±2.29	13.57±2.08	0.936
Hematocrit	39.85±4.99	39.99±6.10	39.9±5.48	0.891
Platelet (10^9/L)	255.10±81.17	272.37±101.46	262.65±90.59	0.305
WBC (×10^9/L)	8.07±2.35	8.89±2.40	8.43±2.40	0.063
Total cholesterol (mg/dL)	186.67± 47.28	172.71±38.97	180.58±44.22	0.90
Triglyceride (mg/dL)	157.49±110.05	147.16±57.40	152.94±90.55	0.544
HDL (mg/dL)	44.68±11.87	44.24±11.39	44.49±11.61	0.838
LDL (mg/dL)	110.98±38.07	99.06±37.95	105.74±38.31	0.096
Creatinine (mg/dL)	1.13±1.02	1.01±0.56	1.08±0.85	0.440
Fasting glucose (mg/dL)	117.20±39.71	129.28±58.61	122.50±49.04	0.193
TSH (mU/L)	2.27±2.05	1.96±0.94	2.11±1.57	0.351
T4 (ng/dL)	1.23±0.26	1.26±0.22	1.25±0.24	0.669
Sodium (mEq/L)	138.78±2.79	138.96±2.50	138.86±2.66	0.712
Potassium (mmol/L)	4.51±0.43	4.57±0.43	4.54±0.47	0.449
LVEF (%)	56.10±7.29	53.27±9.54	54.87±8.42	0.068
sPAP (mmHg)	24.15±11.36	25.17±12.94	24.59±12.02	0.645

SD: Standard deviation; WBC: White blood cell; HDL: High density lipoprotein; LDL: Low density lipoprotein; TSH: Thyroid stimulating hormone; LVEF: Left ventricular ejection fraction; sPAP: Systolic pulmonary artery pressure.

there was no statistically significant difference between the groups (7.7% *vs.* 4.4%; p=0.447). Complication rates according to the access sites were summarized in Table 5.

The rate of patients who stated that they experienced anxiety during the procedure was statistically higher in Group 1 than in Group 2 (19.1% *vs.* 3.8%). The majority of the patients in

Table 4
Treatment

	Right conventional (n=68)		Left distal (n=52)		Total (n=120)		
	n	%	n	%	n	%	*p*
Betablockers	35	51.5	24	46.2	59	49.2	0.564
ACEi's	15	22.1	13	25.0	28	23.4	0.706
ASA	39	57.4	26	50.0	65	54.2	0.423
Clopidogrel	10	14.7	9	17.3	19	15.8	0.699
Ticagrelor	1	1.47	2	3.8	3	2.5	0.409
Prasugrel	2	2.94	0	0	2	1.67	0.212
Oral anticoagulant	7	10.3	2	3.8	9	7.5	0.184
Long acting nitrates	1	1.47	2	3.8	3	2.5	0.409
Statin	24	35.3	10	19.2	34	28.3	0.053
ARBs	6	8.8	4	7.7	10	8.3	0.824
CCB	6	8.8	6	11.5	12	10	0.623
Diuretic	3	4.4	0	0	3	2.5	0.125
Aldosterone antagonist	2	2.94	7	13.5	9	7.5	**0.030**
Digoxin	1	1.47	1	1.9	2	1.6	0.848
OAD	13	19.1	14	26.9	27	22.5	0.310
Insulin	9	13.2	2	3.8	11	9.2	0.077

ACEi: Angiotensin converting enzyme inhibitor; ASA: Acetyl salicylic acid; ARB: Angiotensin receptor blocker; CCB: Calcium channel blocker; OAD: Oral antidiabetic.

Table 5
Comparison of access site complications between groups

	Right conventional (n=68)		Left distal (n=52)		Total (n=120)		
	n	%	n	%	n	%	*p*
Minor bleeding	11	16.2	2	3.8	13	10.8	0.031
Pseudoaneurysm	2	2.9	0	0	2	1.7	0.212
Hematoma	3	4.4	0	0	3	2.5	0.125
Radial spasm	3	4.4	4	7.7	7	5.8	0.447
Occlusion	0	0	0	0	0	0	-
Hand ischemia	0	0	0	0	0	0	-
Major bleeding	0	0	0	0	0	0	-

both groups stated that they did not have any pain during the procedure. The number of patients who had mild and moderate pain was higher in Group 1 than in Group 2 (p=0.047). The rate of patients who had pain that disrupts daily activities was statistically higher in Group 1 compared to Group 2 (17.6% *vs.* 5.8%; p=0.043). When we asked the patients whether they were satisfied with the CAG procedure performed through the radial artery, the group that underwent left distal radial access stated that they were satisfied with the procedure, which had a higher rate than the group that underwent right radial access (94.3% *vs.* 66.2%; p=0.001). When we asked the patients whether they would recommend the transradial CAG method to their relatives if their relatives required CAG, the left distal radial group answered yes more frequently than the right conventional radial access groups,

Table 6
Responses to the questionnaire according to radial access site

	Right conventional (n=68)		Left distal (n=52)		Total (n=120)		
	n	%	n	%	n	%	*p*
Did you have anxiety during the procedure?, yes	13	19.1	2	3.8	15	12.5	**0.012**
Did you have pain during the procedure?							**0.047**
0: Didn't happen	48	70.6	47	90.5	95	79.1	
1: Mild	12	17.6	2	3.8	14	11.7	
2: Moderate	7	10.3	2	3.8	9	7.5	
3: Severe	1	1.5	1	1.9	2	1.7	
Did you have pain in your hand after the procedure that disrupted daily activities?, yes	12	17.6	3	5.8	15	12.5	**0.043**
Were you satisfied with the coronary angiography procedure performed via the arm?							**0.001**
1: Yes	45	66.2	49	94.3	94	78.3	
2: Undecided	18	26.5	2	3.8	20	16.7	
3: No	5	7.3	1	1.9	6	5.0	
If your relatives need angiography, would you recommend radial access for coronary angiography?							**0.001**
1: Yes	42	61.8	48	92.3	90	75.0	
2: Undecided	22	32.3	4	7.7	26	21.7	
3: No	4	5.9	0	0	4	3.3	

which was statistically significant (p=0.001). Survey data are provided in Table 6.

DISCUSSION

This study is one of the rare studies in the literature in terms of comparing the effects of conventional radial access and left distal radial access on patient satisfaction and quality of life in CAG or PCI. With the results of our study, it has been revealed that the risk of major complications, such as occlusion, hand ischemia, and compartment syndrome, is minimal when the CAG procedure is performed through the left distal radial artery by experienced operators and the necessary precautions are taken. It has been revealed that the left distal radial artery access for CAG provides high patient comfort and satisfaction by not causing much pain in daily activities, and the patients can recommend it to their relatives. According to the results of this survey, the left distal radial access appears to be superior to the right radial access in terms of patient satisfaction.

Compared to the right conventional approach, left distal radial access has several significant benefits. Since the dominant hand used by the majority of the population is the right hand, patients who undergo left distal access are not disturbed by the limited mobility of their right hand after the intervention.[11] It will be a comfortable posture for patients to place their left hands close to their navel or right groin throughout the procedure.[12] In addition, in left distal access, the doctor can work at a safe distance from the radiation source.[13]

The radial artery has a superficial course, and thus hemostasis can be easily achieved after the procedure. The end of the radial artery anastomoses with the deep palmar branch of the ulnar artery, forming a deep palmar arch with abundant collateral circulation. In addition, hand ischemia is prevented when occlusion occurs in the radial artery due to the double blood supply of the hand.[4] The incidence of ischemia or necrosis of the hand after transradial artery puncture is low.[14] In our study, no hand ischemia or necrosis developed in any patient. In a study that evaluated the efficacy and safety of distal radial and conventional radial approaches during CAG with 200 patients, hemostasis time was found to be shorter in patients who underwent distal radial access compared to patients who underwent conventional radial access (568±462 *vs.* 841±574; p=0.002).[15] According to the results of this study, the distal radial access is associated with lower successful cannulation rates and shorter manual hemostasis time compared to the conventional radial access. In an observational multicenter study, 177 patients were divided into two groups as conventional radial (n=95) and distal radial (n=82) interventions.[9] Radial artery occlusion was detected by ultrasonography in three (3.1%) patients in the conventional group and none of the patients in the distal group (p=0.25). Vasospasm was found to be similar between the two groups (p=0.54). In our study, no statistically significant difference was found between the two groups in terms of complications other than minor bleeding. We believe that the reason why minor bleeding occurs less in the distal radial group was owing to the bones around the distal radial artery pressing to the artery.

In our study, a similar amount of nitroglycerin was given to the study population during the procedure to prevent radial artery spasms. However, radial artery spasms still occurred, and there was no statistically significant difference between the groups in terms of radial artery spasms. Catheter entrapment associated with radial artery spasms is rare during transradial CAG or PCI, and it has been demonstrated that forearm heating can effectively reverse severe and resistant vasospasm of the radial artery.[16] Accordingly, we applied forearm warming and intra-arterial nitroglycerin readministration in patients who developed radial spasms during the procedure.

The use of the radial artery in coronary artery bypass surgery is becoming increasingly common. It is known that mid-and long-term patency rates are superior when compared to saphenous vein grafts.[17] It has been stated that it should be used as a second graft for complete arterial revascularization, reoperation, and without retraction of the radial artery in young patients.[17] In our study, it was revealed that the distal radial artery should be preferred over the right radial conventional access in CAG or PCI procedures, despite the possibility that the radial artery can be used in future coronary artery bypass surgeries.

In a study in which 100 cases with variable indications for coronary interventions were divided into distal radial access (n=50) and conventional radial access (n=50), the safety profile parameters had statistically significant differences in favor of the distal group in terms of postoperative hematoma, arteriovenous fistula, postprocedural pain, and compression time.[8] Although it was higher in the conventional group, no statistically significant differences were found regarding RAO.[18] In our study, we determined that the distal radial access is an easily applicable and safe method for CAG and PCI compared to the right conventional radial access, and the patients are more satisfied. Therefore, distal radial access in CAG and PCI may be the first choice for interventional cardiologists in the near future.

The main limitation of the study is the small sample size. However, despite the limited number of patients, significant results were demonstrated in favor of the left distal radial artery access being a safe and preferable method for CAG or PCI. In our study, radial Doppler ultrasonography was performed after the procedure; thus, the radial artery diameter and Doppler flow could not be evaluated before the procedure.

In conclusion, left distal radial artery access was a safer method and had less complication risk for CAG and PCI compared to right conventional radial artery access. Left distal radial artery approach provided high patient comfort and satisfaction, did not cause much pain in daily activities, and patients claimed they would recommended it to their relatives for CAG or PCI.

Ethics Committee Approval: The study protocol was approved by the Bakırcay University Non-Invasive Clinical Research Ethics Committee (Date No: 02/16/2022-492). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Effectiveness of directional atherectomy with the drug-coated balloon method for long and heavily calcified superficial femoral artery lesions

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ABSTRACT

Objectives: This study aimed to examine the mid-term results of patients who underwent directional atherectomy (DA) for vascular preparation before drug-coated balloon (DCB) angioplasty with superficial femoral artery lesions longer than 150 mm and severe calcification and compare these patients with those treated with DCB angioplasty alone.

Patients and methods: This prospective study enrolled 76 patients (66 males, 10 females; mean age: 63.3+9.8 years; range 44 to 105 years) with calcific superficial femoral artery lesions longer than 150 mm treated with DA before DCB angioplasty or DCB angioplasty alone between May 2019 and November 2020. The patients were evaluated in two groups according to DA use: the DA+DCB group with 46 patients and the DCB group consisting of 30 patients. The results of these two methods were compared, and the outcomes were followed up for one year after the treatment. Primary outcomes were patency, freedom from target lesion revascularization, and unplanned amputation.

Results: There was no statistically significant difference between the two groups in demographic features, risk factors, comorbidity, and functional capacity assessment tests. At the 12th month, the primary patency of the DCB and DA+DCB group was 66.6% and 82.6%, respectively ($p<0.05$). Although the bail-out stent requirement rate for the treatment of the flow-limiting dissection (type C-F) was lower in the DA+DCB group (8.6% *vs.* 10.0%), there was no statistically significant difference ($p=0.46$).

Conclusion: The DA prior to DCB in long segment severe calcific superficial femoral artery lesions may provide better patency and may decrease rate of flow-limiting and non-flow limiting dissections.

Keywords: Atherectomy, balloon angioplasty, paclitaxel, peripheral artery disease, vascular calcification.

Nowadays, the role of endovascular interventional methods increases in the treatment of superficial femoral artery (SFA) stenosis or occlusion. The choice of endovascular method may vary depending on the calcification burden, the length of the lesion, concomitant vascular involvement in other segments, and the preference of the endovascular surgeon. Balloon angioplasty technologies form the basis of endovascular procedures. Restenosis, which may develop in the target lesion, is one of the main hindrances of endovascular treatments. However, drug-coated balloon (DCB) technologies provide good results in resolving the restenosis problem. In the literature, there are many trials to prove that DCB is more effective than standard balloon angioplasty in solving the restenosis problem.[1,2] It is known that severe calcification is a significant barrier to administering the antiproliferative drug with the DCB into the media layer of the artery.[3] Atherectomy devices reduce the calcium burden in the artery and provide redistribution, thus providing the vascular preparation to deliver the antiproliferative drug from the DCB to the targeted area. In this study, we aimed to examine the mid-term results of patients who underwent directional atherectomy (DA) for vascular preparation before DCB angioplasty in patients with SFA lesions longer than 150 mm and severe calcification and compare these patients with those treated with DCB alone.

PATIENTS AND METHODS

A total of 76 patients (66 males, 10 females; mean age: 63.3+9.8 years; range, 44 to 105 years) treated

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with DA before DCB angioplasty or DCB angioplasty alone at the Prof. Dr. Cemil Tasçıoğlu City Hospital Cardiovascular Surgery Clinic between May 2019 and November 2020 were enrolled in the prospective, single-center study. Inclusion criteria were the presence of a 150 mm or longer SFA lesion with Rutherford clinical category (RCC) 3-6, a ≥70% occlusion of the SFA in computed tomography angiography (CTA) or digital subtraction angiography, and the presence of at least one distal vessel runoff. Exclusion criteria were patients with SFA lesions less than 150 mm in length, acute SFA thrombosis, previous vascular intervention to the target limb less than three months ago, and inability to quit smoking. The patients were evaluated in two groups according to DA use: the DA+DCB group with 46 patients and the DCB group consisting of 30 patients. Study assessment was done at baseline, procedure, first outpatient polyclinic control, and six and 12 months after the procedure.

Preoperative assessments included the evaluation of the patients at the baseline, determination of the physical capacity with RCC and ankle-brachial index (ABI), flow pattern measurements of the distal arteries in duplex ultrasonography (USG), and topographic determination of the SFA and concomitant arterial lesions in CTA. The flow pattern of the target lesion distal artery was measured by duplex USG and classified as monophasic, biphasic, and triphasic. In addition, the calcium burden of the SFA lesion was longitudinally and circumferentially measured as described by Fanelli et al.[3] (numbers ranging from 1 to 4 determined by the quantification of circumferential grading of calcium plaque in four quarters from 0 to 360 degrees and as letters A and B depending on the length of the calcification, longer or shorter than 3 cm, on the longitudinal axis). Calcium gradings of 3A and above were categorized as severe, whereas 2B and below were nonsevere.

Access site was made from the common femoral artery with the retrograde or antegrade approach during the endovascular procedure. The arterial lesion was passed with appropriate guidewires and catheters (support or total occlusion). After passing the target lesion, vascular preparation before DCB application was made with plain balloon angioplasty in the DCB group and with DA in the DA+DCB group. Additional procedures, dissections with or without flow limiting, and complications (arteriovenous fistula, perforation, distal artery thrombus, or debris migration) were recorded separately for both groups during the procedure. The dissections were grouped according to the classification system of the coronary artery dissection patterns described by the National Heart, Lung, and Blood Institute.[4] Letters from A to F in this classification show the severity of the dissection: (A) minor radiolucent areas, (B) linear dissection, (C) contrast outside the lumen, (D) spiral dissection, (E) persistent filling defects, and (F) total occlusion without distal antegrade flow. Types C to F are described as severe dissections. Firstly, the plain balloon angioplasty was used for the treatment of flow-limiting dissections after DCB angioplasty. Drug-coated balloon inflation time was at least 180 sec. The plain balloon inflation time for the treatment of flow-limiting dissections was at least 300 sec, and if the plain balloon inflation did not solve the issue, a bare-metal stent was used.

In the study, HawkOne™ (Covidien, Dublin, Ireland) DA catheters were used. The IN.PACT Admiral (Medtronic Inc., Dublin, Ireland) DCBs were preferred, and the length of the lesion determined how many balloons were required. The numbers of the balloons varied from one to three.

Outpatient control was made in the first week, six months, and 12 months after discharge from the hospital. The physical assessment of the patients was evaluated with the ABI, peripheric pulse examination, and RCC grade. Detailed medical records after the endovascular intervention, such as amputation or surgical debridement, wound healing, and any target lesion reintervention, were also interrogated. The duplex USG was performed at the six- and 12-month controls. The target lesion flow pattern and patency were assessed by sonographic methods. A monophasic flow pattern at the target lesion was considered a severe restenosis of the target lesion. If there was any suspicion of stenosis or patency, they were also assessed with CTA. Severe restenosis was regarded as the need for reintervention if there was restenosis greater than 30% of the lumen diameter in addition to symptoms. Both sonographic and radiologic methods were used to assess primary patency. Adverse events, such as acute thrombosis or embolism of the distal arterial bed, arteriovenous fistula, perforation, and flow-limiting dissection, were diagnosed and recorded during intervention for both groups.

Statistical analysis

The data were evaluated using the IBM SPSS version 20.0 software (IBM Corp., Armonk, NY, USA). The demographic characteristics of the study groups were analyzed with descriptive statistical information, the mean, median, interquartile range, number, percentage, and standard deviation. The suitability of the data to a normal distribution was analyzed with the Shapiro-Wilk test. In the study, chi-square, Mann-Whitney U, Wilcoxon, and Marginal homogeneity tests were used. A *p* value of <0.05 was considered statistically significant.

RESULTS

Demographic characteristics of patients were well matched between two groups, and there was no statistically significant difference among them (p>0.05). The majority of the patients were RCC 3 in both groups (p=0.159); however, the patients with critical limb ischemia (RCC 4 or above) were more common in the DA+DCB group. All demographic features, risk factors, comorbidities, preintervention RCC grading, and ABI measurements were summarized in Table 1.

The mean lesion length of the DA+DCB group was higher than the DCB group (p<0.05). The calcium burden of the groups was evaluated. Approximately one third of the patient in the DCB group had severe calcification (grade 3A and above) while severe calcification was seen in half of the patients in the DA+DCB group; however, there was no statistically significant difference (p>0.05). The lesion length, calcium burden severity, and presence of concomitant lesions in the two groups were summarized in Table 2. In addition, the detailed arterial calcification grading for patients in both groups was demonstrated in Figure 1.

The type A and B (nonflow-limiting) dissection rates were significantly lower in the DA+DCB group (p<0.05). Type C to F dissections were observed in four (13.3%) patients of the DCB group and four (13.3%) patients of the DA+DCB group. The bail-out stent was performed if the balloon angioplasty was not solved by the flow-limiting dissection. A bail-out stent was required in three (10%) of the patients in the DCB group and four (8.6%) in the DA+DCB group to overcome the flow-limiting dissection or residual stenosis. Although the bail-out stent need was lower in the DA+DCB group, the difference was not statistically significant (p=0.461). The detailed dissection grades and bail-out stent needs of the groups were also summarized in Table 2.

Table 1
Baseline characteristics

	DCB (n=30)					DA+DCB (n=46)						All patients				
	n	%	Mean±SD	Median	Range	n	%	Mean±SD	Median	Range	*p*	n	%	Mean±SD	Median	Range
Age (year)			62.1±8.0	62.0	44.0-87.0			64.0±10.9	63.0	50.0-105.0	0.674			63.3±9.8	63	44.0-105.0
Sex																
Male	29	96.6				37	80.4				0.078	66	86.8			
Medical history																
Hypertension	18	60				29	63.0				0.980	47	61.8			
Diabetes mellitus	13	43.3				22	47.8				0.701	35	46.0			
Coronary artery disease	11	36.6				22	47.8				0.470	33	43.4			
Chronic renal failure	4	13.3				7	15.2				1.000	11	14.4			
Hyperlipidemia	13	43.3				29	63.0				0.146	42	55.2			
Smoking	17	56.6				28	60.8				0.900	45	59.2			
Rutherford clinical category											0.159					
<RCC 4	22	73.3				25	54.3					47	61.8			
≥RCC 4	8	26.6				21	45.6					29	38.1			
Foot ulcer	5	16.6				17	36.9					22	28.9			
ABI			0.3±0.1		0.0-0.5			0.2±0.1		0.0-0.4	0.112			0.25±0.1		0.0-0.5

DCB: Drug-coated balloon; DA: Directional atherectomy; SD: Standard deviation; RCC: Rutherford clinical category; ABI: Ankle-brachial index.

Table 2
Angiographic characteristics

	DCB (n=30)					DA+DCB (n=46)						All patients				
	n	%	Mean±SD	Median	Range	n	%	Mean±SD	Median	Range	*p*	n	%	Mean±SD	Median	Range
Lesion length (mm)			181.5±36.5	165.0	150.0-300.0			244.2±75.5	228.5	150.0-550.0				219.5±69.9	210.0	150.0-550.0
Calcium burden											0.106					
Severe	10	33.3				24	52.1					34	44.7			
Mild-moderate	20	66.6				22	47.8					42	55.2			
Concomitant lesion											0.461					
Iliac	10	33.3				6	13.0					16	21.0			
BTK	5	16.6				7	15.2					12	15.7			
Dissection grade (A-F)																
A	3	10				2	4.3					5	6.5			
B	3	10				0	0.0					3	3.9			
C	1	3.3				0	0.0					1	1.3			
D	0	0.0				0	0.0					0	0.0			
E	0	0.0				0	0.0					0	0.0			
F	3	10				2	4.3					5	6.5			
Dissection not need any intervention (Grade A-B)	6	20				2	4.3				<0.05	8	10.5			
Dissection need intervention (Grade C-F)	4	13.3				2	4.3				>0.05	6	7.8			
Bail-out stent use	3	10.0				4	8.6				0.461	7	9.2			

DCB: Drug-coated balloon; DA: Directional atherectomy; SD: Standard deviation; BTK: Below the knee.

In the DCB group, 12 (40%) patients had at least one complication, and there was a statistically significant difference between the groups (p=0.048). The detailed distribution of the complications according to groups was provided in Table 3.

In the follow-up, the ABI values were higher in both groups at the six- and 12-month outpatient controls. However, the ABI increase was higher in the DA+DCB group, which was statistically significant according to preoperative and postoperative ABI measurements (p=0.014). There was no difference between the groups in pre-and postintervention RCC grades (p>0.05 for each). However, the postintervention RCC grades were lower in both procedures when the preoperative and postoperative RCC grades of the groups were compared, which was statistically significant (p <0.05 for each). In duplex USG, the triphasic flow pattern was more frequently detected in the DA+DCB group at the six- and 12-month follow-ups, and the difference was statistically significant (p=0.025). The primary patency of patients evaluated with duplex USG was 80% in the DCB group and 91.3% in the DA+DCB group. However, the flow pattern measurements were inadequate to asses patency of femoral artery because it was affected other region lesions such as below the knee or iliac artery. Therefore, the primary patency was also evaluated with CT angiography. The primary patencies of the DCB and DA+DCB groups at the sixth month were 76.6% and 82.6%, respectively. There was no statistical significance between the groups. However, at the 12th month, the primary patency of the DCB group was decreased to 66.6%,

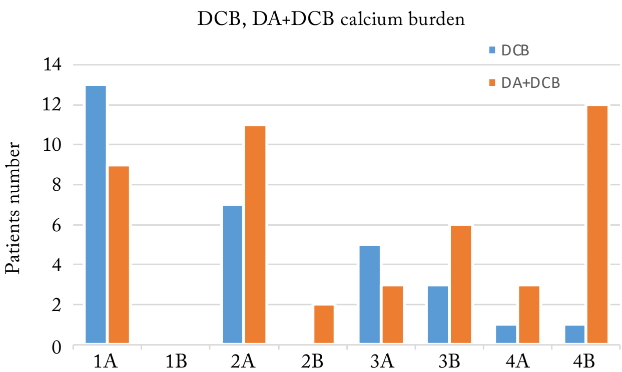

Figure 1. Severity of the calcification according to the grading system (Calcium burden evaluation with CTA (axial) and digital subtraction angiography (longitudinal): "A" <3 cm and "B" >3 cm).

DCB: Drug-coated balloon; DA: Directional atherectomy.

Table 4
Outcomes

	DCB (n=30)					DA+DCB (n=46)					
	n	%	Mean±SD	Median	Range	n	%	Mean±SD	Median	Range	*p*
ABI			0.7±0.2	0.7	0.6-0.8			0.8±0.2	0.8	0.7-0.9	0.014
Rutherford clinical classification			2.6±0.7	3.0	2.0-3.0			2.5±1.3	2.0	2.0-3.0	>0.05
Peripheric pulse examination											0.049
Non-palpable	7	23.33				5	10.86				
One pulse palpable	15	50				16	34.78				
Two pulse palpable	8	26.66				25	54.34				
Duplex USG flow pattern											0.025
Monophasic	6	20				4	8.69				
Biphasic	18	60				19	41.30				
Triphasic	6	20				23	50				
6th month primary patency (CTA)	23	76.66				38	82.60				0.424
12th month primary patency (CTA)	20	66.6				38	82.60				<0.05
Unplanned amputation	2	6.6				2	4.3				>0.05
Mortality (all cause)	0	0.0				0	0.0				

DCB: Drug-coated balloon; DA: Directional atherectomy; SD: Standard deviation; ABI: Ankle-brachial index; USG: Ultrasonography; CTA: Computed tomography angiography.

Table 3
Complications

	DCB (n=30)		DA+DCB (n=46)		
	n	%	n	%	*p*
Distal embolism (need intervention)	2	6.6	1	2.1	
Arteriovenous fistula	0	0.0	1	2.1	
Pseudoaneurysm	0	0.0	1	2.1	
Perforation	0	0.0	1	2.1	0.048
Flow-limiting dissection	4	13.3	2	4.3	
Non-flow limiting dissection	6	20	2	4.3	
All complication	12	40.0	8	17.3	

DA: Directional atherectomy; DCB: Drug-coated balloon.

while that of the DA+DCB group was unchanged (p<0.05). The 6- and 12-month outcomes of the groups were presented in Table 4.

DISCUSSION

In this prospective study, we analyzed the impact of a DA device before DCB angiography for the vascular preparation of calcified long-segment femoropopliteal lesions by comparing two groups of patients treated with a DCB with or without DA. Our analysis showed that vascular preparation with DA before DCB enhanced the primary patency and lowered the rates of both perioperative flow-limiting and nonflow-limiting dissections and the necessity of the bail-out stent according to the DCB method alone.

The lesion length and calcification burden are some of the prime factors affecting the success and durability of the endovascular treatment. Increased length of the diseased segment and severe calcification are associated with unsatisfactory outcomes.[5] The current European Society of Cardiology guideline recommends the endovascular strategy first for femoropopliteal lesions ≤25 cm (Class 1C) with primary stenting (Class IIa) and DCBs (Class IIb). Surgical revascularization with an autologous saphenous vein graft is still the best treatment in lesions >25 cm (Class IB). However, endovascular treatment may also be considered in this group, whether the patient is unfit or at high risk for surgery (Class IIb). Therefore, the endovascular methods have become a preferred 'first' approach in parallel to increasing experience due to short hospital stays and early recovery in long femoropopliteal lesions. The calcification burden has proven its impact on both procedural success and midterm restenosis occurrence. Fanelli et al.[3] reported that both increased cross-sectional calcification burden in CTA and longitudinal calcification burden in digital subtraction angiography are associated with a progressive decrease in clinical success. Additionally, in their study, a cross-sectional calcification burden was found to be a more powerful indicator of poor outcomes than a longitudinal calcification burden. Similarly, the previous studies have demonstrated that severe calcification burden is an independent factor of restenosis following DCB, and this increases bail-out stent implantation.[6-8] The severity of the calcification burden causes an increase in the probability of perioperative flow-limiting dissection and bail-out stenting.[5] Severe calcification may also cause an inadequate opening of stents. There are various devices decreasing the calcification burden or changing calcification distribution, such as cutting and scoring balloons and atherectomy devices that increase patency.[9-13]

Drug-coated balloons decrease restenosis risk with the antiproliferative properties of the drugs on their surfaces. Previous studies have revealed the superiority of DCBs over standard balloon angioplasty in femoropopliteal lesions.[14-21] However, the antiproliferative effects of DCBs depend on the embedding and up-take of drug particles into the media layer of the arteries with the aid of the balloon inflation pressure.[18] At this point, the advanced calcification burden forms a barrier between the drug and the media layer. Some studies in the literature have reported promising results with DA followed by DCB angioplasty in severely calcified lesions.[10,22]

Lesion length is another important determinant of procedural success and patency. In the majority of previous studies, atherectomy was used for lesions <100 mm. The mean lesion length was 74±53 mm in the DEFINITIVE-LE study and patients with lesions >100 mm were only 28% of the study population.[23] Similarly, the DEFINITIVE-AR study compared DCB alone with DA+DCB in patients with a lesion length between 70-150 mm.[24] In the present study, lesion length was >150 mm for all patients.

In this study, the primary endpoint was defined as <30% of restenosis in target lesion assessed with duplex USG and CTA at the 12-month follow-up. The rate of restenosis at 12 months after the procedure was lesser in patients treated with atherectomy for vascular preparation. Similar studies show similar primary patency rates.[10] Clinical assessment with ABI and physical examination showed improved results in comparison with the preprocedural condition in the radiologic evaluation at the 12-month follow-up. A higher increase of ABI was observed in the DA+DCB group than in the DCB group, consistent with radiologic evaluation.

The nonflow-limiting dissections were usually underestimated in previous studies. However, the effect of nonflow-limiting dissection on restenosis rates is still not well known. We separately evaluated the nonflow-limiting dissections for both groups, and we think that they may affect the mid-term patency. As with similar previous studies, the flow-limiting dissections (types C to F) needing intervention were more common in the DCB group (13.3% *vs.* 4.3%), and the relative risk reduction was 67.6%. Bail-out stenting was required in 10% of the DCB group compared to the 8.6% of the DA+DCB group. The bailout stenting rate in the DA+DCB patients was reported as 3.2% in the DEFINITIVE-LE study. In our study, the stenting rate was notably higher in comparison with previous studies. We consider that our study population was composed of patients with longer lesions and a more severe calcification burden. Therefore, we had to use more stents, unlike similar studies. Although bail-out stenting incidence was lower in the DA+DCB group, we found 2.1% perforation, 2.1% pseudoaneurysm formation, and 2.1% arteriovenous fistula, which did not occur in the DCB group. The distal arterial embolization was more common in the DCB group (6.6% *vs.* 2.1%). We used an antiembolic filter in 86.9% of the DA+DCB group. Therefore, this insignificant difference is secondary to the antiembolic filter use.

The major or minor amputation of the extremity and the healing of the ischemic wound rates did not differ between the members of the groups, although the outcomes of the DA group appear more encouraging depending on the target lesion revascularization and primary patency at the 12-month follow-up. Further studies with more patients are required to evaluate amputation and mortality rates.

In conclusion, vascular preparation with the DA prior to DCB in patients with long-segment and severely-calcific lesions may provide better patency, decrease flow-limiting and nonflow-limiting dissections, and lower the need for bail-out stents.

Ethics Committee Approval: The study protocol was approved by the Prof. Dr. Cemil Taşçıoğlu City Hospital Ethics Committee (Date/no: 14.05.2019/1297). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept, data collection and/or processing: S.K.; Design, analysis and/or interpretation, literature review, writing the article, references and fundings:: S.K., H.G.; Control/supervision, critical review: H.G.

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The relationship between left ventricular diastolic dysfunction and hemoglobin A1c levels in the type 2 diabetes mellitus patient population

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ABSTRACT

Objectives: This study aimed to investigate the relationship between hemoglobin A1c (HbA1c) levels, which is a good marker for determining glycemic levels, and left ventricular diastolic dysfunction (LVDD) in the type 2 diabetes mellitus (DM) patient population.

Patients and methods: This retrospective study was conducted with 116 type 2 DM patients (62 males, 54 females; mean age: 58.4±9.5 years; range, 18 to 65 years) between July 2019 and November 2021. The patients were divided into two groups as those without LVDD (n=55, Group 1) and those with LVDD (n=61, Group 2). Early to late diastolic transmural flow velocity (E/A) ratio, the mean ratio (E/e') of mitral inflow (E) and mitral annular (e'), HbA1c levels, other hemogram and biochemical parameters, and demographic data were recorded.

Results: The HbA1c level was significantly higher in the group with LVDD (6.96±1.23 *vs.* 9.00±2.19, p<0.001). While the mean E/e' ratio was 9.69±2.73 in the group without LVDD, it was 16.00±1.69 in the group with LVDD, and there was a significant difference between the two groups (p<0.001). The mean E/A ratio was significantly higher in the group without LVDD (1.25±0.51 *vs.* 1.02±0.53, p=0.021). In regression operating characteristics analysis, a HbA1c cut-off value of 7.35 and was found to be a predictor of LVDD in the type 2 DM patient group with a sensitivity of 80% and specificity of 80% (AUC: 0.805; 95% confidence interval: 0.718-0.892; p<0.001).

Conclusion: Providing close glycemic follow-up and monitoring the HbA1c level can reduce heart failure and other comorbid conditions that may develop, particularly after LVDD.

Keywords: Diabetes mellitus, diastolic dysfunction, hemoglobin A1c.

Diabetes mellitus (DM) is one of the prominent health issues all over the world. Type 2 DM can cause microvascular damage in many organs, particularly the heart and kidney. Cardiovascular complications are the leading cause of mortality in patients with DM.[1] Diabetic cardiomyopathy (DCM) is generally considered to be the result of microvascular damage to the heart.[2] Diabetic cardiomyopathy may be considered in the etiology of heart failure (HF) when no other possible cause can be identified. Left ventricular diastolic dysfunction (LVDD) is the earliest functional change in DCM, followed by a progressive development of heart failure with preserved ejection fraction (HFpEF).[3] An effective treatment protocol for HFpEF has yet to be found. Therefore, it carries similar risks as systolic HF. Hyperglycemia in patients with DM can cause mitochondrial dysfunction, lipotoxicity, and abnormal substrate metabolism, and through this, it may also cause damage to the myocardial tissue.[4] One of the serological markers recommended for periodic glycemic control is Hemoglobin A1c (HbA1c), which has been the subject of research in recent years.[5] Hemoglobin A1c elevation may cause multisystemic adverse effects. In a recent study, it was revealed that the heart rate, cerebral oxygenation and cerebral perfusion were also lower in the group of patients with a higher HbA1c value who underwent cardiac surgery.[6] A 1% increase in HbA1c was associated with an 8% increased risk of developing HF, independent of other cardiovascular risks.[2] In addition, LVDD was found to be quite common in newly diagnosed

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DM patients and was associated with HbA1c levels, obesity, dyslipidemia, and the duration of diabetes.[7] Therefore, early diagnosis, follow-up, and treatment of DM patients before myocardial dysfunction and HF develop is crucial. Hemoglobin A1c can be an effective diagnostic method and screening tool in identifying patients with early changes in myocardial function.

This study aimed to investigate the relationship between HbA1c levels, which is a good marker for determining glycemic level, and LVDD in the type 2 DM patient population.

PATIENTS AND METHODS

This retrospective study was conducted with 116 consecutive type 2 DM patients (62 males, 54 females; mean age: 58.4±9.5 years; range, 18 to 65 years) at the Cardiology Departments of three hospitals, between July 2019 and November 2021. The patients included in the study were enrolled from three different centers. Inclusion criteria for the study were patients with a diagnosis of type 2 DM, who were evaluated by echocardiography (ECHO) and whose HbA1c level was followed. Exclusion criteria from the study were pregnant patients, active infection, malignancy, hematological diseases, rheumatological diseases, life expectancy <1 year, anemia, severe kidney or liver failure, acute coronary syndrome, coronary artery disease, moderate to severe heart valve disease, acute decompensated or cardiac failure, cardiac pacemaker implantation history, patients who were hypertensive at the time of examination (systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg), and patients with severe arrhythmia. The patients were divided into two groups as those without LVDD (n=55, Group 1) and those with LVDD (n=61, Group 2).

Venous blood samples were taken from all patients included in the study after an overnight fasting period. Blood was drawn from the anterior surface of the forearm in the supine position. For the complete blood count, blood was drawn into tubes containing standard EDTA, and measurements were made immediately after blood collection. Drugs used by the patients, demographic data, and echocardiographic data were obtained from hospital records.

Echocardiographic evaluation was performed with a GE Vivid 5 (5-1 MHz multi-frequency probe; GE Medical Systems, Milwaukee, USA) instrument using standard protocol. Echocardiographic images were obtained in four standard views (parasternal long axis, parasternal short axis, apical two chamber, and apical

Table 1
Demographic and comorbid characteristic results

	Group 1 (n=55)			Group 2 (n=61)			Total (n=116)			
Parameters	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			57.8±9.4			59.0±9.7			58.4±9.5	0.459
Sex										
Male			28±50.9			34±55.7			62±53.4	0.603
Systolic BP (mmHg)			124.15±17.8			131.48±18.9			128.0±18.7	0.034
Diastolic BP (mmHg)			69.44 ±10.6			72.67±11.7			71.1±11.3	0.123
Heart rate/min			72.9±11.7			74.0±13.9			73.5±12.9	0.635
Chest pain	28	50.9		32	52.5		60	51.7		0.868
Palpitation	13	23.6		15	24.6		28	24.1		0.905
Dyspnea	11	20.0		27	44.3		38	32.8		0.005
Smoker	21	38.2		29	47.5		50	43.1		0.309
Hypertension	26	47.3		31	50.8		57	49.1		0.703
Stroke/TIA	8	14.5		6	9.8		14	12.1		0.437
Hyperlipidemia	33	60.0		37	60.7		70	60.3		0.943
CKD	3	5.5		8	13.1		11	9.5		0.160

SD: Standard deviation; BP: Blood pressure; TIA: Transient ischemic attack; CKD: Chronic kidney disease.

four chamber) using the methods recommended by the American Society of Echocardiography.[8] The left ventricular ejection fraction was evaluated using Simpson's method from the biplane apical four-and two-chamber views.[8] Pulsed-wave Doppler-derived transmitral inflow velocities were measured in apical four-chamber imaging. While evaluating the diastolic parameters, a single measurement was made from an optimal image.

A detailed medical history was taken from all patients at the time of admission. Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or using antihypertensive medication. Patients with a fasting glucose level ≥126 mg/dL, using antidiabetic agents, or HbA1c >6.5% were considered DM in accordance with the American Diabetes Association.[9] The tests were performed after anemia was excluded. The ratio (E/e') of mitral inflow (E) and mitral annular (e') velocities were obtained in apical four-chamber imaging using pulsed-wave Doppler. Patients with an early to late diastolic transmural flow velocity (E/A) ratio <1, mean E/e' >14, septal e' <7 cm/s, or lateral e' <10 cm/s were considered LVDD due to its high specificity.[10]

Statistical analysis

Data were analyzed using the IBM SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov and Shapiro-Wilk tests

Table 2
Hemogram, biochemical, and echocardiographic results

	Group 1 (n=55)			Group 2 (n=61)			Total (n=116)			
Parameters	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	*p*
Uric acid (mg/dL)			5.30±1.02			5.41±1.02			5.36±1.02	0.590
Creatinine (mg/dL)			0.91±0.20			1.04±0.84			0.98±0.62	0.241
WBC (×10³/L)			8.11±2.06			8.62±2.62			8.98±2.18	0.202
Hemoglobin (g/dL)			13.64±1.28			13.48±1.59			13.55±1.45	0.566
Platelet (×10³/µL)			252.91±42.19			257.72±64.91			255.44±55.14	0.641
Total cholesterol (mg/dL)			195.78±57.18			182.34±48.10			188.72±52.80	0.172
Triglyceride (mg/dL)			156.16±76.54			171.09±135.31			164.01±111.17	0.473
HDL (mg/dL)			44.20±11.73			40.64±11.50			42.33±11.70	0.102
LDL (mg/dL)			118.73±55.64			119.98±93.56			119.38±77.60	0.931
Sodium (mEq/L)			137.58±13.72			139.36±2.79			138.52±9.66	0.324
Potassium (mmol/L)			4.48±0.39			4.51±0.47			4.49±0.43	0.686
HbA1c (%)			6.96±1.23			9.00±2.19			8.03±2.06	<0.001
TSH (µIU/mL)			2.01±1.28			2.25±1.41			2.13±1.35	0.345
LVEF (%)			57.9±5.3			57.8±4.3			57.9±4.8	0.950
LVEDD (mm)			47.09±3.49			47.77±4.81			47.45±4.23	0.390
LVESD (mm)			29.05±4.07			29.67±4.91			29.38±4.53	0.465
LVH	9	16.3		13	21.31		22	18.96		0.497
LA (mm)			35.31±7.25			36.38±5.27			35.87±6.28	0.361
E (cm/s)			104.52±37.32			85.51±29.58			94.53±34.67	0.003
A (cm/s)			87.81±25.14			91.39±24.27			89.7±24.65	0.438
Septal e′ (cm/s)			10.78±2.57			5.34±1.14			7.92±3.35	<0.001
E/A			1.25±0.51			1.02±0.53			1.13±0.53	0.021
E/e′			9.69±2.73			16.00±1.69			13.01±3.87	<0.001

SD: Standard deviation; WBC: White blood cell; HDL: High density lipoprotein; LDL: Low density lipoprotein; HbA1c: Hemoglobin A1c; TSH: Thyroid stimulate hormone; LVEF: Left ventricular ejection fraction; LVEDD: Left ventricular end-diastolic diameter; LVESD: Left ventricular end-systolic diameter; LVH: Left ventricular hypertrophy; LA: Left atrium.

Table 3
The drugs used by patients

	Group 1 (n=55)		Group 2 (n=61)		Total (n=116)		
Parameters	n	%	n	%	n	%	*p*
Beta-blockers	34	61.8	41	67.2	75	64.7	0.544
ACE-I	16	29.1	16	26.2	32	27.6	0.731
ARBs	8	14.5	15	24.6	23	19.8	0.175
MRAs	4	7.3	7	11.5	11	9.5	0.440
Dihydropyridine CCB	11	20.0	8	13.1	19	16.4	0.317
Non-dihydropyridine CCB	5	9.1	2	3.3	7	6.0	0.189
Statin	37	67.3	45	73.8	82	70.7	0.443
Furosemide	4	7.3	7	11.5	11	9.5	0.440
Thiazide diuretic	8	14.5	14	23.0	22	19.0	0.249
Antithrombocyte drugs	44	80.0	52	85.2	96	82.8	0.455

ACE-I: Angiotensin-converting enzyme inhibitors; ARBs: Angiotensin receptor blockers; MRAs: Mineralocorticoid receptor antagonists; CCB: Calcium channel blockers.

were applied to determine whether the study data were normally distributed. Categorical variables were expressed as frequencies and percentages, and quantitative variables were expressed as the mean and standard deviation. Receiver operating characteristics (ROC) analysis was performed to determine the HbA1c cut-off value. The cut-off value was determined according to the Youden index. The significance level was accepted as p<0.05.

RESULTS

There was no significant difference between the groups in terms of mean age and sex (57.8±9.4 *vs.* 59.0±9.7, p=0.459; 50.9% *vs.* 55.7%, p=0.603, respectively). Dyspnea finding was significantly higher in Group 2 (44.3% *vs.* 20%, p=0.005). There was no significant difference between the groups in terms of hypertension (47.3% *vs.* 50.8%, p=0.703) and chronic kidney disease (5.5% *vs.* 13.1%, p=0.160) (Table 1). Other demographic data and comorbid diseases of the groups are given in Table 1.

The HbA1c level was significantly higher in Group 2 (6.96±1.23 *vs.* 9.00±2.19, p<0.001). There was no significant difference between the groups in terms of left ventricular ejection fraction (57.9±5.3 *vs.* 57.8±4.3, p=0.950) and left ventricular hypertrophy (16.3% *vs.* 21.31%, p=0.497). While the E/e' ratio was 9.69±2.73 in Group 1, it was 16.00±1.69 in Group 2, and there was a significant difference between the two groups (p<0.001). A significant difference was observed between the two groups in E/A ratio (1.25±0.51 *vs.* 1.02±0.53, p=0.021, Table 2). Other hemogram, biochemical, and echocardiographic parameters are summarized in Table 2. The patients are compared in terms of the medical treatments they received in Table 3.

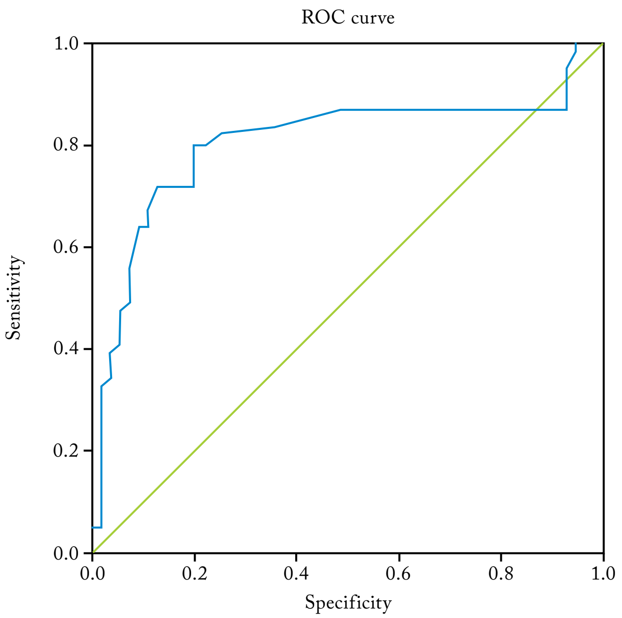

Figure 1. Cut-off value of HbA1c associated with LVDD in ROC curve analysis.
LVDD: Left ventricular diastolic dysfunction; HbA1c: Hemoglobin A1c; ROC: Receiver operating characteristics.

Receiver operating characteristics analysis was used to evaluate the power of HbA1c in predicting LVDD. Hemoglobin A1c was found to be a predictor of LVDD in the type 2 DM patients with a cut-off value of 7.35, sensitivity of 80%, and specificity of 80% (AUC: 0.805; 95% confidence interval: 0.718-0.892; $p<0.001$; Figure 1).

DISCUSSION

In our study, we determined that HbA1c levels may be a predictor of LVDD in type 2 DM patients. Hyperglycemia is a risk factor for HF in individuals with type 2 DM.[11] Structural, functional, and metabolic disorders develop as a result of the relationship between DM and HF. This leads to the emergence of more comorbid diseases and a worse prognosis. In addition, LVDD can be defined as the earliest functional change in type 2 DM patients.[12] Type 2 DM is known as an important factor associated with hypertension or obesity, as well as HFpEF, which often manifests as LVDD. Additionally, higher HbA1c levels have been associated with increased mortality in HF patients.[13] Hyperglycemia has deleterious effects on the myocardium. It up-regulates the renin-angiotensin-aldosterone system, increases oxidative stress, leads to the accumulation of glycation end products, and causes interstitial fibrosis in the heart muscle.[14] The HbA1c level is now recommended as the standard for testing and monitoring diabetes.[15] Giorda et al.[16] found that HbA1c is correlated with LVDD in patients with type 2 DM. Zuo et al.[17] revealed that the correlation between LVDD and HbA1c in type 2 DM patients was higher in patients with a normal body mass index. In a study by Di Pino et al.,[18] elevated HbA1c levels were associated with subclinical cardiac changes in patients with prediabetes, resulting in a lower E/A ratio and higher left atrial volume. Additionally, an independent relationship was found between E/e' ratio and HbA1c in this study.[18] In a recent study, it was emphasized that an E/e' ratio higher than 15 was associated with diastolic dysfunction.[19] This is consistent with our findings and previous studies conducted on patients with alterations in glucose homeostasis. Stahrenberg et al.[20] demonstrated in their study that glucose metabolism is associated with LVDD and HbA1c is associated with E/e' ratio. In another recent study, it was reported that hypoglycemia may also affect diastolic functions.[21] In addition, another study on the risk of atherosclerosis reported that the E/e' ratio was often within the normal range but was also positively associated with HbA1c.[22] These results reveal that HbA1c may be a marker of asymptomatic LVDD, the most prominent feature of DCM.[23] It has also been reported that a 1% increase in HbA1c level is associated with an 8% increase in the risk of HF.[24] Jain et al.[25] reported that the frequency of LVDD increases as the HbA1c level increases. Hameedullah et al.[26] found a strong correlation between HbA1c levels and diastolic indices in their study on 60 patients with type 2 DM. The results we obtained in our study support all these findings in the literature. As mentioned earlier, the pathogenesis of cardiac dysfunction associated with DM is multifactorial. Type 2 DM is thought to play a key role in the development of LVDD-related HFpEF.[23] Since there is still no effective pharmacological treatment in HFpEF patients, the importance of simple glycemic control with HbA1c monitoring becomes evident.

The main limitations of this study are its retrospective design and the relatively limited number of patients. In this respect, the results of the study cannot be generalized. In addition, we did not measure left atrial volume index (LAVI) during ECHO. In this respect, we did not examine all parameters indicative of diastolic dys function. Although we excluded many parameters that may affect diastolic functions, we could not exclude parameters that may affect diastolic functions such as chronic kidney disease, hypertension, and age. However, since there was no significant difference between the groups in terms of these parameters, we think that our study has a limited effect on the results. A single HbA1c value may not reflect the effect of hyperglycemia on diastolic function. In addition, we could not exclude the use of drugs that may have an effect on diastolic parameters.

In conclusion, as LVDD is quite common in the type 2 DM patient population and hyperglycemia is closely related to LVDD, providing close glycemic monitoring with HbA1c levels can reduce HFpEF development due to LVDD. Preventing the development of HFpEF is also of great importance in preventing long-term comorbid conditions.

Ethics Committee Approval: The study protocol was approved by the Bakırçay University Çiğli Training

and Research Hospital Ethics Committee (Date/no: 29.04.2022/580). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Original Article Open Access

Evaluation of a gold nanocomposite hyaluronic acid-based adhesion barrier with antibacterial properties in an animal model

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ABSTRACT

Objectives: In this study, the effects of a gold nanocomposite hyaluronic acid-based adhesion barrier were evaluated in an animal model.

Materials and methods: In our study, a total of 42 rats in seven groups, with six rats in each group, were evaluated. The groups were established according to the application of an adhesion barrier. In the first, second, and third groups, an adhesion barrier was applied by standard median laparotomy in the first, second, and fourth weeks, respectively. The fourth, fifth, and sixth groups underwent the same procedure in the first, second, and fourth weeks; however, no adhesion barrier was applied to these groups. The seventh group was the control group, and no treatment was performed in this group.

Results: There was no significant difference in the formation of inflammatory cells and fibrous tissue between the groups that underwent laparotomy in the first and second weeks with and without the adhesion barrier ($p>0.05$). However, both low inflammatory cells ($p<0.05$) and low fibrous tissue ($p<0.05$) were evaluated in favor of the adhesion barrier group operated at the fourth week.

Conclusion: A gold nanocomposite hyaluronic acid-based adhesion barrier prevents adhesion, particularly in the long term. However, the results need to be supported by clinical studies.

Keywords: Animal, hyaluronic acid, models, surgery-induced tissue adhesions, surgical adhesions.

Adhesions after surgery that require the opening of the peritoneum can often cause significant and distressing results. The incidence of adhesion in surgical procedures in which the abdomen is opened is up to 90%, and in gynecological procedures where the pelvis is opened, it is up to 97%.[1,2] These procedures can induce a broad range of issues, such as infertility, abdominal and pelvic pain, bowel obstruction, and difficulties experienced during reoperative interventions.[3-8] Postoperative adhesions most commonly occur in the early postoperative period. After surgical trauma or other damaging conditions, the inflammatory cascade is triggered, increasing fibrin in the damaged area.[9] Many different materials and medical agents have been produced to prevent adhesions. Some of these products are in the form of membranes, while others are in the form of gel barriers.[10-12] In a study comparing a hyaluronic acid gel and a hyaluronic acid carboxymethylcellulose product, it was demonstrated that the application of hyaluronic acid gel reduced the number of organs undergoing adhesion but did not cause a significant reduction in the degree of adhesion.[13]

In this study, the histopathological effects of a gold nanocomposite hyaluronic acid-based adhesion barrier, designed as a new type of gel barrier, were evaluated on an animal model.

MATERIALS AND METHODS

Animals and experiment method

The study was conducted on a total of 42 Wistar albino rats obtained from the SYLAB Experimental

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Animal Laboratory in seven groups, with six rats in each group. Each group included three adult males weighing 275±10 g (range, 255 to 300 g) and three adult females weighing 225±18 g (range, 200 to 250 g). The rats were kept in cages of equal size for a maximum of four weeks according to the study groups at a constant temperature of 20°C and in a 40-55% humidity laboratory environment on a 12-h daylight, 12-h night cycle. Standard rat chow was used for rats in all groups (25 g/day). The waters of the rats in all groups were changed every other day. At the end of the experiment, all animals were sacrificed by administering a high-dose anesthetic. The rats were cared for and fed using the facilities in the experimental animal laboratory of Sivas Cumhuriyet University.

Control group, and no treatment was performed on the animals. The groups were established according to the application of an adhesion barrier. In the first, second, and third groups, an adhesion barrier was applied in the first, second, and fourth weeks, respectively. The adhesion barrier was applied by standard median laparotomy in these groups. The fourth, fifth, and sixth groups underwent the same standard median laparotomy procedure in the first, second, and fourth weeks; however, no adhesion barrier was applied to these groups. The seventh group was the control group, and no treatment was performed in this group.

After general anesthesia (subcutaneous ketamine 87 mg/kg and intraperitoneal 3 mg/kg xylazine) was administered, the abdominal region of the rats was shaved. After surgical site sterilization, the skin and subcutaneous tissues were passed, and the abdomen was reached. After reaching the abdomen, the intra-abdominal organs were manually manipulated and with surgical forceps in all groups except for the control group. After the manipulation, 4 mL of adhesion barrier (Metrical Medical Devices Software Defense Industry and Trade Limited Company, Sivas, Türkiye) was applied to each rat in the adhesion barrier groups (Figure 1). The same manipulations were performed in the standard surgical groups, but the adhesion barrier was not applied. After the procedures were completed, subcutaneous closure was performed with 2-0 Vicryl sutures for the subcutaneous tissues and 4-0 polyglactin (Vicryl) sutures for the skin. Each operation was performed by the same surgeon to avoid surgical differences during the procedure. Daily dressing was done until the wounds were completely healed. The rats in each group were sacrificed with a high-dose anesthetic at the designed time in the study. Peritoneal tissue samples were taken after the animals were sacrificed. Extracted specimens were histopathologically evaluated, and comparisons were made for each group.

Histopathological method

Peritoneal samples taken from sacrificed rats were fixed in 10% neutral formalin. Tissues were taken into paraffin blocks after routine alcohol-xylol procedures, and 5 µ sections taken on slides with polylysine were stained with hematoxylin-eosin and Masson's trichrome. Histopathological evaluation was evaluated in terms of edema, vascularization, and inflammatory cell infiltration, similar to the study of Papparella et al.[14] The fibrous tissue thickness formed in staining with Masson's trichrome was measured and classified (Table 1). The scoring systems of Zühlke et

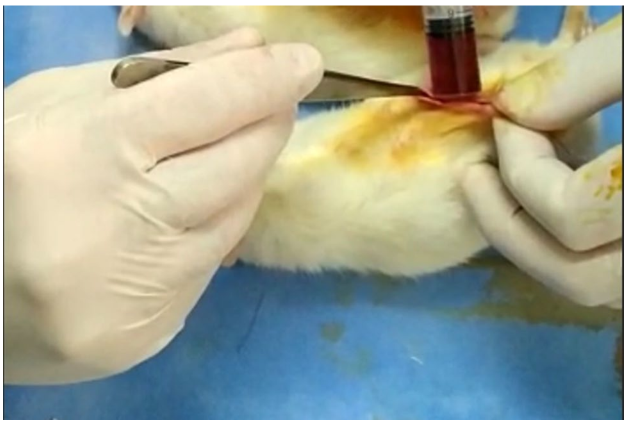

Figure 1. Adhesion barrier application is seen.

Table 1
Histological scoring system[12]

Histopathological scores	
No changes	Absent (-)
Less than 10%	Mild (+)
Between 10-40%	Moderate (++)
More than 40%	Severe (+++)
Fibrous tissue scores	
Less than 20 µm	Absent (-)
20-80 µm	Mild (+)
80-160 µm	Moderate (++)
More than 160 µm	Severe (+++)

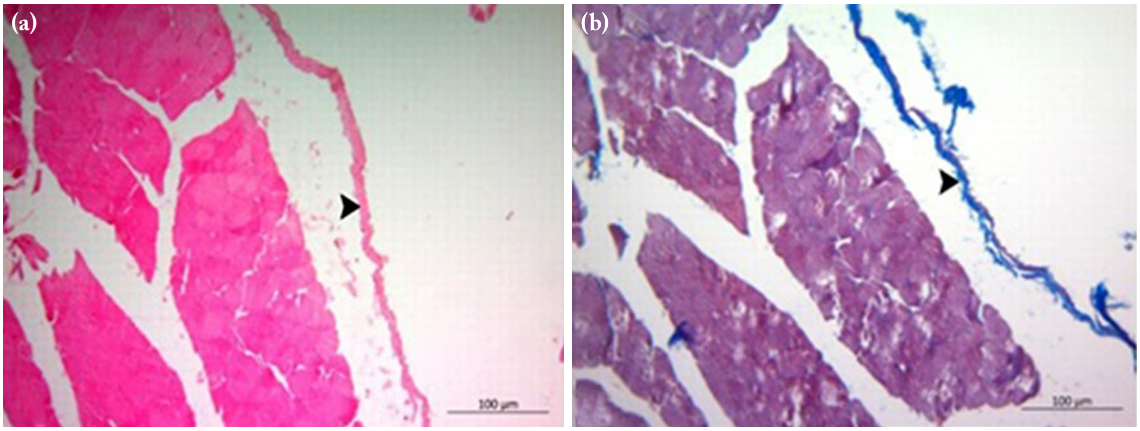

Figure 2. Control group. **(a)** Hematoxylin-Eosin, **(b)** Masson's Trichrome Staining. Normal histological appearance. Mesothelial layer (arrowhead), (×40).

al.[15] and Nair et al.[16] were not used in the study as it was mostly based on observational evaluation in assessing the degree of adhesion. Inflammation (0-3 days, acute), proliferation (3-12 days, subacute), and remodeling (>12 days, chronic) stages used in wound healing were also used in peritoneal wound healing.[17] Histopathological evaluation was based on the study of Kojima et al.[18]

Statistical analysis

The data were analyzed with the IBM SPSS version 20.0 software (IBM Corp., Armonk, NY, USA). The difference between the groups was determined by Student's t-test, which is a nonparametric test. A p value of <0.05 was considered statistically significant.

RESULTS

Peritoneal specimens of rats in the control group had a normal histological appearance (Figure 2). Statistically significant histopathological differences were found between the treatment groups (p<0.05).

Mild edema and inflammatory cell infiltrations were observed in the first and fourth groups. There

Table 2
Histopathological evaluation results.[a,b,c,d] Different letters in the same column indicate statistical difference between groups (p<0.05).[A,B,C] Different letters on the same line indicate statistical difference between groups (p<0.05).

Groups	Edema	Inflammatory cell infiltration	Vascularization
	Mean±SD	Mean±SD	Mean±SD
The group that did not apply an adhesion barrier in the first week.	1.00±0.00[aA]	0.83±0.40[aA]	0.12±0.40[aA]
The group in which an adhesion barrier was applied for the first week.	0.83±0.40[aA]	0.83±0.40[aA]	0.33±0.51[aB]
The group that did not apply an adhesion barrier in the second week.	2.83±0.40[bA]	2.66±0.51[bA]	1.83±0.40[bB]
The group in which an adhesion barrier was applied for the second week.	1.66±0.51[cA]	1.83±0.40[cA]	1.00±0.00[cB]
The group in which no adhesion barrier was applied in the fourth week.	2.66±0.40[bA]	2.83±0.40[bA]	2.66±0.51[dA]
The group in which the adhesion barrier was applied at the fourth week.	1.12±0.40[aA]	1.12±0.40[aA]	1.00±0.00[cA]

SD: Standard deviation.

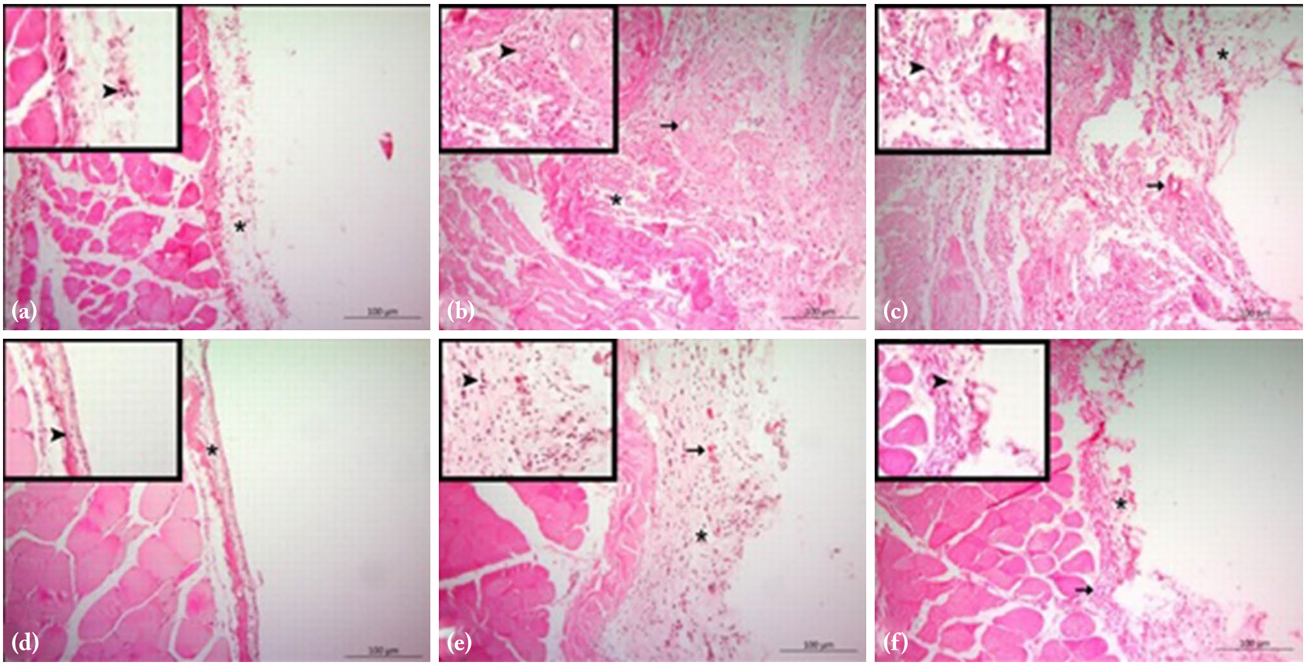

Figure 3. (a) The fourth group: Mild edema (*) and inflammatory cell infiltration; **(b)** The fifth group: Severe edema (*), inflammatory cell infiltration (arrowhead) and moderate vascularization (arrow); **(c)** The sixth group: Severe edema (*), inflammatory cell infiltration (arrowhead) and vascularization (arrow); **(d)** The first group: Mild edema (*) and inflammatory cell infiltration; **(e)** The second group: Moderate edema (*), inflammatory cell infiltration (arrowhead) and mild vascularization (arrow); **(f)** The third group: Mild edema (*), inflammatory cell infiltration (arrowhead), and vascularization (arrow), hematoxylin-eosin, (×40).

was no statistically significant difference between these two groups. While severe edema, inflammatory cell infiltration and moderate vascularization were determined in the fifth group, edema and inflammatory cell infiltration were moderate and vascularization was mild in the second group. The most significant histopathological difference was determined at four weeks. While edema, inflammatory cell infiltration, and vascularization were determined as severe in the group without an adhesion barrier at four weeks (the sixth group), these histopathological findings were mild in the third group, in which an adhesion barrier was applied (Table 2, Figure 3).

Statistically significant differences were detected between the groups in fibrous tissue formation on staining with Masson's trichrome. While mild

Table 3
Masson's trichrome staining findings.[a,b,c] Different letters in the same column indicate statistical difference between groups ($p<0.05$)

Groups	Fibrous tissue formation
	Mean±SD
The group that did not apply an adhesion barrier in the first week.	0.83±0.40[a]
The group in which an adhesion barrier was applied for the first week.	0.83±0.40[a]
The group that did not apply an adhesion barrier in the second week.	1.66±0.51[b]
The group in which an adhesion barrier was applied for the second week.	1.83±0.40[b]
The group in which no adhesion barrier was applied in the fourth week.	2.83±0.40[c]
The group in which the adhesion barrier was applied at the fourth week.	1.00±0.00[a]

SD: Standard deviation.

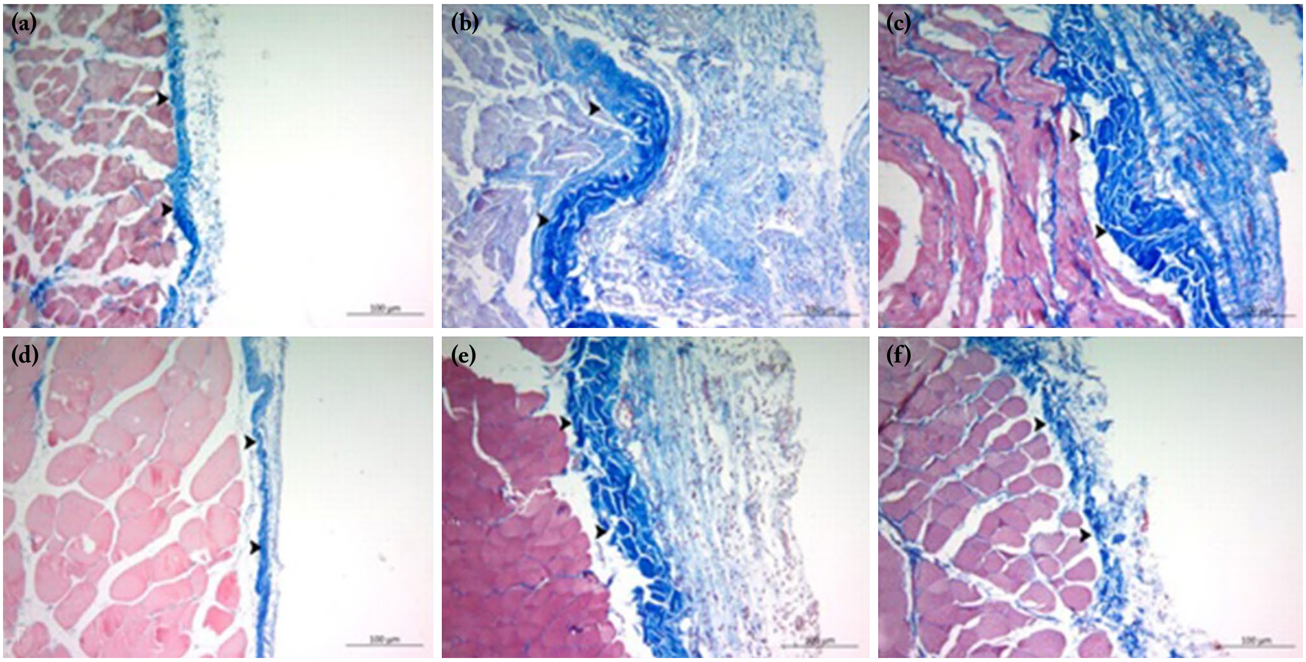

Figure 4. **(a)** The fourth group: Mild fibrous tissue formation (arrowhead); **(b)** The fifth group: Moderate fibrous tissue formation (arrowhead); **(c)** The sixth group: Severe; **(d)** The first group: Mild fibrous tissue formation (arrowhead); **(e)** The second group: Moderate fibrous tissue formation (arrowhead); **(f)** The third group: Mild fibrous tissue formation (arrowhead); Masson's trichrome, (×40).

fibrous tissue formation was detected in the first and fourth groups, moderate fibrous tissue formation was detected in both these groups. There was a significant difference between the third and sixth groups. While severe fibrous tissue formation was observed in the sixth group, mild fibrous tissue formation was observed in the third group (Table 3, Figure 4).

DISCUSSION

Postoperative adhesions are considered a risk factor for redo surgeries.[19] After surgeries in which the solid organs are not covered by the peritoneum or pericardium, adhesions from the previous surgery increase the complexity of the surgical procedure and are associated with increased mortality/morbidity when a new surgery is required. Adhesions seen after any surgery are one of the most important factors affecting the course of redo abdominal surgery.[20,21] The main mechanism of adhesion formation is the migration of inflammatory cells to the surgical site in the acute and chronic phases. Essentially, this migration takes place to speed up recovery, but when surgery is required again, it complicates the surgical process of the patient. Our study was designed based on abdominal adhesions.

Adhesion barriers are currently used to eliminate or minimize the risk of postsurgical adhesion. These barriers prevent the inflammatory cascade or fibrin formation and form a mechanical barrier by preventing the approach and contact between the affected tissues that cause adhesion formation. Abdominal adhesions are associated with significant comorbidities, such as chronic pelvic pain, dyspareunia, infertility, and intestinal obstruction. Adhesions can also cause issues in other specialties, such as gynecology, oncology, or pediatric surgery. There are large financial and public health repercussions associated with hospital readmission costs, and they represent a real public health problem.

There are many products produced to prevent adhesions.[19,22] It has been shown that the use of polyethylene glycol/polylactic acid membrane containing barriers, alone or with other barriers, prevent adhesion to a significant extent.[23] However, polylactide film barrier was found to be ineffective in preventing adhesions.[24] An ideal adhesion barrier prevents the formation of adhesions by allowing the damaged tissue surfaces to separate and heal freely. In addition, the barrier must be nonreactive, antibacterial, biocompatible, biodegradable, and effective *in vivo*.[20,21] In this study, gold nanoparticle/hyaluronic acid nanocomposite was synthesized *in situ* without the use of toxic chemicals and the purification step by green synthesis.

This study evaluated the effectiveness of the adhesion barrier, mainly targeting the acute, subacute, and chronic processes. When the acute period effects were examined, no significant difference was observed between the groups with and without the application of the adhesion barrier in terms of both the density of inflammatory cells and the formation of fibrous tissue. As the process lengthened and the subacute and chronic periods were reached, there was a significant decrease in inflammatory cell and fibrous tissue density in favor of the adhesion barrier group. Furthermore, in terms of edema and vascularization, there was a significant decrease in favor of the adhesion barrier group.

It was shown that the application of an adhesion barrier prevents cellular activities that will cause adhesion in rats. This is promising for patients who will need surgery again. These findings suggest that a gold nanocomposite hyaluronic acid-based adhesion barrier can be successfully applied to prevent postsurgical adhesions. However, clinical studies with long-term follow-up are needed.

There are several limitations in our study. The first of these only conducted research on the The research was only conducted on the laparotomic approach. In addition, the study being an animal experiment limited the chance of long-term follow-up. The study was only tested on peritoneal adhesions. Further studies are needed to investigate its effects on other membranes, such as the pericardium.

In conclusion, the application of the adhesion barrier will cause adhesions in the subacute and chronic periods. It was observed that the adhesion barrier minimizes inflammatory cells, edema, vascularity, and fibrous tissue formation. In terms of these parameters, no statistically significant difference was observed between the two groups in the early period, suggesting that the antibacterial gold nanocomposite hyaluronic acid-based adhesion barrier can be successfully applied to prevent subacute and chronic adhesions. Further clinical studies with long-term follow-up are needed.

Ethics Committee Approval: The study was initiated after the ethics committee decision numbered 65202830-050.04.04-524 of Sivas Cumhuriyet University Animal Experiments Local Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept, critical review: F.K.; Control/supervision, data collection, literature review, writing the article, critical review, references: F.A.; Analysis and/or interpretation, literature review: M.Ö.; Analysis and/or interpretation: A.S.M.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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Cardiovascular Surgery and Interventions

Original Article Open Access

Single center experience with percutaneous peripheral atherectomy with the use of C-arm scopy for the treatment of lower extremity peripheral artery disease

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ABSTRACT

Objectives: This study aimed to present our results of endovascular procedures including balloon angioplasty combined with or without atherectomy for the treatment of iliofemoral and distal lesions with the use of a C-arm scopy.

Patients and methods: The retrospective study was conducted on 153 patients (100 males, 53 females; mean age: 60.2±2.1 years; range, 53 to 82 years) with the diagnosis of peripheral artery disease between January 2017 and January 2020. The symptoms of the patients were claudication, rest pain, or tissue loss. The operations were performed at the operation theatre with local or spinal anesthesia in a supine or prone position according to the lesion status. Lesions were classified as superficial femoral, popliteal, and distal lesions below the knee.

Results: Interventional treatment was applied in all patients, and 272 lesions in 204 extremities were intervened. In 78 patients, 160 right leg lesions were treated, and in 75 patients, a total of 112 lesions were treated. Fifty-one patients had bilateral leg lesions. The number of iliac, superficial femoral, and popliteal and distal segment lesions was 30 (11.1%), 213 (78.3%), and 29 (10.6%), respectively. Most of the lesions were confined to the SFA. We performed percutaneous transluminal angioplasty procedures in all 153 patients; however, 143 of them also received atherectomy with two different reliable devices (Avinger in 45 patients, Invamed in 114 patients). All interventions were done on a standard operating theatre bed with a C-arm scope. Doppler ultrasonography was used for popliteal imaging during the insertion. We did not encounter any problems in 125 patients. In 28 patients, progress was observed in the leg or ischemic wound between 30 and 65 postoperative days. A total of 23 patients required amputation; amputations were minor (finger amputation) in five patients and major (below the knee) in 18 patients.

Conclusion: The perioperative and mid-term follow-up results of our study indicate that atherectomy and drug-coated balloon angioplasty may safely be performed by C-arm scopy with favorable outcomes.

Keywords: Atherectomy, C-arm scope, percutaneous, peripheral artery disease.

Atherosclerotic peripheric arterial disease may present with claudication, rest pain, critical leg ischemia, or gangrene. It is known that over 200 million people worldwide are affected by peripheral artery disease (PAD), and the prevalence significantly increases with age.[1-4] The prevalence of PAD is approximately 20% in the age group above 70 years,[5] and approximately 30% of men and 40% of women above the age of 80 are affected by the disease.[4] The burden of PAD-related treatment on the healthcare system is $4.37 billion in the USA.[6] The most advanced form of PAD is critical leg ischemia, which accounts for 1 to 3% of all patients with PAD.[7]

Treatment options for lower extremity ischemia include conservative treatment, bypass surgery, endovascular options, and primary amputation. Bypass grafting has been the main treatment strategy so far for the treatment of symptomatic PAD.[8,9] However, bypass surgery requires prolonged recovery time and has high complication rates.[10] These complications can be classified as graft infection, thrombosis of the graft, distal embolization, edema in the lower extremity, and complications of the incision site, such as dehiscence and infections.[10] Consequently, endovascular treatment modalities have increased in popularity in the last few years.

In this study, we aimed to present the preoperative and postoperative follow-up results of the patients

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with lower extremity PAD who underwent balloon angioplasty in combination with atherectomy by C-arm scopy.

PATIENTS AND METHODS

The retrospective study was conducted on 153 patients (100 males, 53 females; mean age: 60.2±2.1 years; range, 53 to 82 years) with the diagnosis of PAD at the Department of Cardiovascular Surgery, Bozyaka Training and Research Hospital between January 2017 and January 2020. The pathology was diagnosed by computed tomography angiography or digital subtraction angiography in all patients. The symptoms of the patients were claudication, rest pain, or tissue loss. Exclusion criteria were having a contrast allergy, an allergy to paclitaxel, and a life expectancy of less than six months. In patients with multiple lesions, the treatment was started from the proximal lesion, followed by the management of the distal lesions. Lesions were classified as superficial femoral, popliteal, and distal lesions below the knee.

Percutaneous transluminal angioplasty (PTA) in combination with atherectomy was applied in 143 (93.4%) patients, and sole PTA was applied to 10 (6.6%) patients. Sole PTA was performed in patients with less calcified lesions that could be easily passed through and successful revascularization. However, patients with advanced stenosis or occlusion initially underwent atherectomy to reduce the calcification load and ease the balloon's passage through the lesion. Following atherectomy, PTA was performed for residual stenosis. Percutaneous transluminal angioplasty applications were executed with an Extender drug-eluting balloon (INVAMED, Ankara, Türkiye) in all patients. The atherectomy procedures were performed with Avinger (Avinger Inc., Redwood City, CA, USA) in 45 patients, and Invamed (INVAMED, Ankara, Türkiye) was used in 98 of the patients.

The procedure was performed with a retrograde or antegrade approach. A popliteal retrograde approach was used with spinal anesthesia for patients with superficial femoral artery (SFA) lesions in the prone position only, and the antegrade procedure was performed from the femoral area for patients with SFA and distal lesions under general anesthesia. Doppler ultrasonography (USG) was used to minimalize vascular trauma.

Since the plaque load was heavy in some lesions, it was necessary to increase the duration of the scope acquisition during the procedure when it was difficult to advance the support catheter or wire. In addition, long-term use of the C-arm scope was required in the patient group with iliofemoropopliteal and long-lasting mixed lesions. In such cases, the device was turned off by following the warming warnings to prevent the device from overheating, allowing it to cool for approximately 5 min, and the process was continued when it was noticed that the scope had cooled down. Apart from this heating problem, no technical difficulties were encountered during the C-arm scopy. Angioplasty procedures with the C-arm scope, which can also be found in centers that do not have an angiography unit, were successful. A technician who is present in the operating room is usually required to use the device. In the use of the device, as the primary surgeon, we control the image quality and the opaque amount given by foot control. No complications or technical injuries involving the vascular and surgical team were encountered during the procedure. In the operation room, the graft-covered stents, which are prepared according to the sizes of the iliac arteries of the patients, were ready in case of need during the operation of the patients with iliac lesions.

We aimed to complete revascularization in one session for the patients with multiple lesions. Patients were followed after the first week, twice a week in the first three months, and once a month for the next three months. In the six-month follow-up, the symptoms of the patients, including claudication, were assessed.

Endovascular interventions

The operations were performed at the operation theatre with local or spinal anesthesia in the supine or prone position according to the lesion status. In general, for the patients who only had an iliac lesion, local anesthesia was preferred by the physician and the patients. In patients with only iliofemoral lesions or SFA lesions, spinal anesthesia with the prone position was the chosen modality for the proximal vasculature imaging by popliteal arterial intervention. In patients with SFA lesions beyond the popliteal artery, the antegrade route was preferred from the SFA to its distal with spinal or local anesthesia in the supine position.

All of the interventions were done on a standard operating theatre bed and with a C-arm scope

(Ziehm Imaging GmbH, Nuremberg, Germany). At the beginning of the procedures, the introducer (Invaducer; INVAMED, Ankara, Türkiye) was inserted percutaneously into the vessel to facilitate the insertion of the angiographic balloon and other necessary catheters. Afterward, a 0.035-inch guidewire (InWIRE; INVAMED, Ankara, Türkiye) was inserted through the introducer. Doppler USG was used for popliteal imaging during the insertion. After the insertion of the introducer, a sheath (Jaguar Catheter Long Sheat; INVAMED, Ankara, Türkiye) has been placed by pushing the sheath through the introduer. Either atherectomy or PTA with Extender was decided for the patients according to the status of the lesions, which were assessed by injecting contrast material for the imaging followed by a 1 mL heparin injection. After atherectomy operations, secondary PTA was applied by inserting the balloon through the introducer in cases with residual stenosis. The size of the paclitaxel-covered balloon was adjusted according to the size of the vessel in PTA. The time of the inflation of the balloon was 60-100 secin all patients. In patients with 30 to 40% residual stenosis after primary PTA, additional PTA with an inflation duration of 120-180 sec was applied to the residual stenotic segment. The sequence of the operations is explained in Figures 1 through 6.

In the postoperative period, the patients received 1000 IU/h systemic heparin infusion for the first 24 h and were prescribed 75 mg/day clopidogrel and 100 mg/day acetylsalicylic acid for three months and 40 mg/day atorvastatin at hospital discharge. In patients preoperatively receiving anticoagulants, a single antiplatelet drug, preferably clopidogrel, was preferred. During the follow-up, the result was accepted as a failure if the patient developed vascular stenosis, occlusion, or underwent major amputation.

Statistical analysis

Statistical analysis was carried out using the SPSS version 15.0 software (SPSS Inc., Chicago, IL, USA). The demographic data were expressed in mean ± standard deviation.

RESULTS

Interventional treatment was applied in all patients, and 272 lesions in 204 extremities were intervened. In 78 patients, 160 right leg lesions were treated, and in 75 patients, a total of 112 lesions were treated. Fifty-one patients had bilateral leg lesions.

The demographic features, including age, sex, smoking history, diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, and chronic renal disease, are presented in Table 1. The clinical status of the patients, such as claudication, resting pain, or tissue loss, were also presented in Table 1. The patients with ischemic wounds were compared with the patients with intact extremities, and no statistically significant difference was observed (Table 1).

Usage of at least one antihyperlipidemic, antihypertensive, or antidiabetic agent was accepted as having comorbidity (hyperlipidemia, hypertension, or diabetes mellitus). The patients who previously received hemodialysis and had a history of operation due to coronary artery disease were accepted as coronary artery disease patients in our study. Indications for intervention in the symptom scale were claudication in 110 (71.8%) extremities and rest pain and tissue loss (necrosis) in 43 (28.2%) extremities.

Seven patients with preoperative renal failure or receiving hemodialysis were pre-and postoperatively consulted with the nephrology department. According to suggestions, hemodialysis was scheduled for the morning before the operation or 12 h before the operation and the first postoperative 12 h. The existence of renal damage was controlled

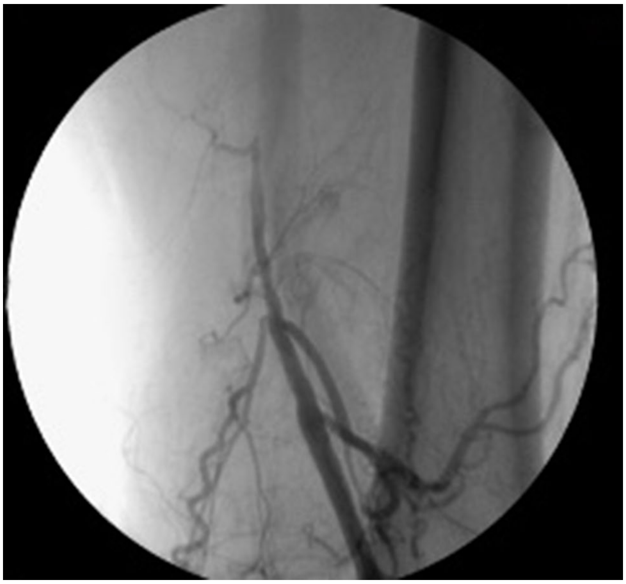

Figure 1. The contrast media image shows the distal lesion in the right SFA, and it is observed that the popliteal artery is open in prone position.

Table 1
Demographic characteristics of the patients according to the presence of ischemic wounds

	Ischemic wound is present	Ischemic wound is not present	
	n	n	Total
Sex			
Male	48	52	
Female	25	28	
History of intervention or operation	24	8	
Diabetes mellitus	40	24	64
Hipertension	43	40	83
Hyperlipidemia	42	39	81
Coronary artery disease	33	38	71
Chronic kidney disease	4	3	7
Cerebrovascular event	6	8	14
Smoking	55	49	104

Mixed lesions: The presence of 60-70% and above lesions in the iliofemoral popliteal and distal below-knee beds.

with biochemical examinations. The postoperative period was uneventful. In addition, we limited the use of opaque to describing the lesion at the beginning of the procedure and observing the result at the end of the operation. We used approximately 40 to 50 mL of opaque in these patients and approximately 70 to 100 mL in other patients.

The length of the patients' extremities and the location of the lesions were recorded. Accordingly, the number of the patients who had iliac lesions was 30 (19.6%), the number of patients with SFA lesions was 94 (61.4%), and the number of patients with popliteal and distal lesions was 29 (18.9%) (Table 2).

The number of iliac, SFA, and popliteal and distal segment lesions was 30 (11.1%), 213 (78.3%), and 29 (10.6%), respectively. Most of the lesions were confined to the SFA. We performed PTA in all 153 patients; however, 143 of them also received atherectomy with two different reliable devices (Avinger in 45 patients, Invamed in 114 patients).

In 23 patients with iliac lesions who had lesions with >70% stenosis, only balloon angioplasty was

Table 2
The locations and the numbers of the lesions treated

	Ischemic lesion is present	Ischemic lesions is not present	
Number of the lesions	n	n	Total
External iliac artery	9	11	20
Common femoral artery	14	17	31
Superficial femoral artery	26	24	50
Popliteal artery	14	18	32
Below the knee	10	10	20
Mixed lesions	140	132	272
Side			
Right	45	59	114
Left	28	21	49

Mixed lesions: The presence of 60-70% and above lesions in the iliofemoropopliteal and distal below-knee beds.

Table 3
Postoperative data

	Ischemic wound is present	Ischemic wound is not present
	n	n
Mortality (independent from the operation)	4	1
Amputation		
Minor	4	1
Major	17	1
Revision	2	1
Infection	12	0

applied. In this group of patients, residual stenosis was not detected, and atherectomy was not required. For the rest of the cases (seven patients), which had approximately ≥90% stenosis, atherectomy in combination with PTA was the chosen modality for the residual stenosis management and stabilization of the plaque in the vessel. In one case, minimal intra-abdominal extravasation of the contrast media was detected, and the stent was implanted, uneventfully finalizing the operation. The patient was followed with abdominal USG and a complete blood count. No complications were observed after three days of hospital stay, and the patient was discharged on the third postoperative day. The mean follow-up period was 596±102 days, ranging from six months to two years. Five (3.2%) patients died due to complications of diabetes mellitus and coronary artery disease, and 23 (15%) patients underwent amputation in the two-year follow-up period. The mean hospital stay of the patients was 2.3 (range, 1-4) days.

No vascular aneurysm, dissection, rupture, pseudoaneurysm, arterial perforation, arterial tear, arterial spasm, arteriovenous fistula, bleeding, emboli, arterial thrombosis, urgent or nonurgent need for arterial bypass surgery, and hematoma were encountered during all procedures. Table 2 demonstrates the lesions and treatment applications in patients with PAD in the cohort.

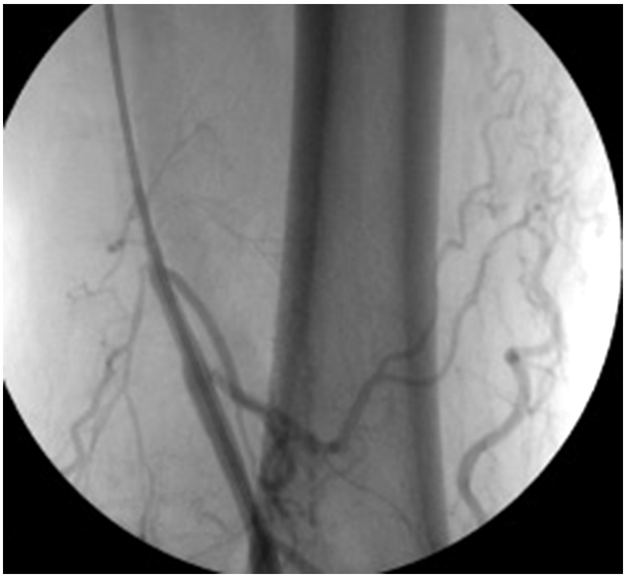

Figure 2. The image shows the movement of the wire inside the support catheter proximal to the popliteal artery.

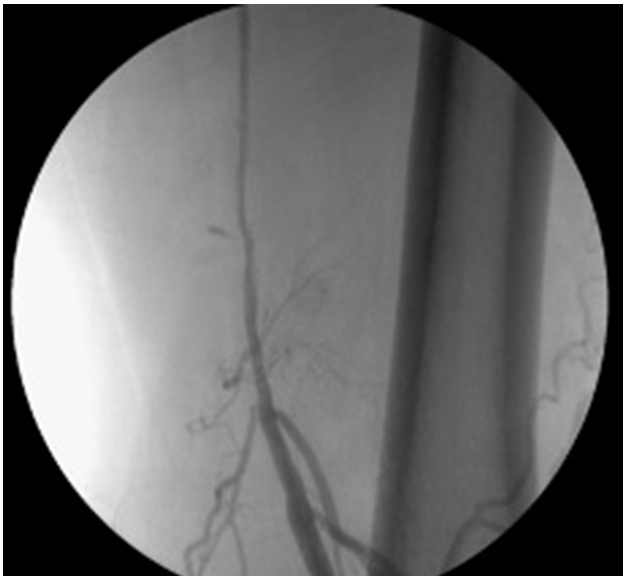

Figure 3. This image shows the wire inside the lesion after retracting the support catheter.

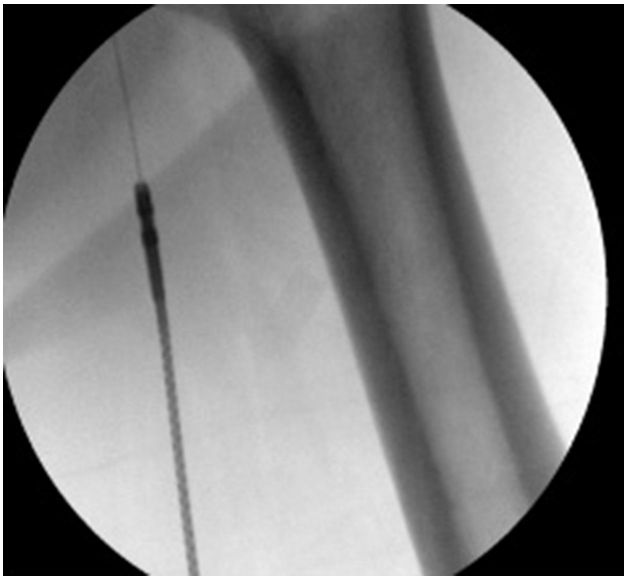

Figure 4. In this image, atherectomy device is pushed forward over the wire inside the SFA through the stenotic lesion.

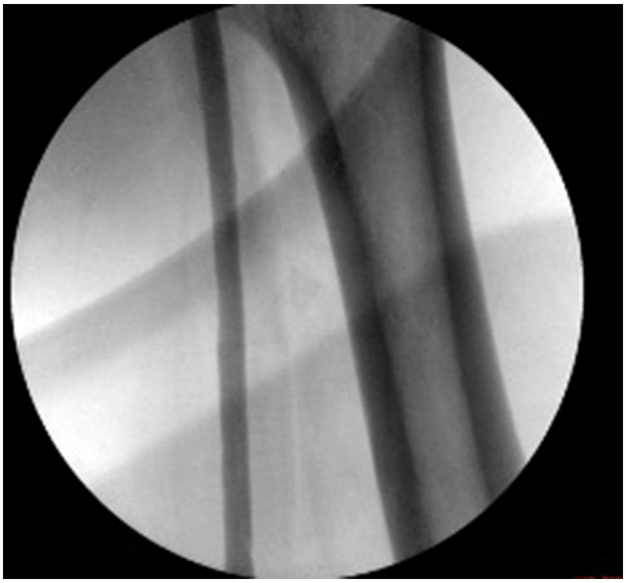

Figure 5. This image shows how PTA is applied to the lesion after the atherectomy.

DISCUSSION

Atherectomy devices and other instruments, such as balloons and stents, have been developed for the treatment of PADs. Balloons and stents are sometimes insufficient when used alone due to the variations in anatomical structures and status of the plaques and

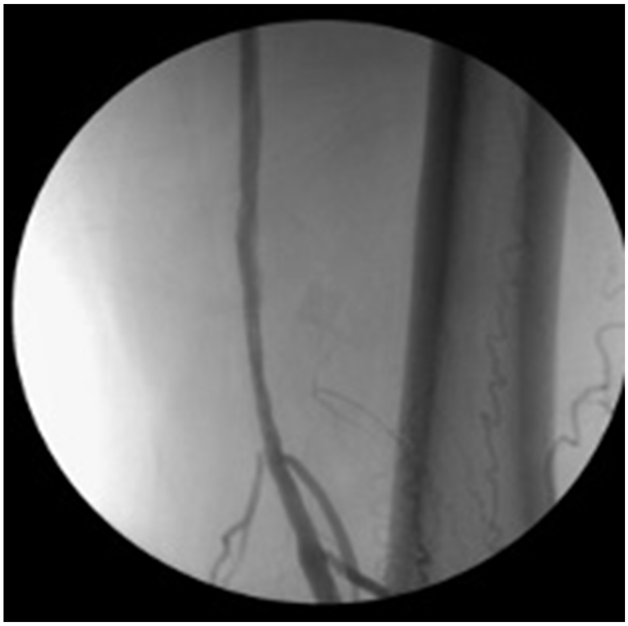

Figure 6. In the image, the SFA can be observed after the lesion is resolved by the procedure.

calcifications in the vascular structures. In general, atherectomy devices are used in circumstances such as high rates of occlusions in the vasculatures caused by the stenosis and hard calcific plaques. Nonetheless, balloons or stents can be used in cases with low levels of stenosis or soft lesions.[11]

In the last 20 years, endovascular treatment options have been the primary modality against claudication and even in critical ischemia of the extremities in several clinics.[12] It has been shown that endovascular treatment has some advantages, such as fast return of the patients to daily activities, decreased time of hospital stay, minimal morbidity, lower hospital charges, and decreased rate of complications to the lower extremity.[13]

It was stated in the DEFINITIVE-LE study that directional atherectomy, which mechanically removes the plaque burden and opens the lumen of the vessel without leaving a stent inside the vessel, is safe and effective in the treatment of the patients, including both the those with claudication and critical leg ischemia.[14] In addition, drug-coated balloons and plain old balloon angioplasty (POBA) were compared in several clinical trials, such as LEVANT 1 and 2, IN.PACT SFA, and ILLIMENATE.[15-18] Thus, it is now known that drug-coated balloons are superior to POBA in treating short to intermediate lesions. Additionally, drug-coated balloons are superior in anatomical outcomes, such as primary patency, binary stenosis, late lumen loss, and target lesion revascularization, compared to POBA.[19-22]

Minimally invasive endovascular treatments include PTA, PTA with additional stent placement, cold-balloon PTA or cryoplasty, and atherectomy with directional, laser, or orbital volume removal methods.[23]

The principal action of atherectomy devices is reducing the plaque burden by shaving or pulverizing the plaque by piercing or sanding it. In the meantime, this procedure causes minimal barotrauma in the vessel. We can classify the acute complications as dissection or acute occlusion. Potential complications of the atherectomy devices are hematoma, pseudoaneurysm, distal embolization, and tearing of the vessel.[23,24]

In our study, 130 patients with SFA and distal lesions underwent atherectomy with PTA, and 23 patients with iliac lesions had pure PTA without atherectomy. Percutaneous transluminal angioplasty was used for residual stenosis or plaque stabilization after the plaque load was reduced by atherectomy in SFA and complicated lesions. In the group with 29 popliteal and distal lesions, the lesion in the distal popliteal artery was approached as an SFA lesion in 11 patients, and an atherectomy was performed on the distal part of the popliteal lesion up to the distal bifurcation, and PTA or only PTA was performed on the area up to the distal bifurcation not to cause injury to the vessel wall.

It is important to know that complicated lesions may cause unfavorable outcomes, particularly in long-term management. In cases with critical leg ischemia, endovascular revascularization increases the rate of survival of the extremity.[24]

Our study mostly contains patients with SFA and distal popliteal lesions. Percutaneous endovascular treatment is more suitable for these patients as it decreases the time of hospital stay and reduces the rate of mortality and morbidity. However, chronic long segment occlusions in arterial vasculature, widespread calcifications, and involvement of more than one segment cause a decrease in the success of percutaneous endovascular interventions.[25]

In the BASIL study done in the United Kingdom, a comparison between the efficacy of bypass surgery and angioplasty in the treatment of patients with severe leg ischemia was evaluated.[13] They determined that there was no difference between the six-month survival and amputation rates between the two groups; however, cost of the treatment was higher in the surgery group. The immediate primary success rate of endovascular therapies was 75%.[26]

In our clinic, we use surgical therapy as an option in appropriate patients. The patients who underwent surgical therapy were not included in this study. The patients who could not tolerate graft insertion due to severely infected ulcers, had unregulated diabetes mellitus, preferred endovascular treatment, and had suitable lesions underwent endovascular therapies. Medical treatment is another option in these patients, particularly in diabetic patients with foot ulcers and PAD, and adjuvant therapies, such as platelet rich plasma (PRP), have been found to be beneficial.[27] We used medical treatment, including antiaggregant drugs, antithrombotic drugs, and cilostazol in the management of some patients.

The cost of the treatment was not evaluated in our study; however, the mean hospital stay of the patients in our study was 2.3 (range, 1-4) days, which is less than the 5.7 days of hospital stay needed after the bypass.

Due to the low rate of long-term patency rates of standard balloon angioplasty and stents, several studies have used drug-eluting stents and drug-coated balloons to search for an effective endovascular treatment modality. Dake et al.[28] suggested in their study that the patency rates of paclitaxel-coated stents used in SFA stenosis were significantly greater than the ones that only PTA was used, and the patency rates were 83.1% and 32.8% respectively. In the last few years, drug-coated balloons have been thought to be effective in percutaneous interventions; however, no significant difference between drug-coated balloons and conventional balloons has been found.[29,30] Rosenfield et al.[20] found that 12-month patency rates of drug-coated balloon angioplasty and standard balloon angioplasty methods are 65.2% and 52.6%, respectively. In our study, we used drug-coated balloons only to eliminate future complications and increase the patency rates.

Unlike the angioplasty and stenting, which push the plaque to the vessel wall, atherectomy, which uses directional and rotational movements in combination with physical or ablative technics, takes out the plaque burden out of the vessel. Atherectomy can be used alone or in combination with stenting or angioplasty. Restenosis after the atherectomy operation has not been fully understood; however, there are some links between few mechanisms.[33] Plasma proteins, C-reactive protein, serum amyloid A and fibrinogen are sensitive, specific and sensitive reaction markers of the acute phase,[31] cytokine-dependent indirectly they indicate the inflammatory process of the arterial wall.[32] Restenosis is mainly due to excessive neointima formation.[33] In our study, no restenosis cases occurred in the early period (first 24 h after the operation). The usage of intraoperative and postoperative antiaggregant and antithrombotic agents was considered to have prevented early restenosis.

Percutaneous intervention causes mechanical trauma to the vessel. Vascular stimulants induce vascular inflammation. The proliferation of smooth muscle cells and extracellular matrix cause neointimal thickening and restenosis.[34] Besides the antithrombotic prescription for the postoperative mechanical trauma, diet, and hyperlipidemic agents, aiming to control LDL to below 100 and triglyceride to below 200, were preoperatively prescribed to the patients with hyperlipidemia.

Risks associated with superficial atherectomy femoral, popliteal, anterior tibial, posterior tibial, and peroneal arteries include arterial dissection, arterial perforation, arterial tear, arterial spasm, arteriovenous fistula, bleeding, emboli, arterial thrombosis, urgent or nonurgent need for arterial bypass surgery, complications of the incision site, restenosis of the treated segment, occlusion in the peripheric vessels, and vascular complications.[35,36] The most common vascular complication is distal embolization; however, the prevalence of the distal embolization can be reduced with the postoperative usage of acetil salisilic acid (ASA) and clopidogrel.[37,38]

Doppler USG-guided popliteal intervention in the prone position was shown to be an alternative to the femoral intervention in patients with iliac and SFA lesions but not in popliteal or distal lesions. For this operation, USG was used to examine the popliteal arterial calcification before the operation. In our study, distal embolic protection devices were not used.

Some recommendations to optimize the outcome of peripheral atherectomy and minimize the risk of procedural complications are as follows: using the contralateral access in cases other than distal lesions, preferring the antegrade approach for better management, making slow and methodical cuts, advancing the cutting blade slowly, and ensuring adequate anticoagulation (aiming for an activated clotting time between 275 and 300 sec) to avoid thrombotic complications during the procedure.[39,40]

The success of endovascular treatments depends on the localization, length, and degree of stenosis. Literature includes many studies that demonstrate the high patency rates of iliac artery stents in the long term, but it is still controversial in the distal region.[41] Drug-coated balloons were related to distal embolism in some studies. However, Fukai et al.[42] revealed that drug-coated balloon-induced distal embolisms were not common in femoropopliteal lesions. We mostly used drug-coated balloons in upper knee lesions and avoided their use in patients with distal gangrenous lesions.

In our cases with an antegrade or retrograde approach, thrombotic complications were tried to be avoided by administering 1 mL of intravenous heparin after sheath placement to the patient without activated clotting time follow-up. All patients were checked for the presence of a thrombus on the sheath tip while the postoperative sheath was withdrawn. Furthermore, the patients' postprocedure foot color and fingers were checked for distal microembolism.

We did not encounter any problems in 125 patients. In 28 patients, progression of the disease was observed in the leg or ischemic wound between 30 and 65 postoperative days. Twenty-three (%15) patients required amputation; 20 of the 40 patients with necrotic wounds showed progression of necrosis leading to amputation after approximately 30 days. Amputations were minor (finger amputation) in five patients and major (below the knee) amputation in 18 patients. These patients with progressive disease had femoropopliteal, distal, and multiple lesions. Most of these patients had advanced calcified lesions with a poor distal vascular bed. More than half of these patients were diabetic.

When it is necessary to share the scope with other departments in the operating room, it can be challenging to determine the surgery day and schedule the patients into one day.

In conclusion, certain interventional endovascular procedures can be performed with the C-arm fluoroscopy. We evaluated the success of our procedures as the satisfaction of the physician and the patient, the short postoperative stay, and, most importantly, the absence of major complications. Moreover, the ergonomics of all the materials used during the procedures, including the use of the C-arm scopy, and their of use facilitated the procedures. In the era of modern hybrid operating rooms, we recommend its use for arterial lesion treatment C-arm for surgeons in centers lacking experienced hybrid theaters I wanted to show that arterial intervention can be done with fluoroscopy.

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Ethics Committee Approval: The study protocol was approved by the Bozyaka Training and Research Hospital Ethics Committee (Date/no: 13.10.2021/ 2021/176). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Cardiovascular Surgery and Interventions

Case Report Open Access

A rare complication of pericardiocentesis: Pneumopericardium

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ABSTRACT

Pneumopericardium is a rare complication of pericardiocentesis and defined as the presence of air in the pericardial space. Pneumopericardium usually occurs after trauma. However, pneumopericardium due to iatrogenic procedures, such as pericardiocentesis, is extremely rare. It can be caused by either direct pleuropericardial connection development or reverse air leakage in the drainage system. Herein, we report the case of a 39-year-old female with cardiac tamponade who developed pneumopericardium after pericardiocentesis.

Keywords: Chylous effusion, pericardial effusion, pneumopericardium, tamponade.

Pneumopericardium is a rare condition in which there is air in the pericardial space. It usually occurs after trauma. However, iatrogenic pneumopericardium during pericardiocentesis is less common.[1-4] Imaging methods are the cornerstone in the diagnosis of pneumopericardium. Posteroanterior chest radiography reveals the typical finding of air-fluid level in the pericardial space. Echocardiography can demonstrate mobile air bubbles around the pericardium. Chest tomography is the gold standard for definitive diagnosis.

Iatrogenic pneumopericardium usually has a good prognosis and does not require specific treatment. Echocardiographic and hemodynamic follow-up is generally sufficient, and it spontaneously wears off over time. However, it rarely progresses to pericardial tamponade. Early diagnosis and therapy, such as percutaneous pericardiocentesis or surgical intervention, may be required in such cases.[5,6] In this paper, we report a case with pneumopericardium, a rare complication of pericardiocentesis.

CASE REPORT

A 39-year-old female patient with no previous chronic disease was admitted to the outpatient clinic with complaints of increased shortness of breath, palpitations, and a recently developed weakness. On physical examination, the patient looked pale and tired. The patient's blood pressure was 105/60 mmHg and pulse rate was 110 bpm. On auscultation, there were muffled heart sounds and a Grade 2/6 pansystolic murmur at the apex with radiation to the axilla. There was no peripheral edema, and other physical findings were unremarkable. Chest X-ray demonstrated an enlarged cardiothoracic ratio with open bilateral costophrenic sinuses and clear lung parenchyma. Normal sinus rhythm was detected on electrocardiography, and there were no signs of hypovoltage. Echocardiography revealed a massive pericardial effusion compromising the diastolic relaxation of the right ventricle. Left ventricular systolic functions were normal with mild mitral insufficiency. The patient was hospitalized in the coronary care unit with the diagnosis of massive pericardial effusion. Pericardiocentesis was performed through the subxiphoid approach with the Seldinger technique under echocardiography guidance. A 6 Fr introducer was inserted into the pericardial space, then a pigtail catheter was advanced over a 0.035 guidewire through the pericardial space. Initially, 700 mL of chylous fluid was drained. Afterward, a total of 1600 mL fluid was drained in five days. The sheath was kept in position until the amount

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of drained fluid was less than 100 mL per day. Laboratory findings of the pericardial fluid were as follows: protein, 5.5 g/dL; albumin, 3.3 g/dL; lactate dehydrogenase, 145 U/L; triglyceride, 872 mg/dL. The serum-fluid albumin gradient was 0.9 g/dL, suggesting an exudative form. In the blood analysis, the leukocyte count was 12,500/mm^3, and the eosinophile ratio was 51%. Sedimentation and C-reactive protein were within normal limits. Other laboratory parameters were in normal range. All tumor markers were negative. Additionally, all autoimmune markers were negative except ANA positivity. Polymerase chain reaction was negative for *Mycobacterium tuberculosis* deoxyribonucleic acid. The adenosine deaminase level in the pericardial fluid was normal. Microbial growth did not occur in the pericardial fluid culture. On the fifth day, the catheter was removed due to reduced fluid drainage and regression of pericardial fluid on echocardiography. The next day, a crackling sound was detected on the patient's chest when moving and leaning forward. Chest X-ray revealed radiolucent space around the heart with a radiopaque demarcation line, suggesting air and fluid surrounding the pericardial space (Figure 1). Echocardiography demonstrated a microbubble appearance (small and bright air vesicles) around the pericardial space and mild pericardial effusion (Figure 2). The diagnosis of pneumopericardium was confirmed by thorax chest tomography (Figure 3). Given the fact that the patient had stable hemodynamics, she was followed by echocardiography. The patient was consulted by a rheumatologist. Autoimmune diseases were ruled out since the ANA positivity was not confirmed by the immunoblot assay. During hospitalization, the pericardial fluid was recollected with a diastolic notch in the right atrium on echocardiography. Since the etiology of the patient could not be elucidated and the fluid was quickly recollected, the pericardial window was opened, and recurrent chylous fluid was

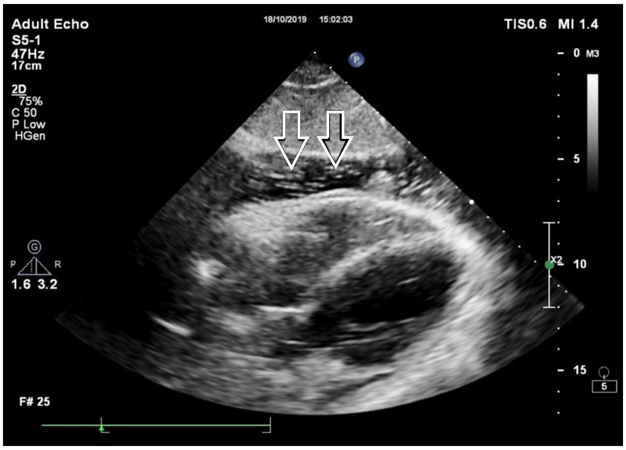

Figure 2. Two-dimensional echocardiography revealing several tiny sparkling echogenic spots swirling in the pericardial sac evoking micro air bubbles (arrows).

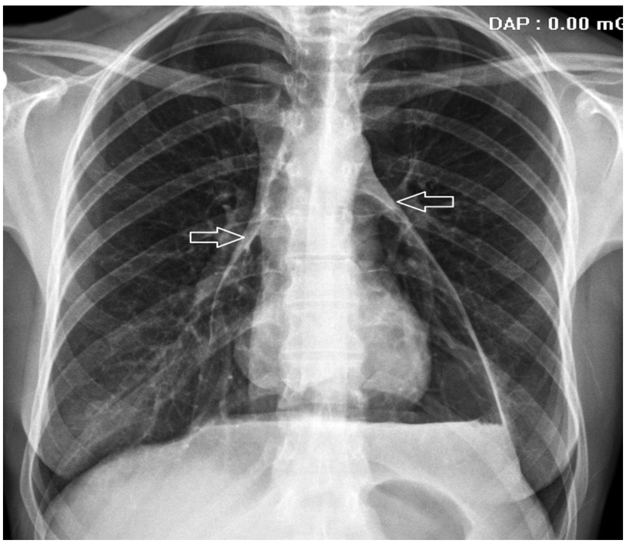

Figure 1. Chest radiograph demonstrating a radiolucent space along with a radiopaque border around the cardiac silhouette (arrows) representing pericardial air.

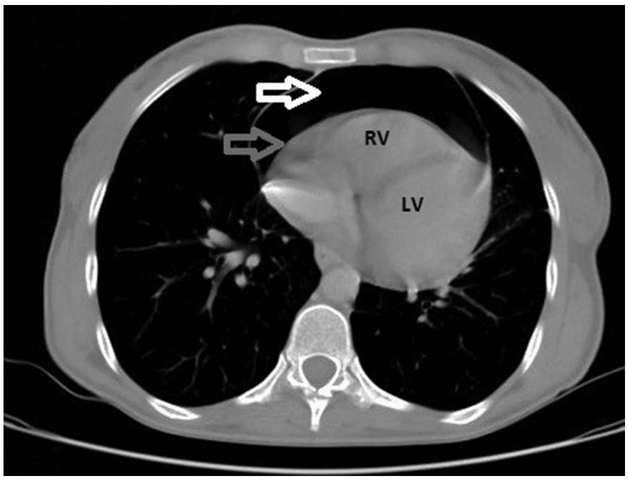

Figure 3. Chest computed tomography section displaying a marked pneumopericardium with an anterior extent (white arrow) associated with a small amount of pericardial fluid (grey arrow).

RV: Right ventricle; LV: Left ventricle.

surgically drained. During the follow-up, there was no pericardial effusion on echocardiography. The patient was discharged uneventfully.

DISCUSSION

Pneumopericardium is the accumulation of air in the pericardial space. It is mostly caused by blunt or penetrating traumas. Rarely, it can occur due to the fistulization of nearby organs, tuberculosis and fungal infections, pacemaker implantation, and pericardiocentesis.[2,4] During pericardiocentesis, pneumopericardium can be caused by direct pleuropericardial connection or reverse air leakage from the catheter.[3] Therefore, the use of under-water drainage systems may be considered to prevent the back-flow of air during fluid drainage. Given the short distance between the pericardium and the skin, cachectic patients may also develop pneumopericardium after the removal of the catheter due to the development of negative pressure during inspiration.[3,5,6] In the present case, there are two possible reasons for pneumopericardium: our patient was thin, and the hub of the pigtail catheter remained open, which might have caused the air leakage into the pericardium.

Pneumopericardium can be asymptomatic or may manifest nonspecific symptoms, such as palpitations, shortness of breath, and chest and shoulder pain. The typical auscultatory finding is the Hamman sign, which is a crackling sound that can be heard with every cardiac beat. Another physical finding is the mill-wheel murmur, or bruit de moulin, which is a succession splash and traducing shaking movement of the heart within the pericardial cavity.[1,6] In cases where pneumopericardium is suspected, imaging should be performed by echocardiography and radiological examinations. Echocardiography can demonstrate two pathognomonic signs: the "air gap sign," a cyclic disappearance of the cardiac shape during systole, coinciding with a cycling appearance of air within the pericardium during this phase as the volume of cardiac cavities decreases,[7] and the "swirling bubbles sign," representing the presence of an air-fluid interface with continuous churning movements in the pericardial cavity due to heart activity, which is revealed on echocardiography by several tiny bright echogenic spots in the pericardial sac evoking micro air bubbles.[5,6,8] The pneumopericardium can easily be diagnosed by chest radiographs, which reveal a radiolucent rim separating the pericardium from the heart, called the "continuous diaphragm sign."[5,6,8] Chest computed tomography can easily confirm the diagnosis and is the mainstay of diagnosis of pneumopericardium in obscure cases. The tomography clearly demonstrates the air-fluid level in the pericardial space, as well as informing about the cause and associated pathologies.[9]

The clinical course in pneumopericardium is highly variable and depends on the etiology, the amount, and the rate of air accumulation. Just as in fluid buildup, a small amount of fast-collected (60 mL) air can cause hemodynamic deterioration, while more slowly collected (500 mL) air can be better tolerated.[1] Iatrogenic pneumopericardium is usually benign. Spontaneous resolution can occur within a few days of follow-up. Bed rest should be exercised in these patients, and hemodynamic parameters should be closely monitored. The patient should be screened until resolution is observed on chest X-ray and echocardiography.[3,5] The most feared and fatal complication is the development of tension pneumopericardium. Drainage should be performed without delay when there is hemodynamic deterioration or an increase in the amount of air or fluid on imaging methods. Drainage can be percutaneously or surgically performed depending on the urgency of the case and the etiology. Surgical treatment is considered if there is direct fistulization with an organ other than the lung or if the fluid is likely to recollect.[3,6]

In this case report, since secondary causes of chylopericardium were ruled out, the patient was considered to have primary idiopathic chylopericardium. Treatment of this disease consists of a diet poor in fatty acids, opening a pericardial window, and, if necessary, thoracic duct ligation.[10]

In conclusion, iatrogenic pneumopericardium, a rare complication of pericardiocentesis, usually has a good prognosis and does not require specific treatment. However, it rarely progresses to pericardial tamponade, which may require percutaneous or surgical intervention.

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Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Case Report Open Access

Metastatic osteosarcoma near-totally occluding the right atrium: A rare cause of cardiovascular emergency

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ABSTRACT

Emergency surgical treatment of metastatic cardiovascular tumors is rarely required in cardiovascular surgery. Metastatic cardiovascular tumors constitute a small portion of open-heart surgeries. Intracardiac metastasis of osteosarcomas is much less common. Herein, we present the diagnosis and management of dyspnea, cyanosis, and respiratory failure secondary to near-total occlusion of the right atrium due to right humerus metastatic osteosarcoma in a 21-year-old female patient.

Keywords: Cardiac tumor, emergency surgery, metastasis, osteosarcoma.

Traumas, acute myocardial infarction and its complications, complications due to interventional procedures, gunshot wounds, stab injuries, aortic dissections/ruptures, thromboembolisms, and acute cardiovascular thromboses are the most common reasons of major emergency cases in cardiovascular surgery. Other causes of emergency surgery are uncommon. As cardiac tumors slowly develop, whether primary or secondary, the patients do not require emergency surgery. Most common metastases of osteosarcomas are to the brain, lymph nodes, skin, and rarely to the heart.[1,2] Herein, we present the diagnosis and management of respiratory failure secondary to near-total occlusion of the right atrium due to right humerus metastatic osteosarcoma.

CASE REPORT

A 21-year-old female patient was admitted to the emergency room with complaints of dyspnea and peripheral cyanosis and hospitalized in the chest diseases department with the suspicion of pulmonary embolism. It was learned from the patient that she was diagnosed with osteosarcoma originating from the right humerus three years ago, and after the diagnosis, the patient received three courses of chemotherapy. In addition, the patient had a total humerus resection and prosthesis implantation operation two years after the diagnosis. Afterward, she received 37 courses of chemotherapy and 32 courses of radiotherapy. The patient was in remission during the last year and was followed up at an external center. Physical examination revealed that the patient was cyanotic and had severe dyspnea. The computed tomography angiography (CTA) taken at the emergency room showed a full-filling thrombus in the right atrium, and the patient was consulted with cardiovascular surgery and then transferred to our department for emergency surgery (Figures 1 and 2). No pathological finding was found in the routine complete blood count, biochemistry, coagulation parameters, and thyroid function tests of the patient. The D-dimer value was 324 ng/mL. The 100% nasal oxygen 6 L/min arterial blood gas was measured as follows: pH, 7.467; pCO_2, 21.6 mmHg; pO_2, 34.5 mmHg; sO_2, 59.5%; actual base excess (ABE), -5.9 mmol/L; lactic acid (Lac), 2.1 mmol/L. Upon these findings, the patient was prepared for an emergency operation, and the patient's peripheral oxygen saturation was 30% when she was taken to the operation. Following routine surgical procedures, the mediastinum was opened with a median sternotomy, and aortic cannulation was

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performed. Venous cannulation could not be performed as the right atrium and superior and inferior vena cava were occluded by the mass. Thereupon, the right atrium was opened, and venous drainage was provided through venous suction. After the partial resection of the mass located in the right atrium, extending from the tricuspid valve to the right ventricle and the inferior cava, the venous cannula was placed through the inferior vena cava from the atrium, partially entering the pump. *En bloc* removal was not possible as the mass was rigid; therefore, it was broken out and removed part by part (Figure 3). The mass extending into the superior vena cava, right subclavian vein, and brachiocephalic vein was consecutively removed (Figure 4). A pericardial patch was required to close the superior vena cava. Then the right atrium was closed, and the partial bypass was finished. The extracted materials were sent to pathology, and the result was osteosarcoma. Postoperative extubated first arterial blood gas was measured as follows: pH, 7.498; pCO_2, 16.7 mmHg; pO_2, 74.9 mmHg; sO_2, 97.5%; ABE, -3.1 mmol/L; Lac: 1.2 mmol/L. The patient was followed up for hemodynamic problems for one week

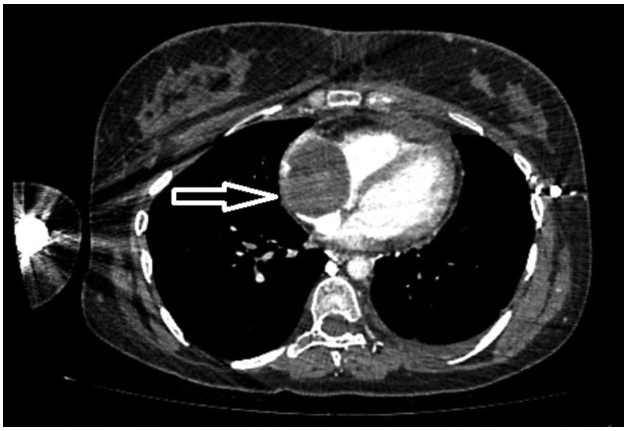

Figure 1. Preoperative computed tomography angiography image of the mass that fills the right atrium almost completely.

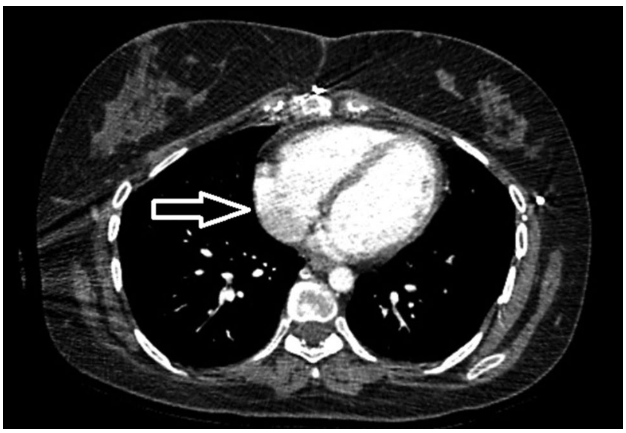

Figure 2. Postoperative computed tomography angiography image of the normal right atrium.

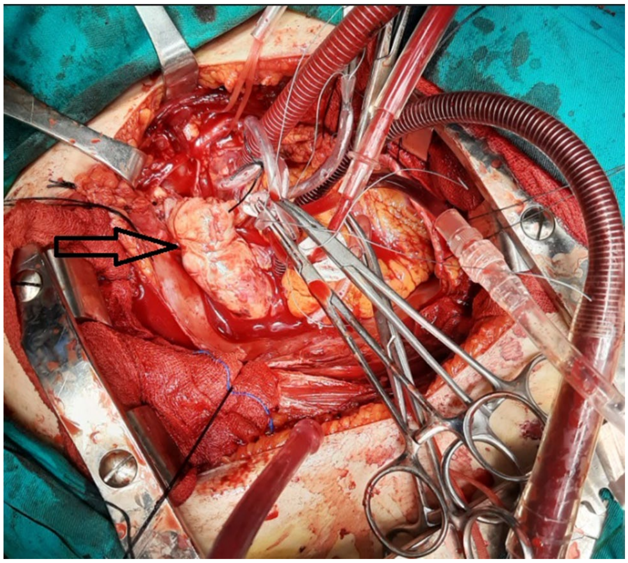

Figure 3. Intraoperative image of the osteosarcoma.

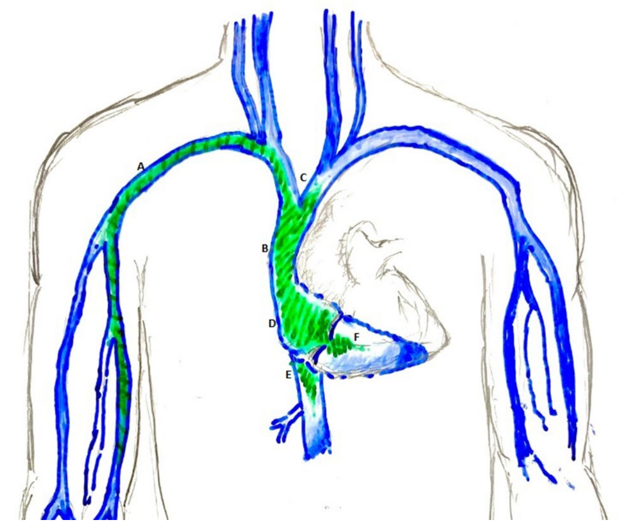

Figure 4. Illustration of the intravascular and intracardiac metastatic osteosarcoma extension (green color indicates tumor extension). The tumor was removed from B, C, D, E, and F regions.

A: Subclavian vein; B: Vena cava superior; C: Innominate vein; D: Right atrium; E: Vena cava inferior; F: Right ventricle.

and discharged. The patient has been followed up for one year without any issues.

DISCUSSION

Cardiac tumors constitute a minority of open-heart surgery cases. Primary cardiac tumors are generally benign and most frequently diagnosed as myxoma.[3] Metastatic cardiac tumors are usually diagnosed at postmortem autopsy. The most common tumors that metastasize to the heart are lung cancers, breast cancers, and hematological malignancies.[4] Osteosarcomas rarely metastasize to the heart. Osteosarcoma cases with cardiac metastasis are rare in the literature. There is a limited number of primary cardiac osteosarcoma cases.[5-7] Intracardiac metastatic osteosarcoma cases can be asymptomatically diagnosed during the follow-up. Additionally, it can be the first symptom of recurrence.[8,9] Symptoms are completely related to the affected chamber of the heart. The most common symptoms are shortness of breath, weakness, and fatigue. Rarely, it may present as peripheral arterial recurrent embolism.[7] The primary osteosarcoma site may be the lower or upper extremities. Due to the low number of cases in the literature, the most common origin of metastasis is not known. However, cardiac metastasis originating from femur osteosarcomas is more frequently encountered in the literature.[8,10] There is no clear ratio concerning metastatic heart tumors. However, metastasis to the right heart chambers is more common in the literature.[8-11] In our case, there was spread to the right chambers of the heart and superior and inferior cava. There are also publications regarding the invasion of the left chambers of the heart.[6,12] Patients are generally young females and adolescents. After the primary diagnosis, early cardiac metastasis may occur, or metastasis may be seen after many years from diagnosis.[11] There was a three-year period between primary diagnosis and cardiac metastasis in our case. Magnetic resonance angiography, CTA, ventriculography, transthoracic echocardiography, and transesophageal echocardiography can be used for diagnosis in symptomatic patients. Positron emission tomography and scintigraphy can be used in asymptomatic patients.[9] In our case, the patient was diagnosed by CTA. However, CTA images appeared more compatible with intracardiac thrombus. In our case, the diagnosis of metastatic osteosarcoma was made based on intraoperative findings and pathology. The main treatment is the surgical resection of the tumor. After surgical treatment, chemotherapy, radiotherapy, or combined treatments can be applied with a multidisciplinary approach. All osteosarcomas with cardiovascular metastasis in the literature were electively operated. However, our patient was urgently operated due to severe dyspnea and respiratory distress, impaired laboratory values, and hemodynamic instability. Although there are tumors that metastasize to the cardiovascular system, they rarely require emergency surgery. There are no intracardiac metastatic osteosarcoma cases requiring urgent surgery in the literature.

In conclusion, although rare, metastatic intracardiac tumors may require emergency surgery. In such cases, a fast and effective preoperative preparation can prevent undesirable results.

Patient Consent for Publication: A written informed consent was obtained from patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Cardiovascular Surgery and Interventions

Case Report Open Access

A right atrial arteriovenous hemangioma excision under a beating heart after percutaneous catheter cardiac ablation

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ABSTRACT

Percutaneous catheter ablation treatment is an interventional treatment method for atrial fibrillation. Herein, we report the case of a 38-year-old male patient who developed a right atrial mass after two percutaneous catheter ablations. The mass was excised by the beating heart technique, later diagnosed as arteriovenous hemangioma. Arteriovenous hemangioma had not been encountered before as a complication of catheter ablation.

Keywords: Arteriovenous hemangioma, atrial mass, paroxysmal atrial fibrillation, pulmonary vein isolation cryoablation, radiofrequency ablation.

Percutaneous catheter ablation is the most effective treatment nowadays for patients with recurrent tachyarrhythmias who are not responding to medical treatment. It can be used for symptomatic supraventricular tachycardia, unifocal atrial tachycardia, atrial flutter, atrial fibrillation with lifestyle-impairing symptoms, and symptomatic idiopathic ventricular tachycardia.[1] However, pulmonary vein stenosis, esophageal perforation, phrenic nerve injury, heart block, stroke, vascular access injury, heart perforation, and rarely death are the possible complications of the catheter ablation.[2,3] Herein, we report a case of a right atrial arteriovenous hemangioma (AVH) in a patient admitted for pulmonary embolism with a history of two percutaneous catheter ablations.

CASE REPORT

A 38-year-old male patient presented to the cardiology outpatient clinic for routine control with minimal symptoms of dyspnea and palpitation. The patient had a history of paroxysmal atrial fibrillation. Two years ago, he underwent percutaneous radiofrequency ablation after unsuccessful cardioversion; however, his palpitation complaints continued. The patient was admitted to another cardiac center four months later, and pulmonary vein isolation cryoablation was done successfully. Anticoagulant medication was discontinued on discharge. On admission to our hospital, electrocardiography revealed atrial fibrillation. At the same time, transthoracic echocardiography was performed, and it demonstrated a right atrial compounded mass (one was about 19×17 mm attached to the interatrial septum, and the other was 18×11 mm), which was not observed in the previous investigations. The appearance was compatible with a thrombus. A pulmonary computed tomography scan with contrast showed a segmentary pulmonary embolism. The patient was admitted to the intensive care unit, and anticoagulant medications were started. When the patient's status became stable, he was taken to the operation theatre for mass excision.

Under general anesthesia and intratracheal intubation, the operation started. After median sternotomy, the pericardium was vertically opened, and under full heparinization, aorto-bicaval cannulation was done. A cross-clamp was not applied, and the operation was carried on under the beating heart technique. The right atrium was opened via its

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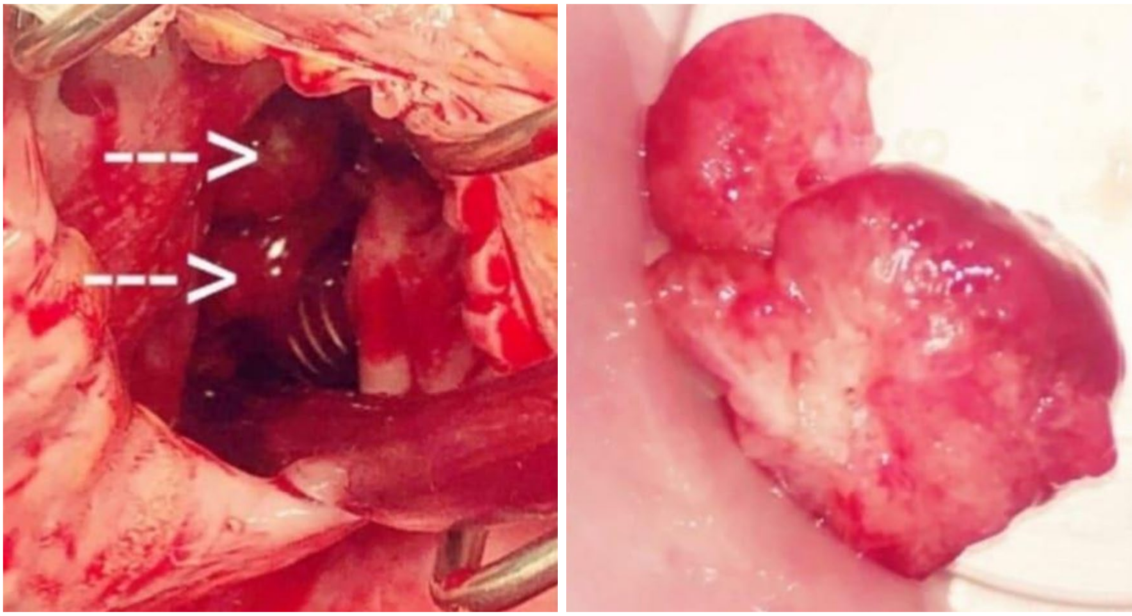

Figure 1. Right atrial mass (arteriovenous hemangioma).

appendage, and a mass of two segments, covered with thrombus, was excised from the interatrial septum (Figure 1). It was attached to the lower part of the interatrial septum above the tricuspid valve by a pedicle. The right atrium was closed, and after decannulation and hemostasis control, the sternum was closed by steel wires. The patient was transferred to the cardiovascular intensive care unit.

On the first postoperative day, the patient's daily dressings and blood investigations were done. One week after the operation, as he was well with no complaints, the patient was discharged on anticoagulant medications to be seen one week later as an outpatient. About 10 days later, the histopathologic report of the cardiac mass revealed an AVH.

DISCUSSION

Cardiac masses can be primary or secondary. The prevalence of primary tumors is about 0.0001 to 0.03%, and 75% of them are benign, while secondary tumors are malign and 20 to 40-fold more common. Myxoma, lipoma, papillary fibroelastoma, and fibroma are the most common benign tumors. Angioma, teratomas, and mesotheliomas are rare primary cardiac tumors.[4]

Cardiac hemangiomas are very rare primary benign cardiac tumors that are usually asymptomatic, and they may originate from any heart layer. They are classified according to the histomorphological structure into capillary, cavernous, arteriovenous, and extremely rare venous ones.[5]

In our case, the patient was young and had several echocardiography reports from before, but none of them showed any cardiac mass. Only the recent echocardiography demonstrated this cardiac mass. Thus, the question was whether there is any relation between this atrial AVH and the transcatheter pulmonary vein cryoablation that he had two years ago. We have browsed the literature but found nothing relating to such complications. Usually, the well-known major complications of such a procedure are pericardial effusion/tamponade, pulmonary vein stenosis, emboly, cardiac block, phrenic nerve injury, vascular access injury, and atrioesophageal fistula.[6]

In our case, there was no early complication of the radiofrequency ablation, which was done 26 months ago, or after pulmonary vein isolation cryoablation 22 months ago.

After the second ablation, the patient had been told to stop his anticoagulant medications. The patient was free of any symptoms for about two years until he suddenly started complaining of dyspnea and palpitation. During the routine investigations, a right atrial mass was accidentally found.

We performed our operation under the heart beating technique, while all preparations were done to switch to complete cardiopulmonary bypass and arrest the heart if needed. Bicaval venous cannulation was selectively performed, making the mass's excision easy. There was a pedicle attaching the mass to the interatrial septum above the tricuspid valve, and the mass was found compounded by two segments with a thrombus above. The tricuspid valve was preserved from any damage during the excision.

In conclusion, cardiac AVHs are very rare benign cardiac tumors that can be excised under the beating heart technique if possible. We suggested a relationship between AVH and catheter cryoablation. However, this relation remains unclear and should be studied widely. We simply wanted to shed light on the possibility of developing atrial AVH after pulmonary vein isolation cryoablation.

Patient Consent for Publication: A written informed consent was obtained from patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept, control/supervision, data collection and/or processing, writing the article, critical review: M.A., M.K.A.; Design, analysis and/or interpretation, literature review, references and fundings, materials, procedure performer: M.A.

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Cardiovascular Surgery and Interventions

Case Report Open Access

Berry syndrome: A rare aortopulmonary malformation

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ABSTRACT

Herein, we present a case of Berry syndrome with successful surgical repair in an infant. A definitive diagnosis was established with appropriate investigative modalities, and a single-stage repair was performed with good results.

Keywords: Aortopulmonary window, Berry syndrome, interrupted aortic arch.

Berry syndrome is an extremely rare aortopulmonary malformation accounting for 0.046% of congenital heart defects.[1] First illustrated by Berry et al.[2] in 1982, it consists of a distal aortopulmonary window (APW), an aortic origin of the right pulmonary artery, an intact ventricular septum, and patent ductus arteriosus (PDA) with hypoplastic or interrupted aortic arch (IAA). Surgery remains the mainstay of treatment. The choice of a single or staged approach is still controversial.[1,3] Herein, we present a case of Berry syndrome with successful surgical repair in an infant.

CASE REPORT

A nine-month-old female child weighing 5 kg presented to our clinic with failure to thrive and recurrent respiratory tract infections. The cardiovascular system examination revealed normal first and second heart sounds. A grade 3/6 continuous murmur was heard in the left second intercostal space.

Chest X-ray revealed cardiomegaly (cardiothoracic ratio: 0.68) and a right ventricular type of apex with plethoric lung fields. Electrocardiography demonstrated a normal sinus rhythm, a heart rate of 145/min, right axis deviation, incomplete right bundle branch block, right ventricular hypertrophy, and left ventricular volume overload. Transthoracic echocardiography (TTE) showed a large APW (1.2 cm) with a bidirectional shunt (Figure 1a), moderate tricuspid regurgitation, and features of pulmonary artery hypertension (PAH). Right ventricular systolic pressure (RVSP) was 97 mmHg, with normal right ventricular function and a left ventricular ejection fraction of 60%. Cardiac catheterization study was performed, which revealed a large APW of 1.6 cm (Figure 1b), arising from the ascending aorta, and a large PDA of 8 mm, supplying the descending thoracic aorta with type B IAA. The ratio of pulmonary blood flow to systemic blood flow (Qp/Qs) was 3.93, and the pulmonary vascular resistance index was 2.81 post oxygen administration.

Intraoperative anatomy was assessed. Type III APW[4] with type B IAA was noted (Figure 2a). Patent ductus arteriosus was observed supplying the descending aorta, and the right pulmonary artery was arising from ascending aorta (Figure 2a).[5]

Cardiopulmonary bypass was established with the high ascending aorta and bicaval venous cannulation. Aorta was cross-clamped, the core was cooled to 18°C, and antegrade cold blood cardioplegia was administered. After satisfactory arrest, the right atrium was opened, and a patent foramen ovale (PFO) was created to vent the left side of the heart. An APW was vertically opened, and the anatomy was noted. The aorta and the main pulmonary artery (MPA) were separated. Once the nasopharyngeal

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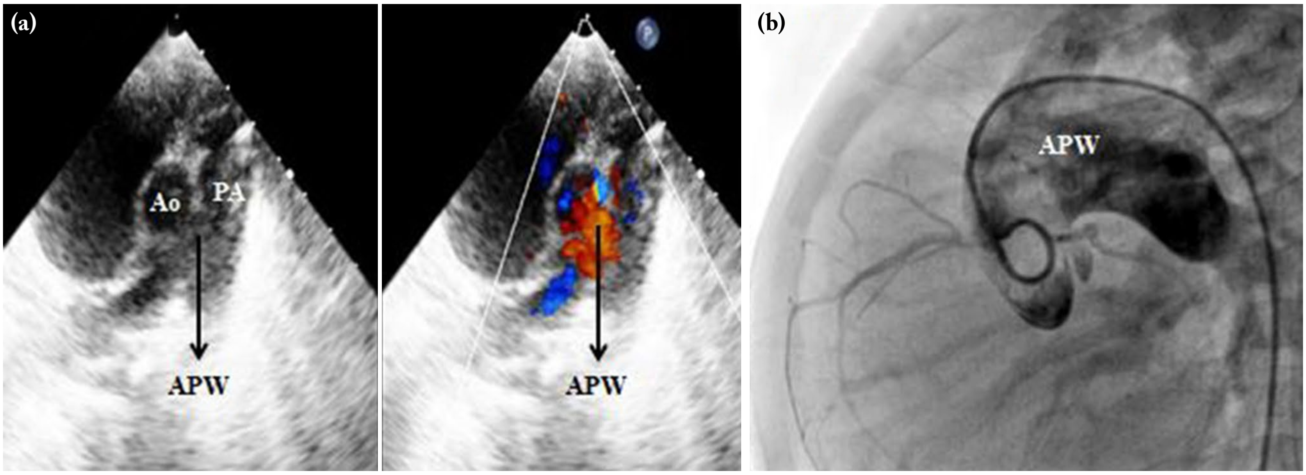

Figure 1. (a) Two-dimensional echocardiography with color Doppler in short axis view shows echo dropout between the aorta and the pulmonary artery indicating APW. **(b)** Catheterization study (catheter course from descending aorta -PDA-through APW to ascending aorta) demonstrating an APW.
Ao: Aorta; APW: Aortopulmonary window; PA: Pulmonary artery.

temperature reached 18°C, total circulatory arrest was initiated. The PDA was ligated, and the proximal stump was transfixed. The distal end of the PDA and remaining ductal tissue was excised. The descending aorta was mobilized (Figure 2b). The left subclavian artery was ligated. The descending aorta was pulled up and anastomosed to the arch of the aorta, and the anterior wall was augmented with autologous untreated pericardium with 6-0 polypropylene sutures. The RPA was disconnected from the ascending aorta, and the proximal ascending aorta was augmented with autologous untreated pericardium. The arterial cannula was reinserted, and rewarming was started. Dearing was done after rewarming. The RPA was anastomosed to the MPA near its bifurcation with 6-0 polypropylene sutures and anteriorly augmented with autologous untreated pericardium (Figure 2c). Tricuspid valve repair was done through the right atrium. The PFO was closed with 5-0 polypropylene sutures, leaving behind a small PFO. The final image after the surgical closure is presented in Figure 2d. The patient was in sinus rhythm after cardiopulmonary bypass with milrinone at 0.5 minimum inhibitory concentration (MIC) and adrenaline at 0.05 MIC and was shifted to the intensive care unit with stable hemodynamics.

The patient was extubated on the first postoperative day and was doing well. She had to be reintubated on the second postoperative day for cardiorespiratory arrest due to a PAH crisis (RVSP=70 mmHg). The PAH crisis was conservatively managed with milrinone infusion, sildenafil, and hyperventilation. The patient was extubated on the 13th postoperative day. In view of low saturation with poor respiratory efforts and left lung collapse consolidation, the patient required prolonged continuous nasal positive airway pressure support, which was gradually weaned off. The rest of the postoperative period was uneventful.

Echocardiography at discharge demonstrated aortic arch continuity without any gradient, unobstructed RPA flow, pulsatile flow in the abdominal aorta, mild tricuspid regurgitation, RVSP of 38 mmHg, good biventricular function, left ventricular ejection fraction of 60%, and no residual APW.

On the last follow-up at one year, the patient was asymptomatic with TTE findings correlating with discharge TTE.

DISCUSSION

Berry syndrome is a rare and complex malformation requiring prompt diagnosis and well-planned, timely surgical treatment to restore normal circulation distal to the IAA supplying the lower part of the body and for the prevention of pulmonary vascular obstructive disease.[1,5]

The clinical presentation is an excessive left-to-right shunt, and most patients present early in life. The development of pulmonary hypertension

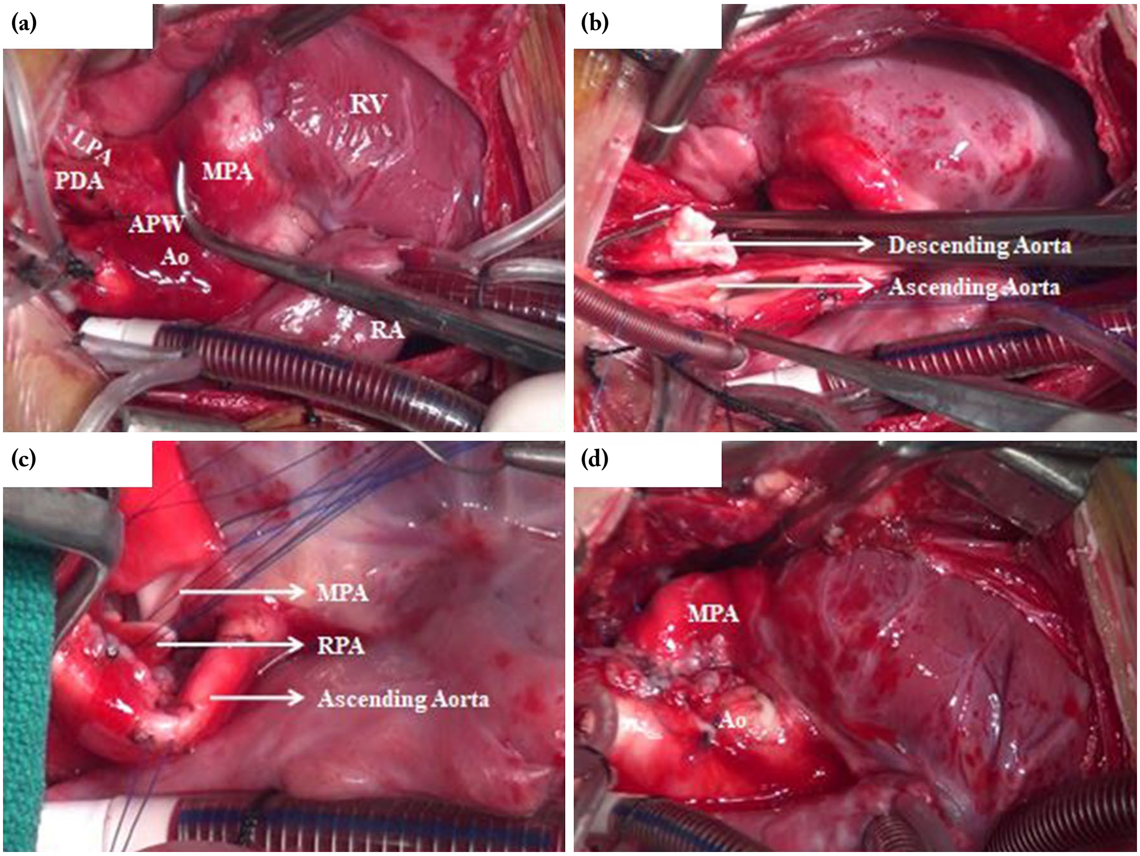

Figure 2. Operative image displaying **(a)** a large-sized APW and PDA; **(b)** mobilized descending aorta and ascending aorta; **(c)** anastomosis of the RPA to MPA; **(d)** the final picture after closure.

RV: Right ventricular; LPA: Left pulmonary artery; MPA: Main pulmonary artery; PDA: Patent ductus arteriosus; APW: Aortopulmonary window; Ao: Aorta; RPA: Right pulmonary artery.

and pulmonary vascular resistance is usually rapid. Fetal echocardiography and TTE are the mainstay of diagnosis in the prenatal and postnatal periods, respectively.[6] Cardiac catheterization provides anatomic details and assesses for pulmonary vascular obstructive disease.[1,2,5]

Single-stage surgery in the neonatal period and infancy is a widely accepted approach, although Ghelani et al.[6] suggested a staged repair in premature infants who present with excessive pulmonary shunts and congestive cardiac failure. In this category of patients, staged repair involves surgical pulmonary artery banding, followed by definitive surgical repair. Single-stage repair includes APW closure, anastomosis of the RPA to MPA, and maintaining the aortic arch continuity.[1] Postoperative PAH crisis is a known phenomenon that can be managed with pulmonary vasodilator therapy, in our case with milrinone infusion and sildenafil.[3]

In conclusion, Berry syndrome is an extremely rare aortopulmonary malformation that can be definitively diagnosed with prenatal fetal echocardiography and neonatal TTE, which warrants prompt and early surgical management. Surgical management can be tailored according to the patient presentation as staged or single-stage procedures. Postoperative PAH crisis is a known complication that can be successfully managed with pulmonary vasodilator therapy in most of the cases.

Patient Consent for Publication: A written informed consent was obtained from patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea, design, data collection and interpretation, literature review, writing the article, references, materials: M.W.A.; Data collection and processing: P.G.; Design, supervision, analysis, literature review, writing the article: S.M.H.; Supervision, critical review: N.D.

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Cardiovascular Surgery and Interventions

Case Report Open Access

Partial posterior leaflet resection for mitral valve endocarditis and valve repair with autologous pericardium

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ABSTRACT

Herein, we present a 55-year-old female who underwent a mitral valve repair procedure for mitral valve endocarditis. Multiple vegetations and leaflet tissues were surgically removed from the P1 and P2 scallops. The defect of the posterior leaflet was repaired using autologous pericardium. Rims of the pericardium supported three artificial chordae to obtain good mitral coaptation. The postoperative course was uneventful. The patient was discharged on the 30th postoperative day.

Keywords: Autologous pericardium, mitral endocarditis, valve repair.

Mitral valve endocarditis (MVE) is defined as the infection of the entirety or portion of one or both mitral valve leaflets. Age, shock, prosthetic valve endocarditis, reduced left ventricular function (ejection fraction <40%), and recurrent endocarditis are considered significant predictors of mortality. However, current evidence regarding the treatment and management strategy of MVE is not univocal and often based on personal experiences.[1] The timing and indications for surgical intervention to prevent systemic embolism in infective endocarditis remain controversial.[2] The rate of stroke is significantly higher during the first two weeks of antibiotic therapy and in those with left-sided infective endocarditis, particularly in the mitral position. The early involvement of an experienced cardiac surgeon is essential to determine the optimal surgical option and timing to provide the best outcome for patients with MVE. Surgical techniques are also controversial. Mitral valve repair can provide better long-and short-term survival.[3] The feasibility of valve repair depends on the extent of tissue destruction. If only one leaflet or scallop is involved, conservative surgery is possible. Herein, we report a case of posterior mitral leaflet endocarditis located on P2 and P1 scallops.

CASE REPORT

A 55-year-old female patient was admitted to our department with a high fever, fatigue, and dyspnea. Coxiella burnetii was yielded from repeated blood cultures. Multiple large (>10 mm) vegetations were found on the posterior mitral leaflet with moderate mitral regurgitation at transesophageal echocardiography (Figure 1a). Tetracycline 500 mg two times daily and vancomycin 2 g daily were administered. Surgical intervention was scheduled for two days later. Ascending aorta and bicaval cannulations were done. A superior septal approach was used for mitral valve exposure. Multiple large vegetations were found on the mitral P1 and P2 scallops (Figure 2a). Vegetations firmly adhered to the posterior leaflet. The P1 and P2 scallops were destructed during the removal of vegetations. Only the P3 segment of the posterior leaflet was free of endocarditis. The P1 and P2 scallops and the adhered chordae were resected. All infected tissues were removed (Figure 2b). The autologous pericardium was processed with 0.001% glutaraldehyde. Measurements were done on the debrided area, and the autologous pericardium was tailored slightly higher than those measurements. The pericardium

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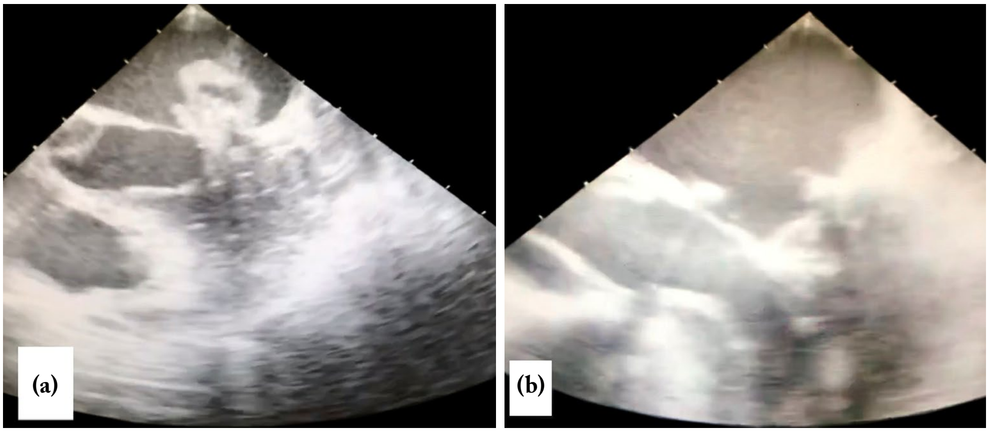


Figure 1. (a) Preoperative transesophageal echocardiography. Arrows indicate multiple large vegetations on the posterior leaflet. **(b)** Postoperative transesophageal echocardiography. Both mitral leaflets' movements and coaptation are good. Arrows indicate good leaflet coaptation and prosthetic ring materials.

was sutured to both the P3 scallop and the mitral annulus of the P1 and P2 scallops (Figure 3). Three artificial chordae were implanted on the sutured pericardium. Satisfactory coaptation was obtained by the saline test. A size 32 rigid ring was used for annular stabilization. The cross-clamp time and total perfusion time were 91 and 124 min, respectively. Mild degree mitral regurgitation was found at the early postoperative transesophageal echocardiograph examination (Figure 1b, Video 1). The postoperative course was uneventful. Vancomycin administration ceased at the end of the fourth postoperative week. The patient was discharged on the 30th postoperative day. Tetracycline therapy was extended to six weeks. The general condition of the patient was good, and the functional capacity was class I.

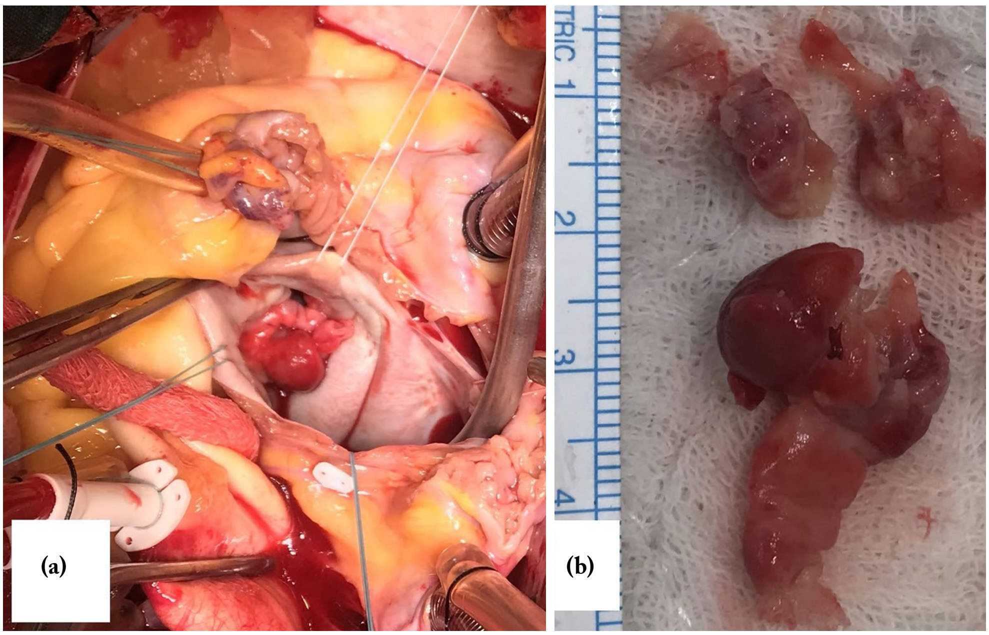


Figure 2. (a) Intraoperative view of the large vegetations located on the posterior mitral leaflet. **(b)** Intraoperative view of the multiple vegetations resected. The largest vegetation is 27×15 mm in size.

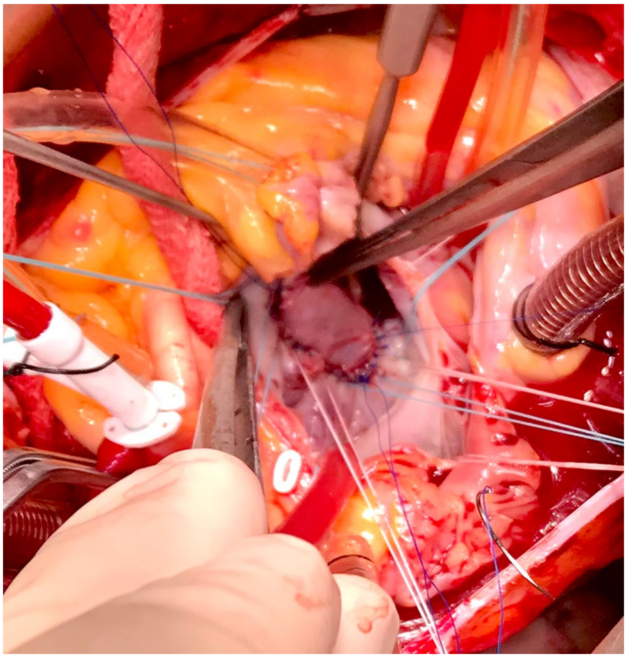
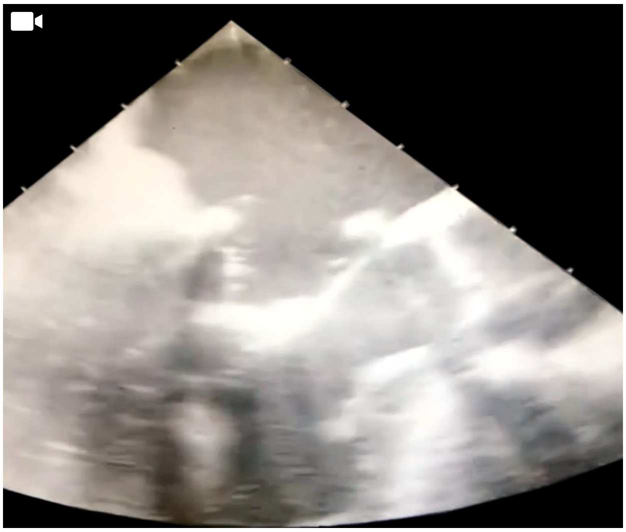


Figure 3. Intraoperative view of the resected P1 and P2 scallops and the glutaraldehyde-processed autologous pericardium sutured to repair the posterior leaflet defect.



Video 1. Early postoperative transesophageal echocardiographic examination revealing sufficient movement and coaptation in both leaflets.

DISCUSSION

The clinical presentation of *C. burnetii* infections (chronic Q fever) is insidious and lacks many of the typical features of subacute bacterial endocarditis. As a result, there is often a significant delay in diagnosis. Despite increasing awareness, recent studies demonstrate a mean delay of seven months from symptom onset to diagnosis. The majority of cases present with congestive heart failure due to valvular dysfunction. Unlike typical cases of endocarditis, fever is absent in a significant proportion and is frequently intermittent or low grade. Although embolic phenomena have been reported in up to one-third of cases, these are usually limited to advanced disease.[1,4] The incidence of infective endocarditis in the general population has ranged from 16 to 62 cases per million person-years.[4] Despite advances in diagnostic techniques and therapeutic strategies, infective endocarditis remains associated with substantial morbidity and mortality, with overall mortality rates for native and prosthetic valve endocarditis as high as 20 to 25%.[1-3] The timing of surgery is crucial for patients with native valve endocarditis. Delaying surgery often increases both the probability of complications (stroke/systemic embolization) and operative mortality. Unfortunately, most surgeons find that cardiologists or other hospitals refer patients with infective endocarditis after the failure of medical therapy, when patients are in intractable heart failure, or when patients have experienced extensive heart tissue damage. In a systematic review of the literature evaluating the morbidity and mortality of mitral valve repair compared to replacement in infective endocarditis, the repair group showed a significantly lower in-hospital mortality (2.3% *vs.* 14.4%) and a markedly better 10-year survival rate compared to the replacement group (long-term mortality, 7.8% *vs.* 40.5%).[3] Similarly, another review of the literature demonstrated better long-term event-free survival.[5,6] The goals of mitral valve repair are to remove the vegetation while restoring a proper line of coaptation on both leaflets to repair the leaflet if perforated and preserve the subvalvular apparatus. Excision of the vegetation can be performed along its cleavage plane on the leaflet. *En bloc* removal of the infective tissue is needed when the infection extends to the leaflet tissue. Extensive removal creates a large leaflet tissue defect. We have used glutaraldehyde-processed autologous pericardium to repair the P1 and P2 area. Three PTFE (polytetrafluorethylene) artificial chordae sutures were placed to obtain satisfactory coaptation. Nonbiological material usage is still controversial in endocarditis surgery. Nonetheless, recently published studies advocate that prosthetic materials can be used after an adequate debridement procedure.[6] We used a rigid prosthetic ring as we were sure that all infected tissues were completely removed.

In conclusion, the primary objective of valve endocarditis surgery is to start surgery before the development of an embolic process and remove all necrotic tissues and continue sufficient antibiotic therapy in the postoperative period.

Patient Consent for Publication: A written informed consent was obtained from the patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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