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ABOUT JOURNAL

Koşuyolu Heart Journal is a peer-reviewed, open access journal that has been published three times a year in April, August and December. This is the scientific journal of the Kartal Koşuyolu High Specialization Training and Research Hospital, (namely in Turkish, Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi, İstanbul, Türkiye).

The aim of the Koşuyolu Heart Journal; is to present advances in the field of cardiology, cardiovascular surgery, congenital cardiac surgery, and cardiovascular anesthesia to the readers. Koşuyolu Heart Journal publishes research articles, reviews, original case reports and images, letters, and critiques on cardiovascular medicine. The target reader population are the doctors specialized to the cardiovascular medicine. As an open access journal, all content is freely available.

Koşuyolu Heart Journal currently has an acceptance rate of 48%. The average time between submission and final decision is 30 days and the average time between acceptance and final printed publication is 60 weeks. However, provisional copy of submissions are published online within 1 month after acceptance.

Journal History

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EDITORIAL POLICIES

Aims and Scope

Koşuyolu Heart Journal aims to present advances in the field of cardiology, cardiovascular surgery, congenital heart surgery, and cardiovascular anesthesia to the readers. To achieve this goal, Koşuyolu Heart Journal will publish research articles (for the clinical or laboratory studies), reviews (by invitation only), case reports, original images, original techniques for cardiovascular surgery or cardiovascular interventions and letters/critiques on cardiovascular medicine. Koşuyolu Heart Journal publishes, after double blinded peer review, the articles for the target reader population consisting of cardiologists, cardiovascular surgeons and cardiac anesthesiologists. The official language of journal is either Turkish or English. Editorial and publication process of Koşuyolu Heart Journal are congruent with the standards of ICMJE, WAME, and COPE. Koşuyolu Heart Journal is an open access journal.

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The corresponding author must certify that their article is original, has not been published previously, and is not under consideration for publication by another journal. The corresponding author should affirm originality of the work in the Article Submission Form. If the work has been presented previously at a meeting as an oral or poster presentation, corresponding author must state the name, date and place of the meeting at the Title Page.

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Scope of the Journal

The Koşuyolu Heart Journal is published three times a year (april, august, and december). The journal accepts articles in English language. However, the articles have the titles and abstracts written in English and Turkish language. Terms written in another language should be indicated within quotation marks in articles.

All manuscripts submitted for publication should comply with Uniform Requirements for Manuscripts Submitted to Biomedical Journals produced and updated by the International Committee of Medical Journals Editors (http://www.icmje.org/).

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Example: Suárez De Lezo J, Medina A, Pan M, Romero M, Segura J, Pavlovic D, et al. Transcatheter occlusion of complex atrial septal defects. Catheter Cardiovasc Interv 2000;51:33-41.

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Example: Parsonnet V, Lean D, Bernstein AD. A method of uniform stratification of risk for evaluating the results of surgery in acquired adult heart disease. Circulation 1989;79(Suppl 1):S3-S12.

If the reference is a book;
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Example: Borrow K, Braunwald E. Heart Disease. 1st ed. Philadelphia, PA, USA: WB Saunders, 1988:976.

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CONTENTS / İÇİNDEKİLER

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CONTENTS / İÇİNDEKİLER

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New Predictors in Determining the Need for Invasive Treatment in NSTEMI During the COVID-19 Pandemic? A Retrospective Study

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ABSTRACT

Introduction: The non-invasive approach has become the first choice for the acute non-ST elevation myocardial infarction-acute coronary syndrome (NSTEMI-ACS) during the Coronavirus Disease-2019 (COVID-19) pandemic. However, most of these patients require interventional treatment. In this study, the possible role of hematological inflammatory markers in differentiating medium-high risk NSTEMI-ACS patients according to the GRACE risk classification in need of interventional treatment was investigated.

Patients and Methods: Patients who underwent coronary angiography with the diagnosis of NSTEMI-ACS in a tertiary cardiology clinic between January 2018 and December 2019 were included in the study, which was designed as a retrospective cohort study. NSTEMI-ACS patients (n= 276), except for patients with exclusion criteria (n= 32), were divided into two groups as those in need of invasive treatment (n= 217) and medical treatment (n= 59) according to the results of coronary angiography. The hematological inflammatory markers were compared between groups.

Results: Neutrophil to lymphocyte ratio (NLR) (AUC: 0.637, 95% CI: 0.563-0.712, p= 0.001) and systemic immune-inflammation index (SII) (AUC: 0.622, 95% CI: 0.545-0.699, p= 0.004) predicted the requirement of interventional treatment in NSTEMI-ACS.

Conclusion: It is unclear whether the NLR and SII elevation, which may be a predictor of the need for invasive treatment, is a cause or a consequence of the pathophysiological process in patients with NSTEMI-ACS. However, elevated NLR and SII values can help distinguish NSTEMI-ACS patients who need invasive treatment during the COVID-19 pandemic. The results of this study, show the need for large-sized studies to determine the ideal cut-off point of NLR and SII levels in determining the treatment strategy for NSTEMI-ACS.

Key Words: Non-ST elevation myocardial infarction; invasive treatment; neutrophil to lymphocyte ratio; systemic immune-inflammation index.

COVID-19 Pandemisi Sırasında NSTEMI Hastalarında İnvaziv Tedavi İhtiyacını Belirlemede Yeni Öngörücüler? Geriye Dönük Bir Çalışma

ÖZ

Giriş: Noninvaziv yaklaşım, "Coronavirus Disease-2019 (COVID-19)" pandemisi sırasında akut ST yükselmesiz miyokart infarktüsü-akut koroner sendrom (NSTEMI-AKS) için ilk seçenek haline gelmiştir. Ancak bu hastaların çoğu girişimsel tedaviye ihtiyaç duyar. Bu çalışmada, girişimsel tedaviye ihtiyaç duyan GRACE risk sınıflandırmasına göre orta-yüksek riskli NSTEMI-AKS hastalarını ayırt etmede hematolojik inflamatuvar belirteçlerin olası rolü araştırılmıştır.

Hastalar ve Yöntem: Geriye dönük kohort çalışması olarak tasarlanan çalışmaya Ocak 2018-Aralık 2019 tarihleri arasında üçüncü basamak kardiyoloji kliniğinde NSTEMI-AKS tanısı ile koroner anjiyografi yapılan hastalar dahil edilmiştir. AKS hastaları (n= 276), dışlama kriterleri olan hastalar (n= 32) dışındaki sonuçlara göre invaziv tedavi (n= 217) ve medikal tedavi (n= 59) olmak üzere iki gruba ayrılmıştır. Hematolojik inflamatuvar belirteçler gruplar arasında karşılaştırılmıştır.

Bulgular: Nötrofil lenfosit oranı (NLR) (EAA: 0.637, %95 CI: 0.563-0.712, p= 0.001) ve sistemik immün inflamasyon indeksi (SII) (EAA: 0.622, %95 CI: 0.545-0.699, p= 0.004) NSTEMI-AKS'de girişimsel tedavi gerekliliğini öngörmüştür.

Sonuç: İnvaziv tedavi ihtiyacının bir göstergesi olabilecek NLR ve SII yükselmesinin, NSTEMI-AKS'li hastalarda patofizyolojik sürecin bir nedeni mi yoksa bir sonucu mu olduğu açık değildir. Bununla birlikte,

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yüksek NLR ve SII değerleri, COVID-19 pandemisi sırasında invaziv tedaviye ihtiyaç duyan NSTEMI-AKS hastalarını ayırt etmeye yardımcı olabilir. Bu çalışmanın sonuçları, NSTEMI-AKS için tedavi stratejisini belirlemede NLR ve SII seviyelerinin ideal kesme noktasını belirlemek için büyük ölçekli çalışmalara olan ihtiyacı göstermektedir.

Anahtar Kelimeler: ST yükselmesiz miyokart infarktüsü; invaziv tedavi; nötrofil lenfosit oranı; sistemik immün inflamasyon indeksi.

INTRODUCTION

Non-ST elevation myocardial infarction-acute coronary syndrome (NSTEMI-ACS) is one of the cardiac emergencies where early diagnosis and treatment are important. In the guidelines, diagnostic coronary angiography is recommended within 24 hours at the latest in patients with NSTEMI-ACS[1]. However, in the national consensus statement published in the period of Coronavirus Disease-2019 (COVID-19), non-invasive treatment was recommended as an alternative therapy in patients with non-very high risk NSTEMI-ACS[2,3]. Unfortunately, risk scoring systems are not sufficient to differentiate these patients. Therefore, it is important to discover markers that can be used to differentiate NSTEMI-ACS patients with increased invasive treatment during the COVID-19 pandemic.

Inflammation plays an active role in the development and progression of atherosclerotic plaque in the coronary artery. It has been reported that coronary artery patients with severe atherosclerotic involvement and high mortality rates may be distinguished with the help of hematological markers closely related to inflammation[4,5]. To the best of our knowledge, there is a lack of literature on the correlation between the need for invasive treatment strategy and the hematological markers in patients diagnosed with NSTEMI-ACS.

In this study, the potential role of hematologic inflammatory markers in differentiating those requiring invasive treatment in patients with medium-high risk NSTEMI-ACS according to the Global Registry of Acute Coronary Events (GRACE) risk classification was investigated[6].

PATIENTS and METHODS

The study was designed as a retrospective cohort study. Study data were obtained from medical records. Between January 2018 and December 2019, patients treated with a diagnosis of NSTEMI-ACS in the cardiology clinic of a tertiary hospital were consecutively evaluated. NSTEMI-ACS was defined as ischemic chest pain with troponin-I levels > 0.01 ng/mL and non-ST segment elevation on 12-lead chest electrocardiography (ECG).

Inclusion criterias: Patients who do not have exclusion criteria and who underwent coronary angiography with the diagnosis of NSTEMI-ACS.

Exclusion criterias: Being under the age of 18, chest pain that persists despite medication, hemodynamic instability, fatal ventricular arrhythmias, and the presence of dynamic ST-T wave changes, heart failure (ejection fraction < 40), severe anemia, malignancy, sepsis, obesity [body mass index (BMI) > 30 kg/m^2], renal failure (glomerular filtration rate < 60 mL/min/1.73 m^2), chronic hematological disease, collagen tissue disease, moderate to severe hepatic failure, severe valvular heart disease, electrolyte disturbance, chronic anti-inflammatory drug use, history of chronic inflammatory disease, and a history of serious infection in the last month.

NSTEMI-ACS patients (n= 276), except for patients with exclusion criteria (n= 32), were divided into two groups as those in need of invasive treatment (n= 217) and medical treatment (n= 59) according to the results of coronary angiography (Figure 1).

BMI was calculated by dividing the weight in kilograms by the square of height in meters. GRACE risk scores for each patient at admission were calculated with the help of a computer program (http://www.outcomes-umassmed.org/grace). We admitted to the Clinicaltrials.gov with the aprotocol number 05.08.2020-2020/15/10 and we are waiting for approval.

Complete blood count parameters obtained from the blood taken during hospitalization using an automatic hematological analyzer (XN 3000; Sysmex Corp., Kobe, Japan) were obtained from the records. Among these parameters, hemoglobin, hematocrit, red cell distribution width (RDW), mean platelet volume (MPV), platelet distribution width (PDW), thrombocyte (P), white blood cells (WBC), immature granulocyte count (IGC), lymphocyte (L) and neutrophil (N) counts was recorded. The N/L ratio (NLR) was determined by dividing the N number by the L number. The P/L ratio (PLR) was determined by dividing the P number by the L number. Systemic Immune-inflammation Index (SII) was calculated using P x NLR formula[7]. Routine biochemical tests of each patient, were carried out the next morning after hospitalization, after 12 hours of fasting.

Two interventional cardiologists blinded to the study made angiographic assessments and calculated the Gensini score of each patient[8]. TIMI 0-1 flow in the coronary arteries on angiography was defined as complete occlusion.

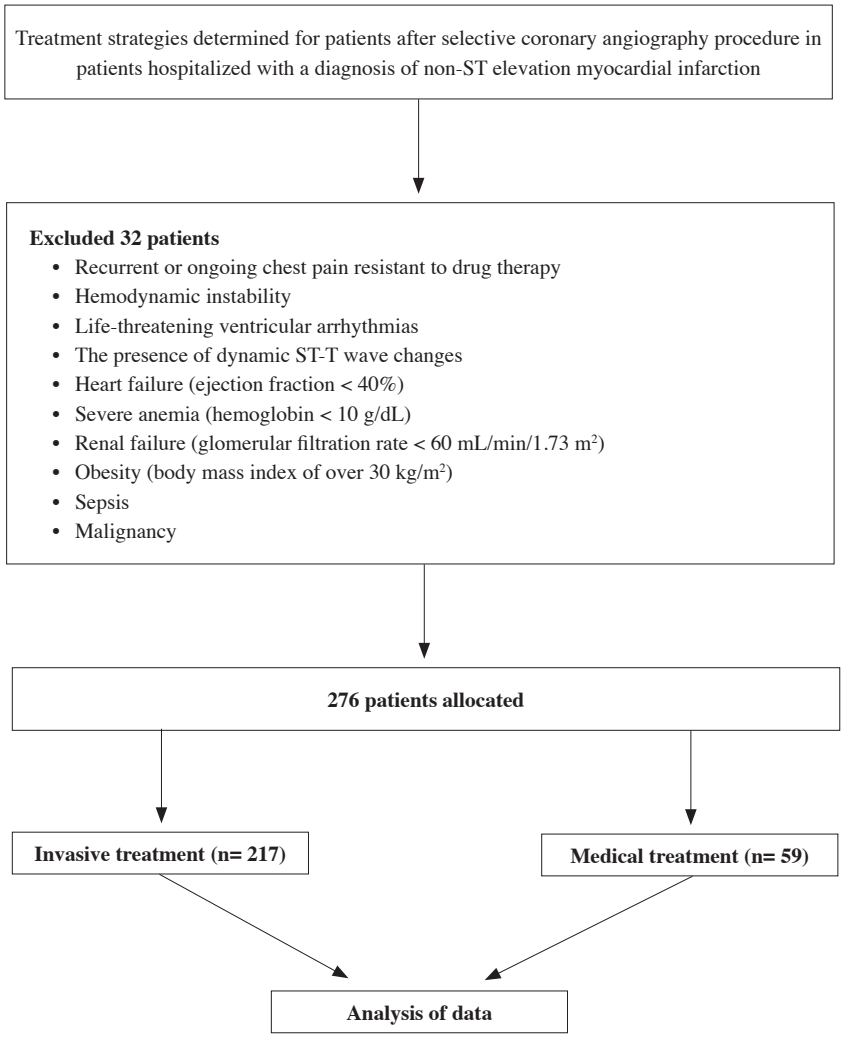

Figure 1. The enrollment of the study population was shown in flow chart.

All echocardiographic assessments were made in line with the recommendations of the guidelines by the American Heart Association[9].

Whether the continuous variables fit the normal distribution was evaluated using the Shapiro-Wilk test and histograms. Continuous variables were presented as mean and standard deviation, and as median (25^{th} percentile-75^{th} percentile) if they were not normally distributed. In the comparison between groups, Student's t-test was used in accordance with normal distribution, if not, the Mann-Whitney U test was used. Chi-square test or Fisher's exact test was used to compare categorical variables. The power of the parameters to predict the type of treatment or total occlusion was measured by receiver operating characteristic curves (ROC) calculations. The statistical significance limit was chosen as $p< 0.05$. All statistical calculations were carried out using SPSS v.23.

RESULTS

Participants were divided into two groups as an invasive treatment and medical treatment. Demographic data, comorbidities and the drugs they used were similar between the groups (Table 1).

The main concern in the study was the comparisons of markers that indicate inflammation between the two groups. There was a significant difference between the two groups in terms of WBC ($p< 0.001$), SII ($p= 0.004$), and NLR ($p= 0.004$) (Table 1). Multivariate analyses and ROC analyzes were performed to evaluate the predictive power of these parameters for invasive treatment. WBC, NLR, and SII were found to predict moderately invasive treatment in patients. It was observed that IGC values, which were found to be significantly higher in multivariate analysis, did not have predictive value in ROC analysis (Figure 2, Table 2, 3).

Table 1. Demographic and laboratory findings of patients in need of invasive and medical treatment strategies

	Treatment groups		
	Invasive treatment (n= 217)	**Medical treatment (n= 59)**	**p value**
Age (years) [mean ± SD (min-max)]	67.00 ± 12.56 (59-76)	68.44 ± 15.27 (60-80)	0.509[A]
Male/Female (gender)	69.6%/30.4% (n= 151/66)	54.2%/45.8% (n= 32/27)	***0.027***[C]
BMI (kg/m^2) [median (25%-75%)]	27.36 (26.5-28.2)	27.27 (26.8-28)	0.504[B]
Systolic TA (mmHg) [median (25%-75%)]	130 (125-135)	130 (125-135)	0.918[B]
Diastolic TA (mmHg) [median (25%-75%)]	72 (70-76)	74 (72-76)	0.184[B]
Hypertension	67.3% (n= 146/217)	64.4% (n= 38/59)	0.678[C]
Dyslipidemia	29.0% (n= 63/217)	27.1% (n= 16/59)	0.773[C]
DM	32.3% (n=70/217)	33.9% (n=20/59)	0.812[C]
GRACE score	120 (110-135)	122 (115-125)	0.385[B]
Gensini score	32 (16-44)	8 (4-12)	***< 0.001***[B]
ACE/ARBs	52.1% (n= 113/217)	59.3% (n= 35/217)	0.322[C]
Beta-blockers	43.8% (n= 95/217)	37.3% (n= 22/217)	0.371[C]
HCT [median (25%-75%)]	40.7% (36.8-43.9)	38.1% (35.45-42.65)	0.11[B]
CCB	25.3% (n= 55/217)	23.7% (n= 14/59)	0.799[C]
Statins	28.6% (n= 62/217)	27.1% (n= 16/59)	0.826[C]
OAD	30.4% (n= 66/217)	27.1% (n= 16/59)	0.623[C]
Insulin usage	12.9% (n= 28/217)	11.9% (n= 7/59)	0.832[C]
EF [median (25%-75%)]	55% (50-60)	55% (55-55)	0.591[B]
WBC (10^3/mm^3) [median (25%-75%)]	9.84 (8.33-11.79)	8.58 (7.17-10.21)	***< 0.001***[B]
IGC (/mm^3) [median (25%-75%)]	40 (20-55)	40 (20-60)	***0.648***[B]
RDW-CV [median (25%-75%)]	13.5% (12.9-14.8)	14 (13.25-14.9)	0.128[B]
MPV (fL) [median (25%-75%)]	10.4 (9.7-11.1)	10.2 (9.8-10.85)	0.247[B]
PDW [median (25%-75%)]	12.3% (11-13.6)	12.2 (11.2-13.75)	0.914[B]
SII [median (25%-75%)]	945.93 (602.15-1518.79)	738.79 (450.55-1085.98)	***0.004***[B]
NLR [median (25%-75%)]	3.71 (2.47-6.42)	2.72 (2.09-3.91)	***0.001***[B]
PLR [median (25%-75%)]	129.56 (96.36-187.24)	126.74 (19.44-552.02)	0.858[B]

A: p< 0.05 according to Student t-test.
B: p< 0.05 according to Mann-Whitney U test.
C: p< 0.05 according to Chi-square test.

TA: Blood pressure arterial, BMI: Body mass index, ACE/ARBs: Angiotensin converting enzyme inhibitors/Angiotensin receptor blockers, HCT: Hydrochlorotiazid, CCB: Calcium channel blockers, OAD: Oral antidiabetics, EF: Ejection fraction, WBC: White blood cell count, IGC: Immature granulocyte count, RDW: Relation of red cell distribution width, MPV: Mean platelet volume, PDW: Platelet distribution width, SII: Systemic immune-inflammation index, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio.

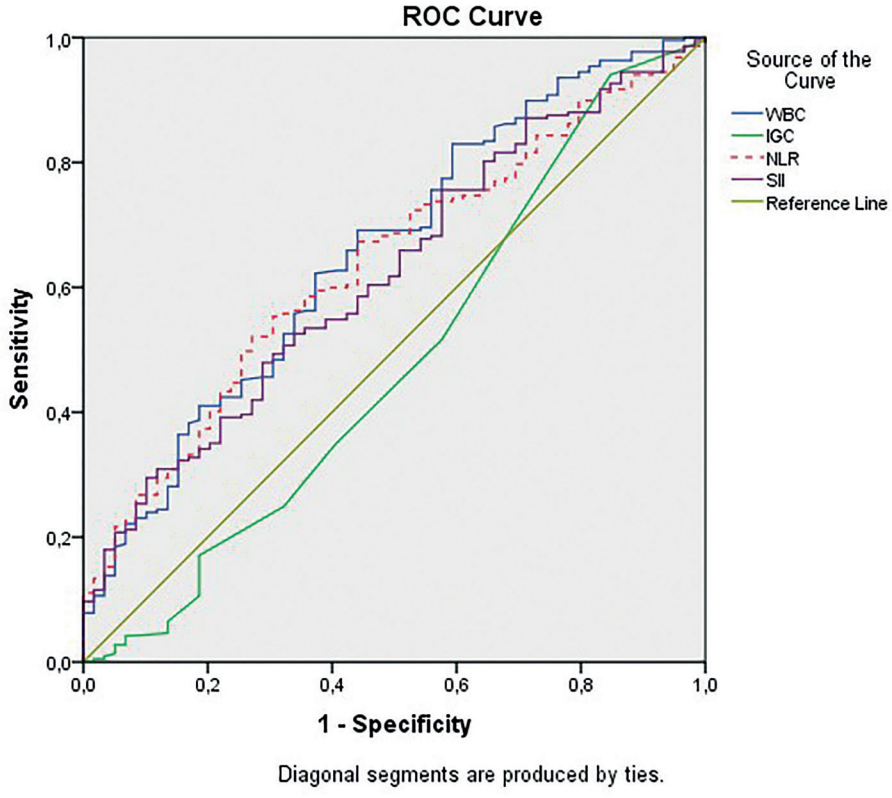

Figure 2. The relationship of WBC, IGC, NLR, and SII levels with the need for invasive treatment in NSTEMI-ACS.

Table 2. Multivariate analyses results of inflammatory markers for prediction of patients in need of invasive treatment strategies

				95% CI	
	Odds Ratio	B value	p value	Lower Bound	Upper Bound
WBC	0.915	10.373	***< 0.001****	9.996	10.749
NLR	0.351	5.792	***< 0.001****	4.855	6.729
IGC	0.986	10.471	***< 0.001****	10.321	10.620
SII	0.359	1426.354	***< 0.001****	1199.723	1652.986

WBC: White blood cell count, NLR: Neutrophil to lymphocyte ratio, IGC: Immature granulocyte count, SII: Systemic immune-inflammation index, CI: Coefficient Interval.
* The difference is statistically significant.

Table 3. ROC analyzes results of inflammatory markers for prediction of patients in need of invasive strategies

					Asymptotic 95% CI		
	ARUC	Cut-off value	Sensitivity (%)	Specificity (%)	Lower Bound	Upper Bound	p value
WBC (10^3/mm^3)	0.657	≥ 9	69.1	52.5	0.578	0.735	***< 0.001****
NLR	0.637	≥ 2.81	66.8	55.9	0.563	0.712	***0.001****
IGC (/mm^3)	0.481	≥ 35	51.6	42.4	0.391	0.571	0.245
SII	0.622	≥ 757.96	60.4	54.2	0.545	0.699	*0.004**

* p< 0.05
ARUC: Area under curve, WBC: White blood cell count, NLR: Neutrophil to lymphocyte ratio, IGC: Immature granulocyte count, SII: Systemic immune-inflammation index, CI: Coefficient interval.

DISCUSSION

This study demonstrated that a high SII value and a high NLR may be possible predictors of the need for invasive treatment in patients with NSTEMI-ACS.

Distinguishing NSTEMI-ACS patients who need invasive treatment from others may be important in terms of decreasing cardiovascular mortality, under COVID-19 pandemic conditions. In the literature, there is a lack of literature about the roles of inflammatory hematological markers with predictive properties for cardiovascular mortality in these patients.

One of the main mechanisms that play a role in increasing the tendency of the atheroma plaque to rupture is inflammation[10,11]. Leukocytosis, neutrophilia and lymphopenia have been reported to indicate a poor prognosis in ACS[12-14]. NLR, a potential inflammation biomarker, is a marker that provides information about the complex inflammatory activity in the vascular bed in NSTEMI-ACS[14]. In recent years, it has been reported that the number of immature granulocytes may be used as a prognostic indicator, especially in malignancies[15]. It has also been shown to predict high syntax score in patients with ACS[16].

Platelet activation is one of the main mechanisms involved in the etiopathogenesis of ACS. It has been reported that a high platelet count and a decreased lymphocyte count may be associated with a potential thrombotic state and increased inflammation[17]. Thrombocytosis, PLR, MPV, and PDW has also been reported to be associated with adverse cardiovascular events[18,19]. However, none of these parameters had a significant correlation with the invasive treatment method.

Recently, it has been reported that increased levels of SII, which was developed to evaluate the inflammatory and immune status of patients simultaneously, are associated with poor prognosis in cancer disease[9,20,21]. Also, in coronary patients undergoing percutaneous coronary intervention, it was observed that the high SII value predicts major cardiovascular events better than traditional risk factors[7].

This study is probably the first to investigate hematological markers of inflammation in distinguishing patients with NSTEMI-ACS who need invasive therapy. It is vital to differentiate these patients during the COVID-19 pandemic period when invasive treatment strategies cannot be applied to all patients. In this study, it was seen that high WBC, NLR value and SII moderately predicted the need for an invasive treatment strategy in the initial evaluation of NSTEMI-ACS patients.

Its main limitations are that the design of the study is retrospective and the study volume is not large. Especially the relatively smaller number of patients, for whom medical treatment decisions were made, might be a limitation. Another limitation is that the biomarkers commonly used for atherosclerosis were not used in this study.

CONCLUSION

It is unclear whether the NLR and SII elevation, which may be a predictor of the need for invasive treatment, is a cause or a consequence of the pathophysiological process in patients with NSTEMI-ACS. However, elevated NLR and SII values can help distinguish NSTEMI-ACS patients who need invasive treatment during the COVID-19 pandemic. The results of this study, show the need for large-sized studies to determine the ideal cut-off point of NLR and SII levels in determining the treatment strategy for NSTEMI-ACS.

Ethics Committee Approval: The research protocol in line with the Helsinki Declaration was approved by the local ethics committee (Approval Date: 05.08.2020; Protocol No: 2020/15/10).

Informed Consent: Due to the design of the study, consent to volunteer could not be obtained from the patients.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - EA, MB; Analysis/Interpretation - EA, DA, MB; Data Collection - EA, EÇ, BÖ; Writing - EA; Critical Revision - EA, DA, KG, AA; Final Approval - EA, AA; Statistical Analysis - DA, MB; Overall Responsibility - EA.

Conflict of Interest: The authors have no conflicts of interest to declare

Financial Disclosure: The authors declared that this study has received no financial support.

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Does Concomitant Tricuspid Annuloplasty Increase the Need for Permanent Pacemaker Implantation Following Mitral Valve Replacement?

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ABSTRACT

Introduction: This study compared the frequency of permanent pacemaker implantation (PPI) following mitral valve replacement (MVR) with tricuspid annuloplasty (TAP) and isolated MVR.

Patients and Methods: This retrospective study analysed 409 patients who had undergone MVR with or without concomitant TAP, from January 2015 through May 2020. Patients were divided into two groups (the isolated MVR group and the MVR plus TAP group). The two groups were compared according to whether PPI was present or not.

Results: A total of 409 consecutive patients [in the isolated MVR group, n= 212 patients; 129 (60.8%) female and in the MVR plus TAP group, n= 197 patients; 138 (70.1%) female] were assessed. The number of female, functional mitral regurgitation, mixed mitral disease, and the use of bio-prosthetic valve was higher in the MVR plus TAP group (p< 0.01). A total of 8 (2%) patients needed a PPI. There was no statistically significant difference between the two groups in terms of PPI (p> 0.01). The frequency of postoperative PPI was 2.2% (7 of 311 patients) in patients with rheumatic etiology and 1.1% (1 of 98 patients) in patients with non-rheumatic etiology (OR: 2.026, 95% CI: 0.24-16.68, p= 0.5). The median time to implantation was seven days [minimum postoperative days (POD) 5 , maximum POD 45].

Conclusion: When isolated MVR is considered and if the patient also has tricuspid regurgitation (TR), it is apparent that TAP will be inevitable, because TR inflicts a considerable burden on the patient's quality of life. Recent studies reported varying frequencies of PPI after TAP accompanying left valve surgery. The present study observed no increase in the use of PPI after MVR accompanied by TAP as compared with isolated MVR.

Key Words: Mitral valve replacement; tricuspid annuloplasty; permanent pacemaker implantation.

Mitral Kapak Replasmanına Eşlik Eden Triküspid Annuloplasti Kalıcı Pacemaker İhtiyacını Arttırır mı?

ÖZ

Giriş: Bu çalışmada, mitral valve replasmanı (MVR) ile birlikte triküspid annuloplasti (TAP) ve izole MVR sonrası kalıcı pacemaker implantasyonu (KPI) sıklığı karşılaştırılmıştır.

Hastalar ve Yöntem: Bu retrospektif çalışmada, Ocak 2015 tarihinden Mayıs 2020 tarihine kadar TAP ile birlikte MVR veya TAP olmadan MVR uygulanan 409 hasta analiz edilmiştir. Hastalar izole MVR ve MVR + TAP olarak iki gruba ayrılmıştır. İki grup KPI olup olmamasına göre karşılaştırılmıştır.

Bulgular: Çalışmada toplam 409 ardışık hasta [izole MVR grubu: 212 hasta, 129 (%60.8)'u kadın, MVR + TAP grubu: 197 hasta, 138 (%70.1)'i kadın] değerlendirilmiştir. Kadın hasta sayısı, fonksiyonel mitral yetmezliği ve biyoprotez kapak kullanımı MVR + TAP grubunda daha yüksek bulunmuştur (p< 0.01). Toplam 8 (%2) hastanın KPI'ya ihtiyacı olmuştur. İki grup arasında KPI açısından istatistiksel olarak anlamlı bir fark tespit edilmemiştir (p> 0.01). Romatizmal etiyolojisi olan hastalar için postoperatif KPI sıklığı %2.2 (311 hastanın yedisi), romatizmal olmayan etiyolojisi olan hastalar için %1.1 (98 hastadan biri) olarak saptanmıştır (OR= 2.026, %95 CI= 0.24-16.68, p= 0.5). Ortalama implantasyon süresi yedi gün olarak belirlenmiştir (minimum postoperatif beşinci gün, maksimum postoperatif 45. gün).

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Sonuç: İzole MVR düşünüldüğünde ve hastada triküspit yetmezliği varsa, triküspit yetmezliğinin hastanın yaşam kalitesine önemli bir yük getireceği için TAP'ın kaçınılmaz olacağı açıktır. Son çalışmalar, sol kapak cerrahisine eşlik eden TAP sonrası değişen sıklıklarda KPI bildirmişlerdir. Bu çalışmada, izole MVR'ye kıyasla TAP eşliğinde MVR sonrası KPI kullanımında artış gözlemlenmiştir.

Anahtar Kelimeler: Mitral kapak replasmanı; triküspid annuloplasti; kalıcı pacemaker implantasyonu.

INTRODUCTION

Permanent pacemaker implantation (PPI) is performed with frequencies of 5.6% and 7.9% after dual and triple valve replacements, respectively, leading to an increased risk of PPI requirement, as the number of valves replaced rises. Following valve surgeries, temporary pacemaker (TPA) is usually required[1]. PPI does not frequently appear to be necessary, which is 5% after cardiac surgery[2-5]. PPI is associated with a long period of mechanical ventilation, intensive care unit (ICU) stay and hospital stay[2-4]. Older age (> 60 years of age), male sex, emergency surgery and comorbidities such as diabetes mellitus (DM), heart failure and kidney injury were independent predictors for PPI[1].

PPI is more frequent following multiple valve surgeries[1,6]. Anterior mitral valve leaflet and septal tricuspid valve leaflet are in close proximity to the conduction systems, which can be damaged by surgical trauma[1,7].

The current study compared the frequency of PPI following mitral valve replacement (MVR) with tricuspid annuloplasty (TAP) and isolated MVR.

PATIENTS and METHODS

This retrospective study analysed 409 patients who had undergone MVR with or without concomitant TAP at the same centre, from January 2015 through May 2020. The data were retrieved from follow-up files and hospital records. A total of 409 consecutive patients who electively had undergone isolated MVR or MVR plus TAP were included into the study, being divided into two groups (the isolated MVR group n= 212 patients; and the MVR plus TAP group n= 197 patients). Additionally, the two groups were compared according to whether PPI was present or not.

The data included the demographics characteristics and past clinical history, types of surgery and specifics, pre- and post-operative electrocardiographic (ECG) features. Additionally, we followed up the patients who had PPI following surgery up to five years.

The exclusion criteria were: emergency surgery, mitral valve repair, pre-operative PPI, concomitant surgical ablation (such as maze procedures), concomitant other cardiac surgeries (coronary artery bypass grafting, aortic valve surgeries, aortic surgery or adult congenital surgeries), unstable cardiac condition and preoperative infective endocarditis.

Echocardiographic Evaluation

All patients underwent echocardiographic examination before and after the operation. The echocardiographic findings were evaluated by echocardiographic cardiologists. Mitral valve pathologies were assessed with respect to etiology (rheumatic or degenerative etiology). Tricuspid regurgitation was evaluated with color Doppler imaging to assess jet area by using parasternal short axis view, the right ventricular inflow view, and the apical four chamber view.

Outcomes and Follow-up

All patients were observed by echocardiographic examination, evaluation of ECG features, valve functions and the requirement of PPI in the postoperative period. The two groups were compared with respect to post-operative findings and long-term survival rates.

Surgical Procedure

All surgeries were performed using aortic arterial and bi-caval venous cannulations for cardiopulmonary bypass (CPB). Myocardial protection with mild hypothermia was achieved by intermittent antegrade cardioplegia and/or retrograde cardioplegia. While the mechanical prosthetic valve was the most commonly used material as the artificial valve, biological prosthetic valve replacement was performed in elderly patients or women considering pregnancy. Tricuspid annuloplasty was performed through the right atriotomy. The choice of the technique for TAP was left to the surgeons. When the ring annuloplasty was planned for tricuspid valve repair we used a 3D rigid tricuspid ring for all patients. During the postoperative period, warfarin was recommended as a life-long oral anticoagulant treatment to all patients with a mechanical prosthetic valve.

Statistical Analysis

Due to the inability of randomization with regard to tricuspid valve intervention, a propensity score (PS) was generated for

each patient from a multivariable logistic regression model based on preoperative and intraoperative covariates as independent variables with isolated MVR versus MVR via TAP as a binary dependent variable. Covariates included in the PS model were age, gender, DM, hypertension, chronic obstructive pulmonary disease, chronic kidney disease, severe pulmonary hypertension (PABs > 55 mmHg), LV dysfunction (ejection fraction < 45%) preoperative medications (beta-blockers, calcium canal blockers, digoxin, other antiarrhythmics) usage, etiology (degenerative, rheumatic, functional), mitral valve pathology (stenosis, regurgitation, mixt), pre-existing rhythm disturbance (atrial fibrillation or any other conduction disorders), and prosthetic valve type. Pairs of patients were derived nearest neighbour 1:1 matching with a calliper of a width of 0.2 SD of the logit of the PS. The quality of the match was assessed by comparing selected variables in PS-matched patients using the standardized mean difference, for this, an absolute standardized mean difference greater than 10% is proposed to represent a significant covariate imbalance. Matching was performed using the "MatchIt" package, and covariate balance was assessed using "cobalt", balance improvements presented using the "love.plot" command. Categorical variables were presented as counts and frequencies; continuous variables as mean (Standard deviation, SD) or median (Interquartile range, IQR) as appropriate. The Chi-square test or the Fisher's exact test was used for comparison between categorical variables. The Student t-test or Mann-Whitney U test was used to compare continuous variables. A two-tailed p value of 0.05 was considered statistically significant. R Statistical Software (version 3.6.3; R Foundation for Statistical Computing, Vienna, Austria) was used for all statistical analysis[8-10].

RESULTS

A total of 409 consecutive patients [in the isolated MVR group: 212 patients; 129 (60.8%) female and in the MVR plus TAP group: 197 patients; 138 (70.1%) female) were assessed. Thirty-nine patients (18.4%) were > 65 years of age in the isolated MVR group, 38 (19.3%) patients were > 65 years age in the MVR plus TAP group (p= 0.81). Patients were stratified according to the presence or absence of TAP. Severe pulmonary hypertension, degenerative mitral disease, regurgitation and stenosis were more pronounced in the isolated MVR group (p< 0.01). The number of women, functional MR, mixed mitral disease, the use of bio-prosthetic valve were higher in the MVR plus TAP group (p< 0.01). After PS matching, the two groups of 120 patients were obtained. Balance improvement after the propensity match is illustrated in Figure 1.

The two groups were comparable for all pre-treatment variables after being matched. Table 1 shows the variables of the patients.

Postoperative TPM was warranted in 95 patients (23%). There was no statistically significant difference between the two groups in terms of TPM and in the PS matched population (p> 0.01). A total of 8 patients (four patients in the isolated MVR group, four patients in the MVR plus TAP group) needed PPI (2%). The frequency of postoperative PPI was 2.2% (7 of 311 patients) in patients with rheumatic etiology and 1.1% (1 of 98 patients) in patients with non-rheumatic etiology (OR: 2.026, 95% CI: 0.24-16.68, p= 0.5) (Table 2).

PPI was implanted in 6 of 8 patients due to a complete AV block. The time to median implantation was 7 days [minimum postoperative days (POD) 5, maximum POD 45]. The PPI and TPM data are presented in Table 3.

DISCUSSION

PPI requirement following heart operation is associated with increased rate of morbidity, longer hospital stay and higher costs[1,11]. We examined whether concomitant TAP increases the frequency for PPI following MVR. Functional MR, mixed mitral disease, the use of bio-prosthetic valve and the number of female patients were higher in the MVR plus TAP group. The frequency of postoperative PPI was 2% and there were no difference between the groups with respect to etiology. Of eight patients who underwent PPI, six had a complete AV block. The two groups showed no statistically significant difference with respect to PPI. Moreover, patients in the two groups who underwent PPI showed no difference with respect to etiology.

The frequency of PPI was about 7% in patients undergoing aortic valve replacement and was about 4% in patients undergoing MVR and 21% in patients undergoing tricuspid valve operations (replacement or repair)[11-14]. Jouan et al. found that the incidence of PPI was 2.6% following isolated MV repair[15]. The current study showed that the frequency of PPI was 2% following MVR with/without TAP. There was no between-group difference at the follow up at five years.

Several studies reported that female gender and older age (> 75 years) were predictive risk factors for PPI[16-18]. However, some studies showed no difference in the frequency of PPI in two sexes, which is consistent with our findings[18]. The preoperative arrhythmia, conduction disturbances and chronic comorbidities were linked to an elevated risk for PPI, which occurred within 30 days after operation[19]. We found

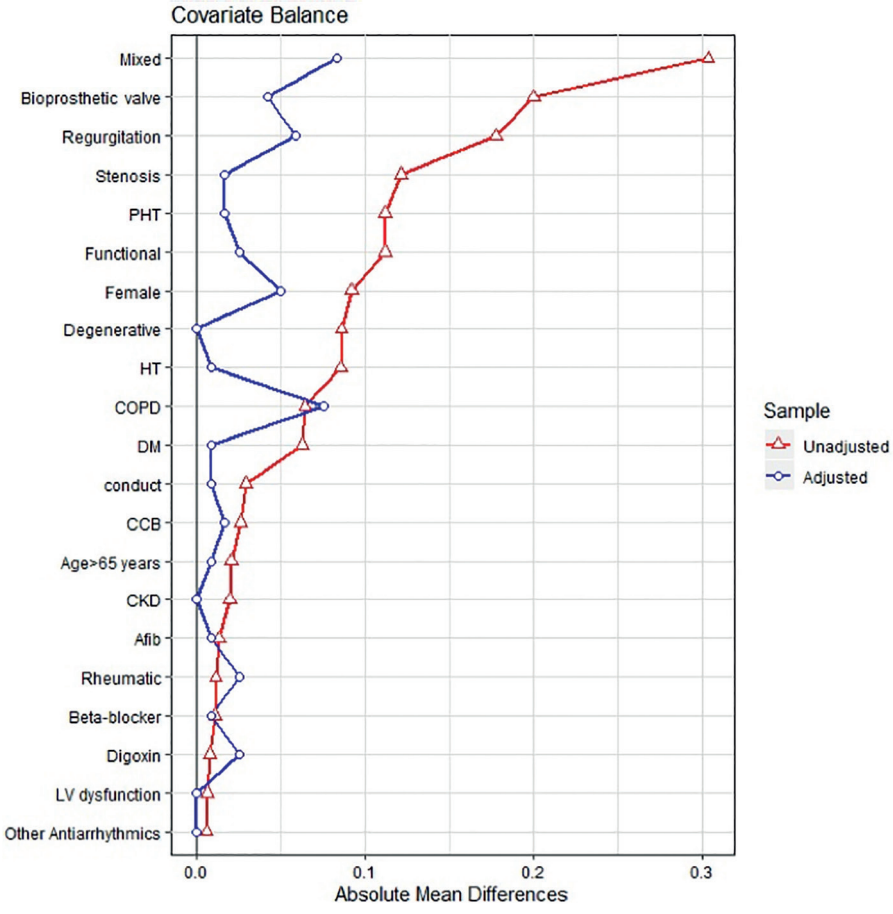

Figure 1. Balance improvements for baseline variables before and after propensity matching.

Pulmonary hypertension (PHT): Severe pulmonary hypertension (PABs > 55 mmHg), HT: Hypertension, COPD: Chronic obstructive pulmonary disease, DM: Diabetes mellitus, CCB: Calcium channel blockers, CKD: Chronic kidney disease, Conduct: Any other conduction disorders, Afib: Atrial fibrillation, LV Dysfunction: Left ventricular dysfunction, ejection fraction < 45%.

that advanced age (> 65 years of age) and gender showed no difference between the two groups.

Several studies reported that preoperative conduction disorders such as right or left bundle branch block and first-degree AV block or left anterior fascicular block warranted PPI[11,17]. The presence of bradycardia further increases the risk for PPI[20,21]. Of eight patients who underwent PPI, six had a complete AV block in this study.

Operative trauma to conduction system has been shown to bring about PPI, posing a risk factor for conduction disorders associated with AV node[20-23]. Following aortic, mitral and tricuspid valve surgeries, PPI are more widely mandated[5,24]. Ghamdi et al. showed that prolonged CBP and cross-clamping time raised the risk for PPI[18]. Chronic kidney disease was linked to conduction disturbances and atrial fibrillation based on pathological myocardial remodelling and fibrosis[25,26]. Jouan et al. showed that prolonged cross clamping time and TAP were independent predictors for conduction disorders, unlike our findings[15]. PPI was an increased risk factor for mitral valve surgery with concomitant TAP different from our findings. The frequency of PPI was higher in tricuspid valve replacement than in aortic and mitral valve replacements[12,27].

The European Society of Cardiology guideline recommends an observation of seven days for AV block and from five days to several weeks for sinoatrial dysfunction after cardiac surgery prior to PPI[28,29]. Permanent pacemaker was reported to be implanted at day five postoperatively after valve surgery[28]. However, Jouan et al. recommended that, prior to performing PPI, patients should be observed up to 14 days following mitral valve surgery with TAP[15]. In this study, PPI was implanted, on overage, on the 7th postoperative day (ranging from 5 to 45 days postoperatively). In early

Table 1. Baseline characteristics of study population

	Before Match			After Match				
Variables	**Isolated MVR**	**MVR + TAP**	**p value**	**Isolated MVR**	**MVR + TAP**	**p value**	**Before**	**After**
Number of patients	212	197		120	120			
Female gender, n (%)	129 (60.8)	138 (70.1)	0.02	84 (70.0)	78 (65.0)	0.4	0.092	-0.05
Age > 65 years, n (%)	39 (18.4)	38 (19.3)	0.81	70 (58.3)	71 (59.2)	0.89	-0.05	0.0083
DM, n (%)	94 (44.3)	75 (38.1)	0.19	51 (42.5)	52 (43.3)	0.86	-0.0627	0.0083
COPD, n (%)	89 (42.0)	70 (35.5)	0.18	43 (35.8)	52 (43.3)	0.235	-0.0645	0.075
HT, n (%)	27 (12.7)	42 (21.3)	0.02	19 (15.8)	20 (16.7)	0.86	0.0858	0.0083
CKD, n (%)	12 (5.7)	15 (7.6)	0.42	6 (5)	6 (5)	1	0.0195	0
PHT, n (%)	84 (39.6)	56 (28.4)	0.01	36 (30.0)	38 (31.7)	0.78	-0.112	0.0167
LV dysfunction, n (%)	3 (1.4)	4 (2.0)	63	2 (1.7)	2 (1.7)	1	0.0062	0
Beta-blocker, n (%)	144 (67.9)	136 (69.0)	0.8	85 (70.8)	84 (70.0)	0.88	0.0111	-0.0083
CCB, n (%)	27 (12.7)	20 (10.2)	0.41	15 (12.5)	13 (10.8)	0.68	-0.0258	-0.0167
Digoxine, n (%)	20 (9.4)	17 (8.6)	0.88	15 (12.5)	12 (10)	0.54	-0.008	-0.025
Other antiarrhythmics, n (%)	12 (5.7)	10 (5.1)	0.79	8 (6.7)	8 (6.7)	1	-0.0058	0
Rheumatic, n (%)	166 (78.3)	152 (77.2)	0.78	99 (82.5)	96 (80)	0.62	-0.0114	-0.025
Degenerative, n (%)	29 (13.7)	10 (5.1)	0.004	8 (6.7)	8 (6.7)	1	-0.086	0
Functional, n (%)	14 (6.6)	35 (17.8)	0.001	13 (10.8)	16 (13.3)	0.55	0.1116	0.025
Regurgitation, n (%)	127 (59.9)	79 (40.1)	0.001	70 (58.3)	63 (52.5)	0.36	-0.1777	-0.0583
Stenosis, n (%)	58 (27.4)	20 (10.2)	0.001	24 (20)	22 (18.3)	0.74	-0.1213	-0.0167
Mixed, n (%)	25 (11.8)	98 (49.7)	0.001	25 (20.8)	35 (29.2)	0.13	0.3034	0.0833
Afib, n (%)	19 (9.0)	15 (7.6)	0.62	10 (8.3)	9 (7.5)	0.81	-0.0135	-0.0083
Other conduction disorders, n (%)	11 (5.2)	16 (8.1)	0.233	10 (8.3)	11 (9.2)	0.81	0.0293	0.0083
Bioprosthetic valve, n (%)	34 (16.0)	71 (36.0)	0.001	30 (25)	25 (29.2)	0.46	0.2	0.0417

MVR: Mitral valve replacement, TAP: Tricuspid annuloplasty, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, HT: Hyperytension, CKD: Chronic kidney disease, PHT: Pulmonary hypertension, LV: Left ventricle, CCB: Calcium channel blocker, Afib: Atrial fibrillation.

Table 2. Postoperative PPI and TPM requirements according to the type of operation in the overall study cohort and PS-matched population

	Unmatched (n= 409)	**MVR (n= 212)**	**MVR + TAP (n= 197)**	**p value**	**Matched (n= 240)**	**MVR (n= 120)**	**MVR + TAP (n= 120)**
PPI, n (%)	8 (2)	4 (1.9)	4 (2.0)	0.36	4 (2.1)	2 (1.7)	3 (2.5)
TPM, n (%)	95 (23.2)	46 (21.7)	49 (24.9)	0.44	55 (22.9)	26 (21.7)	29 (24.2)

MVR: Mitral valve replacement, TAP: Tricuspid annuloplasty, PPI: Permanent pacemaker implantation, TPM: Temporary pacemaker, PS: Propensity score.

postoperative period TPM was warranted in 23% of patients. However, after postoperative seven days, PPI was required in 2% of patients, of whom fourwere in the isolated MVR group and four in the MVR plus TAP group. The two group did not differ with respect to PPI.

Jouan et al. showed that requirement for PPI was enhanced after concomitant TAP, different from our results[15]. Jokinen and collogues followed up 136 consecutive patients undergoing tricuspid valve operations for nearly eight years and they reported that PPI may prevent from fatal bradyarrhythmia following tricuspid surgery in the long term follow-up. However, PPI appears to have a risk for endocarditis and thromboembolic complications[14]. Several studies examined TAP with left sided valve surgeries and found that concomitant

Table 3. The PPI and TPM data presentation

Patients	Age (years)	Sex	Pathology	Operation	Indication for PPI	Postoperative day of PPI
1	48	F	Rheumatic-Stenosis	MVR (mechanical)	3rd degree AV block	5
2	37	F	Rheumatic-Stenosis	MVR (mechanical)	3rd degree AV block	8
3	48	F	Functional-Regurgitation	MVR (mechanical) + Tricuspid ring annuloplasty	3rd degree AV block	7
4	64	F	Rheumatic-Stenosis	MVR (mechanical)	3rd degree AV block	5
5	54	M	Rheumatic-Regurgitation	MVR (mechanical) + Tricuspid de vega annuloplasty	2nd degree AV block	45
6	35	M	Rheumatic-Regurgitation	MVR (mechanical)	3rd degree AV block	5
7	55	F	Rheumatic-Stenosis	MVR (mechanical) + Tricuspid ring annuloplasty	3rd degree AV block	24
8	55	F	Rheumatic-Regurgitation	MVR (bioprotesis) + Tricuspid ring annuloplasty	2nd degree AV block	27

PPI: Permanent pacemaker implantation, TPM: Temporary pacemaker, F: Female, M: Male, MVR: Mitral valve replacement, AV block: Atrioventricular block.

TAP with left sided surgeries did not increase the incidence of PPI or other morbidities such as bleeding, low cardiac output syndrome and kidney diseases[30,31]. We found no difference in the frequency of PPI between the two groups.

It is vital to protect patients from adverse effects of late TR, because it is known that elevated TR is associated with increased morbidity and mortality following mitral valve surgery[32,33].

CONCLUSION

When isolated MVR is considered and if the patient also has TR, it is apparent that TAP would be inevitable, because TR inflicts a considerable burden on the patient's quality of life. Recent studies reported varying frequencies of PPI after TAP accompanying left valve surgery. This study did not observe an increased use of PPI after MVR operations accompanied by TAP as compared with isolated MVR operations.

STUDY LIMITATIONS

There are many limitations in this study because, it has a retrospective design and included observational data from a single-center with a relatively small cohort and short follow up period. Further prospective and multi-center studies are needed to clarify the frequency for PPI following MVR plus TAP.

Ethics Committee Approval: This study was approved by Kartal Kosuyolu High Specialization Training and Research Hospital, Clinic of Cardiovascular Surgery Ethics Committee (2020/8/358).

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - RA, DÇ; Analysis/Interpretation - ES, VB; Data Collection - AK, ÜY, FB; Writing - RA, ES; Critical Revision - MR; Final Approval - RA; Statistical Analysis - ES; Overall Responsibility - RA, MR.

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Determination of Predictors of Acute Kidney Injury in Patients with Coronary Bifurcation Lesions Revascularized with the Two-Stent Strategy

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ABSTRACT

Introduction: Acute kidney injury (AKI) is an important complication that increases mortality, morbidity, hospitalization and costs after the invasive cardiac procedures. The incidence of AKI and the factors affecting the development of AKI after the revascularization of coronary bifurcation lesions with the two-stent strategy remain unclear.

Patients and Methods: We retrospectively evaluated 230 consecutive non-ST elevation myocardial infarction (NSTEMI) patients who underwent revascularization with the two-stent strategy for the true coronary artery bifurcation lesions between January 2015 and September 2020, and did not meet the exclusion criteria. AKI was defined as meeting Acute Kidney Injury Network (AKIN) group criteria with the development of creatinine changes within the first 48 hours after the procedure. ACEF (age, serum creatinine, left ventricular ejection fraction) score was calculated for all patients.

Results: AKI developed in 28 (12.2%) patients after the procedure. As a result of the multivariable analysis, hypertension, ACEF score ≥ 1.14 and contrast agent volume ≥ 252 mL were determined as independent predictors for AKI. The coronary anatomical factors and technique related factors had no effect on AKI development. ACEF score ≥ 1.14 had sensitivity of 82.1%, specificity of 60.9% and negative predictive value of 96.1% for detecting AKI development. Moreover, the rate of AKI in the group with high ACEF score was significantly higher than the group with low ACEF score (22.5% vs. 3.9%, p< 0.001).

Conclusion: The simple and extremely user-friendly ACEF score can accurately describe the risk of AKI development after the revascularization of coronary bifurcation lesions with the two-stent strategy.

Key Words: ACEF score; acute kidney injury; coronary bifurcation.

İki-Stent Stratejisi ile Revaskülarize Edilen Koroner Bifurkasyon Lezyona Sahip Hastalarda Akut Böbrek Hasarı Prediktörlerinin Belirlenmesi

ÖZ

Giriş: Akut böbrek hasarı (ABH) kardiyak invaziv girişimler sonrası mortalite, morbidite, hastanede kalış süresi ve maliyeti arttıran önemli bir komplikasyondur. İki-stent stratejisi ile revaskülarize edilen koroner bifurkasyon lezyonları sonrası görülme sıklığı ve ABH gelişimini etkileyen faktörler belirsizliğini korumaktadır.

Hastalar ve Yöntem: Çalışmada Ocak 2015-Eylül 2020 tarihleri arasında kurumumuzda gerçek koroner arter bifurkasyon lezyonlarına iki-stent stratejisi ile revaskülarizasyon uygulanan ve dışlama kriterlerini karşılamayan 230 ardışık non-ST elevasyonlu miyokart infarktüsü (NSTEMI) hastası retrospektif olarak incelenmiştir. ABH, işlem sonrası ilk 48 saat içinde kreatinin değişikliklerinin ortaya çıkması ile "Acute Kidney Injury Network (AKIN)" grubu kriterlerinin karşılanması olarak tanımlanmıştır. Tüm hastalar için ACEF (yaş, serum kreatinin, sol ventrikül ejeksiyon fraksiyonu) skoru hesaplanmıştır.

Bulgular: İşlem sonrası hastaların 28 (%12.2)'inde ABH gelişmiştir. Yapılan çok değişkenli analiz sonucunda hipertansiyon, ACEF skoru ≥ 1.14 ve kontrast volümü ≥ 252 mL ABH için bağımsız prediktörler olarak saptanmıştır. Koroner anatomiye dair faktörlerin ve teknik ile ilişkili faktörlerin ise ABH üzerine herhangi bir etkisi bulunamamıştır. ACEF skoru 1.14 değerinin üstünde %82.1 duyarlılık, %60.9 özgüllük ve %96.1 negatif prediktif değeri ile ABH gelişimini tespit etmiştir. Ayrıca yüksek ACEF skoru olan grupta ABH oranı, düşük ACEF skoru olan gruba göre anlamlı düzeyde daha yüksek bulunmuştur (%22.5'e karşın %3.9, p< 0.001).

Sonuç: Basit ve son derece kullanıcı dostu ACEF skoru, iki-stent stratejisi ile revaskülarize edilen koroner bifurkasyon lezyonları sonrası ABH gelişme riskini doğru bir şekilde tanımlayabilir.

Anahtar Kelimeler: ACEF skoru; akut böbrek hasarı; koroner bifurkasyon.

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INTRODUCTION

Acute kidney injury (AKI) which commonly occurs after the percutaneous coronary intervention (PCI), is the third leading cause of hospital-acquired renal failure[1,2]. AKI has been associated with important adverse effects such as longer hospitalization, permanent renal failure, need for dialysis, increased risk of mortality, and recurrent ischemic events[3-5]. It is important to predict the patients who may develop AKI, in terms of taking necessary precautions.

Coronary bifurcation lesions represent a particularly challenging lesion subgroup for PCI. Although the current recommendation is a temporary side branch stenting strategy, a number of coronary bifurcation lesions require treatment of both the side branch and the main branch[6-9]. The two-stent strategy applied to the coronary bifurcation lesion leads longer operation durations and higher contrast agent volume when compared to the standard PCI procedure. Although it is assumed that this situation will increase the risk of AKI development, the incidence of AKI after the procedure and the factors affecting the development of AKI in patients with bifurcation lesions treated with the two-stent strategy still remain unclear.

This study aimed to investigate the effect of anatomical factors, technique-related factors and ACEF (age, serum creatinine, left ventricular ejection fraction) score on AKI development in patients with non-ST elevation myocardial infarction (NSTEMI) who underwent revascularization with two-stent strategy to true coronary artery bifurcation lesions.

PATIENTS and METHODS

Study Population

In this retrospective study, all consecutive NSTEMI patients who underwent revascularization with a two-stent strategy for true coronary artery bifurcation lesions at our institution between January 2015 and September 2020 and did not meet the exclusion criteria, were included. A true coronary bifurcation lesion was described as stenosis of > 50% in both the main branch and the ostium of the side branch according to Medina classification (1,1,1; 1,0,1; 0,1,1)[10]. Patients on dialysis, patients with ST elevation in the last 48 hours, cardiogenic shock, Killip 3-4, intense thrombus burden, and patients with missing data that would interfere with ACEF score calculation and AKI detection were excluded from the study. After exclusion, a total of 230 patients (179 males, 51 females; mean age 59.3 ± 10.8 years) were accepted as the study population. The study was approved by the local ethics committee (date: January 26 2021; decision no: 2021/01) and was conducted in accordance with the requirements of the Declaration of Helsinki.

Stent Implantation Procedure

The coronary procedures were performed from femoral approach by using 6-Fr or 7-Fr diagnostic and guiding catheters. All patients received loading doses of acetylsalicylic acid (300 mg) and clopidogrel (300 to 600 mg) or ticagrelor (180 mg) before or during the procedure. Dual antiplatelet therapy was given for at least 12 months (acetylsalicylic acid: 100 mg once daily and clopidogrel: 75 mg once daily or ticagrelor: 90 mg twice daily). Glycoprotein IIb/IIIa inhibitors (GPI) were used according to the the operator's decision. Unfractionated heparin was administered as an intravenous bolus at a dose of 50-70 U/kg with GPI and 70-100 U/kg without GPI. All the technical choices during the stenting procedure were decided by the operator. Intravascular ultrasound was not used routinely. Angiographic success was defined as achieving Thrombolysis In Myocardial Infarction (TIMI) 3 flow with < 30% final residual stenosis for the main branch and < 50% for the side branch.

Data Collection and Definitions

Patients' intensive care and inpatient clinic follow-up files and digital records in the hospital information system were retrospectively examined. Age, gender, co-morbidities, smoking status, pre- and post-procedural laboratory results, echocardiographic parameters, procedure date, procedure duration, stenting technique, length and size of the stents, and the amount of contrast agent were recorded. In addition, the SYNTAX score and ACEF score: Age/Left ventricular ejection fraction (%) + 1 (if serum creatinine ≥ 2.0 mg/dL) based on the original study conducted by Ranucci et al. were calculated for all patients[11].

Co-morbidities were defined as follows: Diabetes mellitus (DM) as a recent use of insulin or antidiabetic drugs, fasting blood glucose value ≥ 126 mg/dL and/or HbA1c 6.5%, hypertension (HT) as a recent use of antihypertensive drugs, systolic blood pressure 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, hyperlipidemia (HL) as a recent use of cholesterol-lowering drugs and/or low-density lipoprotein cholesterol (LDL-C) value 140 mg/dL, peripheral artery disease as a previous peripheral artery revascularization, presence of lower extremity claudication with arterial disease detected on doppler ultrasound, cerebrovascular disease (CVA) ischemic stroke or history of transient ischemic attack.

End-point

The primary end-point of the study was the development of AKI after contrast agent administration, without any other possible etiology. The definition of AKI was a raise

of 0.3 mg/dL or 50% in post-procedure (24-72 h) creatinine compared to baseline, proposed by the Acute Kidney Injury Network (AKIN) as a standardized definition of AKI[12].

Statistical Analysis

Data was analyzed using the Statistical Package for the Social Sciences, version 24.0 (SPSS Inc., Chicago, Illinois, USA). Whether the variables show normal distribution; visual (histograms, probability curves) and analytical methods (Kolmogorov-Smirnov or Shapiro-Wilk) were evaluated. Numerical variables showing normal distribution were mean ± standard deviation (SD), numerical variables not showing normal distribution were expressed as median (interquartile range) and categorical variables as percentage (%). Numerical variables were evaluated using Student t-tests and the Mann-Whitney U test between the two groups. Chi-quare or Fisher exact test were used to compare categorical variables. In order to determine the independent predictors of AKI, univariate logistic regression analysis was performed which was followed by a multivariate logistic regression analysis with the parameters found to be significant in univariate analysis. Receiver operating characteristic (ROC) curves and Youden index [max (sensitivity + selectivity-1)] were used to determine the cut-off values of parameters such as ACEF score, and the area under the ROC curve > 0.5 and p value < 0.05 were considered as statistically significant.

RESULTS

A total of 230 patients' mean age was 59.3 ± 10.8 years. 179 (77.8%) of the patients were male and 51 (22.2%) were female. Ninety-two (40.0%) patients were revascularized by T-stenting, 57 (24.8%) patients by culotte stenting, and 81 (35.2%) patients by crush stenting technique. AKI developed in 28 (12.2%) patients after the procedure. The comparison of patient groups with and without AKI in terms of basic characteristics was presented in Table 1. Patients in the AKI (+) group were older, and the rates of DM and HT were higher in the AKI (+) group. Left ventricular ejection fractions (LVEF) were lower and fluoroscopy durations were higher. In addition, contrast agent volume usage during the procedure was higher in these patients compared to patients in the AKI (-) group. On the other hand, ACEF score median values were also found to be significantly higher in the AKI (+) group (Figure 1). In Figure 2, patients were grouped according to stent strategies, and there was no significant difference between T-stenting, culotte stenting and crush stenting techniques (p= 0.872).

First, univariate logistic regression analysis was performed to determine the parameters predicting the development of AKI after the procedure in patients with coronary bifurcation lesions revascularized with the two-stent strategy (Table 2). In this analysis, age (p= 0.003), DM (p= 0.036), HT (p= 0.002), LVEF (p< 0.001), hematocrit level (p= 0.045), creatinine level (p= 0.023), contrast agent volume (p= 0.001) and ACEF score (p< 0.001) were determined as possible risk factors for the development of AKI. Among these parameters, age, LVEF and creatinine level were not included in the multivariate analysis since they were the components of the ACEF score. On the other hand, the cut-off values for the numerical data such as ACEF score, hematocrit level and contrast agent volume were determined using ROC curves and Youden index, and these data were categorized. As a result of the multivariate logistic regression analysis, HT (OR: 2.778, 95% CI: 1.065-7.244, p= 0.037), ACEF score ≥ 1.14 (OR: 4.949, 95% CI: 1.735-14.122, p= 0.003) and contrast agent volume ≥ 252 mL (OR: 2.637, 95% CI: 1.072-6.486, p= 0.035) remained significant and were found to be independent predictors of AKI development (Table 3).

Figure 3 showed the ROC curve of ACEF score for the development of AKI. ACEF score ≥ 1.14 can detect AKI development with 82.1% sensitivity, 60.9% specificity and 96.1% negative predictive value (AUC: 0.775, 95% CI: 0.685-0.865, p< 0.001). On the other hand, when the patients were divided into two groups according to this cut-off value, the rate of AKI development in the group with ACEF score ≥ 1.14 was significantly higher than the group with ACEF score < 1.14 (22.5% vs. 3.9%, p< 0.001).

DISCUSSION

In this study, we investigated the predictors of AKI development in NSTEMI patients who underwent revascularization with two-stent strategy for the true coronary artery bifurcation lesions. AKI developed in 12.2% of the patients after the procedure. As a result of the multivariate analysis, HT, ACEF score ≥ 1.14 and contrast agent volume ≥ 252 mL were determined as independent predictors for AKI. The coronary anatomical factors and technique related factors had no effect on AKI. The ACEF score ≥ 1.14 could detect the development of AKI with 82.1% sensitivity, 60.9% specificity and 96.1% negative predictive value.

Nowadays, transcatheter interventions have become the preferred treatment choice for a growing number of heart diseases. One of the most common complications after these interventions is the contrast-induced AKI, which is defined as an acute decrease in kidney function after iodinated contrast agent administration. The pathophysiology of AKI includes

Table 1. Comparison of characteristics of study patients with and without acute kidney injury

	All patients (n= 230)	AKI (-) (n= 202)	AKI (+) (n= 28)	p value
Age, years	59.3 ± 10.8	58.5 ± 10.5	65.2 ± 11.0	0.002
Male	179 (77.8%)	160 (79.2%)	19 (67.9%)	0.175
Current smoking	114 (49.6%)	98 (48.5%)	16 (57.1%)	0.392
Comorbidities				
Diabetes mellitus	89 (38.7%)	73 (36.1%)	16 (57.1%)	0.032
Hypertension	107 (46.5%)	86 (42.6%)	21 (75.0%)	0.001
Hyperlipidemia	100 (43.5%)	86 (42.6%)	14 (50.0%)	0.458
Prior PCI	71 (30.9%)	65 (32.2%)	6 (21.4%)	0.249
Prior CABG	13 (5.7%)	12 (5.9%)	1 (3.6%)	1.0
Peripheral artery disease	16 (7.0%)	15 (7.4%)	1 (3.6%)	0.700
Cerebrovascular disease	1 (0.4%)	0 (0.0%)	1 (3.6%)	0.122
Atrial fibrillation	8 (3.5%)	7 (3.5%)	1 (3.6%)	1.0
LVEF (%)	52.9 ± 10.0	54.0 ± 9.4	45.5 ± 11.2	< 0.001
Laboratory data				
Hematocrit (%)	40.6 ± 5.3	40.9 ± 5.1	38.7 ± 6.3	0.043
White blood cells (10^3/uL)	9.56 ± 2.90	9.49 ± 2.76	10.06 ± 3.79	0.335
Platelet (10^3/uL)	259 ± 62	257 ± 60	273 ± 74	0.204
Creatinine (mg/dL)	0.86 (0.72-0.96)	0.86 (0.72-0.95)	0.90 (0.78-1.14)	0.165
Total cholesterol (mg/dL)	188 ± 49	188 ± 49	193 ± 53	0.636
LDL-C (mg/dL)	107 (84-132)	107 (84-131)	109 (81-142)	0.435
HDL-C (mg/dL)	43.0 ± 10.7	43.7 ± 10.7	46.2 ± 10.9	0.254
Triglyceride (mg/dL)	152 (100-229)	152 (102-235)	161 (94-183)	0.448
ACEF score	1.07 (0.90-1.37)	1.06 (0.88-1.28)	1.45 (1.17-2.09)	< 0.001
SYNTAX score	15.7 ± 4.6	15.5 ± 4.4	17.0 ± 5.6	0.105
Bifurcation location				0.714
LAD-LCx	15 (6.5%)	12 (5.9%)	3 (10.7%)	
LAD-Diagonal	133 (57.8%)	119 (58.9%)	14 (50.0%)	
LCx-OM	73 (31.7%)	63 (31.2%)	10 (35.7%)	
PDA-PLA	9 (3.9%)	8 (4.0%)	1 (3.6%)	
Bifurcation angle > 70°	90 (39.1%)	80 (39.6%)	10 (35.7%)	0.693
Procedural data				
Stenting strategy				0.872
T-stenting	92 (40.0%)	81 (40.1%)	11 (39.3%)	
Culotte stenting	57 (24.8%)	49 (24.3%)	8 (28.6%)	
Crush stenting	81 (35.2%)	72 (35.6%)	9 (32.1%)	

Table 1. Comparison of characteristics of study patients with and without acute kidney injury (continues)

	All patients (n= 230)	AKI (-) (n= 202)	AKI (+) (n= 28)	p value
Main branch stent length (mm)	25.3 ± 6.5	25.2 ± 6.6	25.9 ± 5.9	0.607
Side branch stent length (mm)	19.3 ± 5.0	19.2 ± 5.0	19.7 ± 5.2	0.635
Main branch stent size (mm)	2.88 ± 0.29	2.88 ± 0.29	2.83 ± 0.25	0.372
Side branch stent size (mm)	2.61 ± 0.23	2.62 ± 0.23	2.58 ± 0.23	0.482
Predilation	185 (80.4%)	162 (80.2%)	23 (82.1%)	0.808
POT	195 (84.8%)	173 (85.6%)	22 (78.6%)	0.397
Final kissing	223 (97.0%)	197 (97.5%)	26 (92.9%)	0.204
Procedural time (min)	70 (55-92)	68 (54-90)	84 (61-110)	0.138
Fluoroscopy time (min)	23 (18-35)	23 (17-34)	29 (22-44)	0.044
Contrast volume (mL)	239 ± 67	234 ± 65	281 ± 70	< 0.001

Data are presented as percentage, mean ± standard deviation or median (interquartile range). AKI: Acute kidney injury, PCI: Percutaneous coronary intervention, CABG: Coronary artery bypass graft, LVEF: Left ventricular ejection fraction, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, LAD: Left anterior descending artery, LCx: Left circumflex artery, OM: Obtuse marginal artery, PDA: Posterior descending artery, PLA: Posterolateral artery, POT: Proximal optimisation technique.

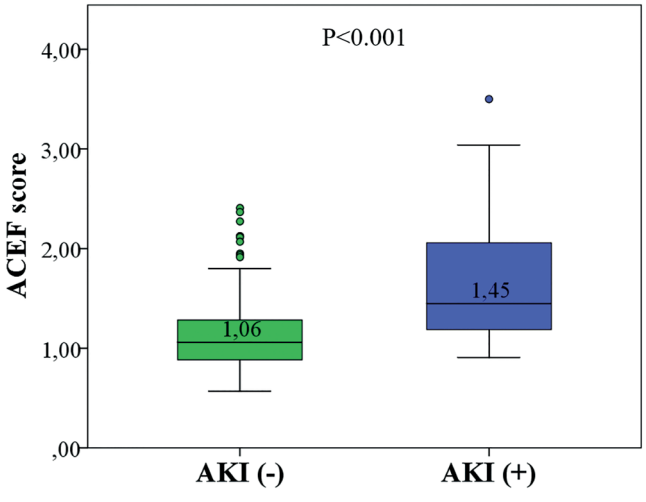


Figure 1. ACEF score box plot graph according to the presence of acute kidney injury.

AKI: Acute kidney injury.

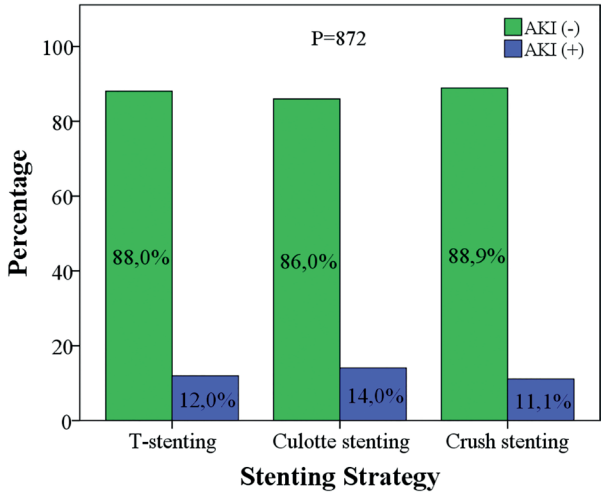


Figure 2. Comparison of acute kidney injury rates according to stenting strategy.

AKI: Acute kidney injury.

several mechanisms. First, the contrast agent shifts the balance between vasodilator and vasoconstrictive factors towards vasoconstriction, leading to cortical and medullary renal ischemia and consequently a decrease in GFR[13]. Second, the contrast agent exerts a direct cytotoxic effect and disrupts various functions of tubular epithelial cells. Third, the contrast agent increases blood viscosity, leading to further reduction of microcirculatory flow and changes in blood osmolality, resulting in impaired renal function[14].

It has been reported that patients who underwent PCI with a diagnosis of acute coronary syndrome and developed AKI after the procedure had significantly higher rates of 30-day mortality, recurrent myocardial infarction (MI), target lesion revascularization, target vessel revascularization, and major bleeding compared to patients without AKI[15]. In addition to increase in major adverse cardiovascular events rates, since we lack effective treatments for AKI, the detection of factors that can predict the development of AKI will be effective in taking necessary precautions to prevent AKI. Many studies

Table 2. Univariable logistic regression analysis for the development of acute kidney injury

	Univariable analysis		
	OR	**95% CI**	**p value**
Age	1.060	1.020-1.101	0.003
Male	0.554	0.234-1.313	0.180
Current smoking	1.415	0.637-3.142	0.394
Diabetes mellitus	2.356	1.057-5.252	0.036
Hypertension	4.047	1.646-9.950	0.002
Hyperlipidemia	1.349	0.611-2.977	0.459
Prior PCI	0.575	0.222-1.486	0.253
Prior CABG	0.586	0.073-4.691	0.615
Peripheral artery disease	0.462	0.059-3.637	0.463
Atrial fibrillation	1.032	0.122-8.713	0.977
LVEF	0.926	0.891-0.962	< 0.001
ACEF score	9.244	3.763-12.704	< 0.001
SYNTAX score	1.066	0.986-1.153	0.108
Hematocrit	0.928	0.863-0.998	0.045
White blood cells	1.065	0.937-1.211	0.335
Platelet	1.004	0.998-1.010	0.205
Creatinine	5.883	1.276-27.119	0.023
Bifurcation location			0.722
LAD-Diagonal*	0.471	0.118-1.872	0.285
LCx-OM*	0.635	0.152-2.654	0.534
PDA-PLA*	0.500	0.044-5.700	0.577
Bifurcation angle > 70°	0.847	0.372-1.929	0.693
Stenting strategy			0.872
Culotte stenting#	1.202	0.452-3.195	0.712
Crush stenting#	0.920	0.361-2.348	0.862
Main branch stent length	1.016	0.957-1.078	0.605
Side branch stent length	1.019	0.944-1.099	0.633
Main branch stent size	0.495	0.107-2.298	0.369
Side branch stent size	0.521	0.085-3.163	0.480
Predilation	1.136	0.407-3.172	0.808
POT	0.615	0.230-1.645	0.333
Final kissing	0.330	0.061-1.788	0.198
Procedural time	1.003	0.994-1.013	0.478
Fluoroscopy time	1.015	0.994-1.038	0.169
Contrast volume	1.010	1.004-1.016	0.001

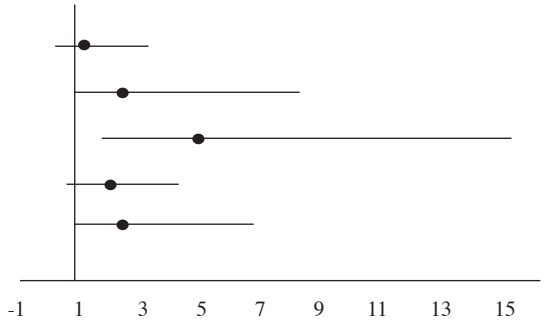
OR: Odds ratio, CI: Confidence interval, PCI: Percutaneous coronary intervention, CABG: Coronary artery bypass graft, LVEF: Left ventricular ejection fraction, LAD: Left anterior descending artery, LCx: Left circumflex artery, OM: Obtuse marginal artery, PDA: Posterior descending artery, PLA: Posterolateral artery, POT: Proximal optimisation technique.

* Compared to LAD-LCx.

Compared to T-stenting.

Table 3. Multivariable logistic regression analysis for the development of acute kidney injury

	Multivariable analysis		
	OR	95% CI	p value
Diabetes mellitus	1.524	0.629-3.693	0.351
Hypertension	2.778	1.065-7.244	0.037
ACEF score ≥ 1.14	4.949	1.735-14.122	0.003
Hematocrit ≤ 37.1%	2.140	0.873-5.246	0.096
Contrast volume ≥ 252 mL	2.637	1.072-6.486	0.035



OR: Odds ratio, CI: Confidence interval.

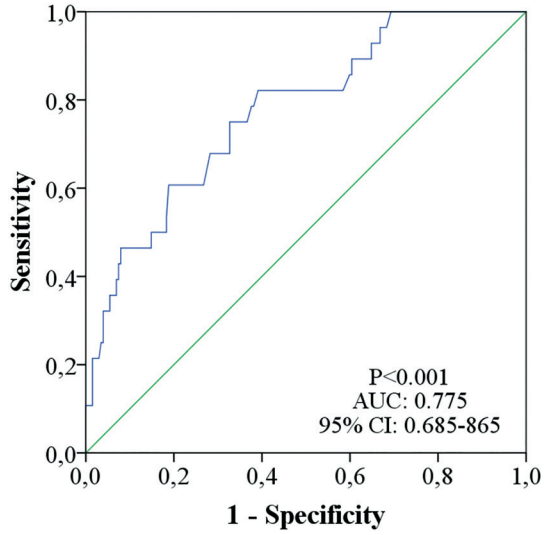


Figure 3. ACEF score ROC curve for the development of acute kidney injury.

AUC: Area under curves, CI: Confidence interval.

searching a prediction model for AKI have been conducted to help identifying the high-risk patients who can benefit from pre-procedural strategies and preserve kidney or improve pre-intervention counseling[16-23]. To the best of our knowledge, there is no study conducted for this purpose in a specific patient subgroup such as patients with PCI to the bifurcation lesion.

Challenging coronary bifurcation disease composes 15-20% of the lesions treated with PCI[24]. PCI for bifurcation is associated with a higher incidence of procedural complications, a higher rate of restenosis, and worse clinical outcomes when compared to non-bifurcation PCI[25-27]. Drug-eluting stents contributed to a significant reduction in the incidence of restenosis and target vessel revascularization. There might be several problems during bifurcation PCI due to the anatomical structure: plaque shift, carina shift, jail of side branch, the protruded stent strut in the lumen, and so on[24,28]. Therefore, many interventional techniques for bifurcation lesions have been developed and used[24]. These techniques are mainly categorized, according to the strategy for the side branch, into one-stent versus two-stent strategy. To date, no study showed clear advantages on one strategy. Mainly simpler techniques are slightly favored in the randomized trials[29,30]. Previous studies demonstrated that one-stent strategy could be recommended as the routine bifurcation stenting technique[29-31]. Based on these study results, the strategy of stenting main vessel with provisional side branch stenting is currently favored by most interventional cardiologists. However, we occasionally use two-stent strategy with various reasons, expecting more favorable side branch outcomes. For example, we could perform side branch stenting in advance, if side branch is so stenotic and large that we might be concerned with the jail of that vessel during main vessel stenting. Although the complications such as short and long-term mortality, recurrent MI, target lesion revascularization, target vessel revascularization have been well established in patients undergoing the two-stent strategy, the incidence and the predictors of AKI after the procedure are not clear.

Previous studies have reported different incidence rates ranging from 0.7% to 19% for AKI after PCI[16,19,32,33]. However, most of these studies were single-center studies and were conducted more than a decade ago, and many used different definitions of AKI. Historically, different cut-off levels have been adopted to define AKI; the most recent definition includes any of the following: increase in serum creatinine by 0.3 mg/dL within 48 hr; or increase in serum creatinine to 1.5 times baseline within the prior 7 days; or

urine volume < 0.5 mL/kg/hr for 6 hr following contrast media administration. In our study, we defined AKI as the development of creatinine changes within the first 48 hours after the procedure and meeting the AKIN group criteria, and we detected AKI in 12.2% of the patients[12]. Although our rate was high, it was not contrary to the literature. In Azzalini et al. study comparing patients with complex PCI with other patients for the development of AKI, they found the AKI rate in the complex PCI group as 12.1%, very similar to our rate[34]. The higher rates in these patient groups are likely to be explained by the longer operation durations and the higher amount of contrast agent compared to standard procedures.

In our study, we concluded that the factors of coronary anatomy and the technical differences used while revascularization of bifurcation lesions with the two-stent strategy did not affect the development of AKI. This result may relax the clinicians while deciding the treatment strategy for bifurcation lesions. We determined that HT, contrast agent volume and ACEF score were the predictors of AKI. In previous studies, ACEF score has been proven to be a predictor of AKI in patients who underwent transcatheter aortic valve implantation (TAVI), mitral repair, coronary artery bypass grafting (CABG), and PCI[23,35-37]. The ACEF score combines three important clinical variables; age, serum creatinine (renal failure) and LVEF. These three preoperative clinical variables are well known independent risk factors for postoperative AKI in patients undergoing PCI. Therefore, the ACEF scoring system can be a useful and feasible risk model for predicting postoperative AKI. It is also more suitable for non-elective PCI, as it uses clinical variables that can be obtained easily and quickly. A recent study showed that the ACEF score can identify patients at the risk of early fatal or non-fatal complications and long-term mortality who underwent PCI due to coronary bifurcation lesions[38]. In another study, Ando et al. showed that ACEF score can be used as a predictor of AKI in patients who underwent primary PCI[23].

According to recent guidelines on myocardial revascularization, treatment of patients at high risk for AKI includes saline hydration and avoidance of excessive contrast agent usage[39]. In our study, we found a negative predictive value of 96.1%. This means that an operator can get more projection to get a good angiographic result in patients with low ACEF scores. In another scenario, over-hydration can be avoided in the patients at risk of pulmonary edema with a low ACEF score.

There were some limitations in our study. First of all, it was a small-sized, single-center, retrospective observational study. The only end-point was AKI development. The inclusion of different end-points would diversify the results of the study. The reduction in urine output wasn't included in the definition of AKI, which may lead to an underestimation of the incidence of AKI. For AKI estimation, we did not make a comparison with other risk models because we didn't have the data of some variables necessary for their calculations. Finally, the cut-off value of each parameter used in this study was initially developed by using ROC curves. Therefore, our results must be interpreted carefully until they will be confirmed in subsequent studies.

The ACEF score is a practical and simple user-friendly tool that independently predicts AKI in patients with coronary bifurcation lesions revascularized with the two-stent strategy. Moreover, a low ACEF score has an excellent negative predictive value for AKI, which might be clinically significant. On the other hand, the development of AKI is not affected by the anatomical location of the lesion and the technical differences used for revascularization of coronary bifurcation lesions.

Ethics Committee Approval: The study was approved by the Istanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital Clinical Research Ethics Committee (Date: 26.01.2021; Decision No: 2021/01).

Informed Consent: Informed consent was obtained.

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Evaluation of Interatrial Block in Patients Presented with Acute Pulmonary Embolism

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ABSTRACT

Introduction: Interatrial block (IAB), which is defined as a conduction delay between the right and left atrium, is characterized by the prolongation of P wave on the electrocardiography (ECG). In this study, we aimed to investigate the relationship between the presence of IAB and acute pulmonary embolism (APE) in patients admitted to emergency department with a preliminary diagnosis of APE.

Patients and Methods: In this retrospective case-control study, a total of 82 patients with a preliminary diagnosis of APE were enrolled. Of these patients, 42 patients were diagnosed with APE via pulmonary computed tomographic angiography. In all patients, the ECGs were recorded on admission.

Results: Our study findings revealed that P wave dispersion, P wave duration of ≥ 120 ms, and notched P wave were significantly higher in patients with APE ($p< 0.05$ for all). Also, elevated heart rate and lower systolic blood pressure were found in patients with APE ($p= 0.022$ and $p= 0.043$, respectively). In multivariable logistic regression analysis, P wave duration of ≥ 120 ms was found to be an independent predictor of APE (OR: 3.958; 95% CI: 1.095-14.308; $p= 0.036$). In a receiver operating characteristics curve analysis, IAB predicted the APE with a sensitivity of 40.5% and a specificity of 85%.

Conclusion: Prolonged P wave duration was observed more frequently in patients with APE. The study findings showed that IAB may be an important predictor of APE in patients with a preliminary diagnosis of APE.

Key Words: Interatrial block; pulmonary embolism; electrocardiography.

Akut Pulmoner Emboli ile Başvuran Hastalarda İnteratriyal Blok Varlığının Değerlendirilmesi

ÖZ

Giriş: Sağ ve sol atriyum arasında bir iletim gecikmesi olarak tanımlanan interatriyal blok (IAB), elektrokardiyografi (EKG)'deki P dalgasının uzaması ile karakterize edilir. Bu çalışmada, acil servise başvuran hastalarda akut pulmoner emboli (APE) ön tanısıyla IAB varlığı ile APE arasındaki ilişkinin araştırılması amaçlanmıştır.

Hastalar ve Yöntem: Bu retrospektif olgu kontrol çalışmasına, APE ön tanısı ile acil servisimize başvuran toplam 82 hasta dahil edilmiştir. Bu hastaların 42'sine APE tanısı pulmoner bilgisayarlı tomografik anjiyografi ile konulmuştur. Tüm hastaların başvuru sırasındaki EKG kayıtları alınmıştır.

Bulgular: Çalışma bulgularımız P dalga dispersiyonunun, P dalga süresinin ≥ 120 ms ve çentikli P dalgasının APE hastalarında anlamlı olarak yüksek olduğunu göstermiştir ($p< 0.05$). Ayrıca APE tanısı alan hastalarda kalp atım hızı daha yüksek ve sistolik kan basıncı daha düşük tespit edilmiştir (sırasıyla $p= 0.022$ ve $p= 0.043$). Çok değişkenli lojistik regresyon analizinde, P dalga süresinin ≥ 120 ms olması APE'nin bağımsız bir belirleyicisi olduğu bulunmuştur (OR: 3.958, %95 CI: 1.095-14.308, $p= 0.036$). Yapılan ROC eğri analizinde, IAB, APE'yi %40.5 duyarlılık ve %85 özgüllük ile öngörmüştür.

Sonuç: Uzamış P dalga süresi, APE tespit edilen hastalarda daha sık gözlenmiştir. Çalışma bulguları, IAB'nin APE ön tanısı alan hastalarda önemli bir APE belirleyicisi olabileceğini göstermiştir.

Anahtar Kelimeler: İnteratriyal blok; pulmoner embolizm; elektrokardiyografi.

INTRODUCTION

Acute pulmonary embolism (APE) is one of the life-threatening disease that may cause considerable morbidity and mortality. In addition, APE is a challenging emergency condition because the clinical presentation in patients with APE may range from mild chest pain to shock[1-3]. Even though the definitive diagnosis of APE is based on computerized tomographic pulmonary angiography (CTPA), some electrocardiographic (ECG) findings such as $S_1Q_3T_3$

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pattern, negative T-wave in precordial leads and atrial arrhythmias have been shown to have high specificity for APE[4-6].

Interatrial block (IAB), which is a conduction delay between right and left atrium, was defined as a positive P wave duration longer than 120 ms on the surface ECG, or manifested as P wave duration longer than 120 ms plus biphasic (±) morphology in leads II, III, and aVF[7]. Some previous studies concluded that IAB was related with the occurance of atrial fibrillation in acute coronary syndrome patients[8]. However, it has been unknown whether IAB is a marker of APE in patients presented with signs and symptoms of APE. Therefore, in our study, we aimed to evaluate the potential diagnostic utility of IAB in patients with a preliminary diagnosis of APE.

PATIENTS and METHODS

Study Patients

In this retrospective case-control study, the patients who presented to emergency department with signs and symptoms of APE from January 2016 to June 2018 and underwent CTPA were reviewed. The patients who had end-stage liver and renal disease, active infection, acute coronary syndrome, chronic inflammatory disease, and coagulopathy were not included in this study. In addition, the patients whose ECG morphology indicating atrial fibrillation or pace rhythm were also excluded from the study. After evaluation regarding with exclusion criteria, 82 patients were enrolled in our study. Of these patients, APE diagnosis was confirmed in 42 patients by CTPA. Control group consisted by remaining 40 patients with a final diagnosis other than APE. Among these patients, 10 patients had been treated as acute heart failure, four patients as pneumonia, and 16 patients as acute asthma or exacerbation of chronic obstructive pulmonary disease. In the remaining 10 patients, there was no detected organic pathology. All patients who had a diagnosis of APE were treated with the standard medical therapy in accordance with the recent guidelines. Our study protocol was confirmed by the local ethics committee of our hospital in accordance with the principle of the Declaration of Helsinki. Due to the retrospective design of the study, an informed consent was not needed.

Electrocardiographic Analysis

The standard 12-lead ECGs were achieved on a paper with speed of 25 mm/s, amplitude of 10 mm/mv, and a filter range between 0.5 to 150 Hz from whole patients on admission. The beginning of the P wave was defined as the initially detected upward or downward deflection calculated from baseline. The returning point of the P wave to the baseline was defined as the P wave offset. IAB was defined as the duration of P wave longer than 120 ms with or without presence of notching. The P wave maximum was calculated in each leads, and the algebraic difference between the two was accepted as the P wave dispersion. The ECGs were analyzed by two independent cardiologists who were blind to the patients' clinical data.

Echocardiographic and CTPA Examination

All echocardiographic examinations were obtained by an experienced cardiologist using an ultrasound machine (Vivid 7, GE Healthcare, USA) within 24 hours during hospitalization. The peak systolic pressure of pulmonary artery was calculated using the simplified Bernoulli equation. The left ventricular ejection fraction (LVEF) was calculated in accordance with the Simpson method.

In the present study, APE was diagnosed by CTPA with a standard APE protocol (which was a contrast material volume: 135 mL, contrast material injection rate: 4 mL/sec, field of view: 35 cm and section thickness: 3 mm). Two radiology specialists confirmed the diagnosis of APE if there was thrombus at the main pulmonary artery or its major branches.

Statistical Analysis

Categorical variables were stated as percentage (%), whereas continuous variables were stated as mean ± standard deviation or median. Kolmogorov-Smirnov test was used to test the normality distribution of continuous variables. Chi-square or Fisher exact test were used for comparison of categorical data. Correlation of continuous variables was analyzed by Pearson correlation test. Correlation of non-continuous variables was analyzed by Spearman test. Student t-test or Mann-Whitney U test was used to compare continuous variables between the two groups. In order to find the independent predictors of APE, a multivariate logistic regression analysis was performed. A 2-sided p value of < 0.05 was accepted as significant. The IAB value which predicted the best sensitivity and specificity of APE was calculated with receiver operating characteristic (ROC) curve analysis. The effect size (Cohen's d) and power value ($1–\beta$) for IAB, which was compared between patients with and without APE, were measured via G*Power software. The power value and effect size were 0.92 and 0.77, respectively. Statistical analysis were performed with SPSS version 21 (IBM Corp., Armonk, NY).

RESULTS

A total of 82 patients [43 females (52.4%), mean age 56 ± 18 years] were included in our study. The baseline clinical and laboratory characteristics of all patients are shown in Table 1. The level of heart rate, respiratory rate, systolic

Table 1. Baseline demographic characteristic and laboratory findings of all patients and patients with or without PTE

	All patients (n= 82)	PTE (-) (n= 40)	PTE (+) (n= 42)	p value
Age, years	56 ± 18	56 ± 17	56 ± 19	0.714
Female gender (%)	43 (52.4)	20 (50)	23 (54.8)	0.666
History				
Diabetes mellitus, n (%)	12 (14.6)	6 (15)	6 (14.6)	0.927
Hypertension, n (%)	20 (24.4)	7 (17.5)	13 (31)	0.156
COPD, n (%)	10 (12.2)	4 (10)	6 (14.3)	0.553
Coronary artery disease, n (%)	12 (14.6)	6 (15)	6 (14.3)	0.927
Chronic heart failure, n (%)	6 (7.3)	4 (10)	2 (4.8)	0.363
History of PTE, n (%)	2 (2.4)	1 (2.5)	1 (2.4)	0.972
Malignancy, n (%)	4 (4.9)	0 (0)	4 (9.5)	0.116
Deep vein thrombosis, n (%)	4 (4.9)	2 (5)	2 (4.8)	0.96
Smoking, n (%)	38 (46.3)	19 (47.5)	19 (45.2)	0.837
On admission				
Surgery or immobilization within past four weeks, n (%)	17 (20.7)	6 (15)	11 (26.2)	0.211
Hemoptysis, n (%)	8 (9.8)	3 (7.5)	5 (11.9)	0.503
DVT symptoms, n (%)	17 (20.7)	6 (15)	11 (26.2)	0.211
Heart rate (rate/min)	91 ± 22	87 ± 24	95 ± 19	0.022
Systolic blood pressure (mmHg)	126 ± 22	131 ± 23	121 ± 20	0.043
Body temperature (°C)	36.6 ± 0.6	36.6 ± 0.6	36.6 ± 0.6	0.985
Respiratory rate (rate/min)	22 ± 5	20 ± 4	23 ± 5	0.014
O_2 saturation (%)	93 (86-96)	94 (91-96)	91 (82-96)	0.011
Laboratory findings				
Glucose (mg/dL)	118 (101-146)	114 (95-153)	124 (106-142)	0.489
Creatinine (mg/dL)	0.8 ± 0.2	0.8 ± 0.2	0.8 ± 0.2	0.568
BUN (mmol/L)	36 (28-51)	36 (27-48)	35 (29-53)	0.849
ALT (U/L)	17 (13-30)	16 (13-31)	18 (13-30)	0.86
Potassium (mEq/L)	4.3 ± 0.5	4.3 ± 0.5	4.3 ± 0.5	0.97
Sodium (mEq/L)	137 ± 4.3	136 ± 4.6	138 ± 3.8	0.034
Calcium (mEq/L)	8.9 ± 0.6	8.9 ± 0.5	8.8 ± 0.6	0.173
WBC count ($x10^3/mm^3$)	9.5 ± 4.1	9.2 ± 4.6	9.8 ± 3.5	0.202
Hemoglobin (mg/dL)	13.8 ± 2.2	13.7 ± 1.9	13.8 ± 2.4	0.933
Platelets ($x10^3/mm^3$)	226 (173-298)	231 (195-278)	211 (165-312)	0.639
Positive D-Dimer test, n (%)	72 (87.8)	33 (82.5)	39 (92.9)	0.152
Positive troponin value, n (%)	32 (39)	11 (27.4)	21 (50)	0.037
Wells score	3 (3-5)	3 (3-4.5)	3 (3-6)	0.185
Geneva score	5 (3-8)	4 (1-6.5)	6 (4-8)	0.016

Continuous variables are presented as mean ± SD or median; nominal variables presented as frequency. COPD: Chronic obstructive pulmonary disease, PTE: Pulmonary thromboembolism, DVT: Deep vein thrombosis, BUN: Blood urea nitrogen, ALT: Alanine aminotransferase, WBC: White blood cell.

blood pressure, oxygen saturation, sodium level, and positive troponin level were significantly different between the patients with and without APE (p< 0.05, for all). Comparing the echocardiographic findings showed that patients with APE had significantly higher prevalence of more than mild degree of tricuspid regurgitation, increased systolic pulmonary artery pressure, right ventricle dilatation, and increased right ventricle/left ventricle ratio (p< 0.05, for all) (Table 2). In terms of electrocardiographic parameters, the frequency of; increased P wave duration, P wave dispersion, P wave duration of > 120 ms, and P wave notching were significantly higher in patients with APE compared to controls (p< 0.05, for all). However; there was no significant difference in terms of negative T wave on the precordial leads, P wave maximum duration, and presence of fragmented QRS (p> 0.05, for all).

After the exclusion of patients who had chronic obstructive lung disease and chronic heart failure, electrocardiographic findings of patients with and without APE were compared and showed in Table 3. Heart rate, complete or incomplete right bundle brunch block, P wave duration, P wave dispersion, P wave duration of ≥ 120 ms, and P wave notching were remained different significantly between patients with and without APE (p< 0.05, for all).

In univariable regression analysis; right bundle branch block, heart rate, P wave dispersion, and P wave duration of ≥ 120 ms were found to be correlated with APE (Table 4). These parameters were entered to the multivariable logistic regression analysis. According to these analysis; heart rate (OR: 1.052, 95% CI: 1.021-1.084, p= 0.001) and P wave duration of ≥ 120 ms (OR: 3.958, 95% CI: 1.095-14.308, p= 0.036) were found to be independently associated with APE in the study population. ROC curve analysis showed that, IAB may predict the APE with sensitivity and specificity of 40.5% and 85% respectively.

Table 2. Comparison of echocardiographic and electrocardiographic findings of all patients and patients with or without PTE

	All patients (n= 82)	PTE (-) (n= 40)	PTE (+) (n= 42)	p value
Echocardiographic findings				
LVEF (%)	58 ± 8	58 ± 8	58 ± 7	0.809
TR more than mild degree, n (%)	34 (41.5)	9 (22.5)	25 (59.5)	0.001
Pulmonary artery pressure (mmHg)	39 ± 12	29 ± 5.5	48 ± 9.6	< 0.001
Right ventricle dilatation, n (%)	36 (43.9)	8 (20)	28 (66.7)	< 0.001
Right ventricle (mm)	37 ± 7.7	33 ± 5.5	41 ± 8.1	< 0.001
Left ventricle (mm)	38 ± 6.4	38 ± 5.9	37 ± 6.8	0.264
Right ventricle/Left ventricle ratio	1.0 ± 0.2	0.8 ± 0.2	1.1 ± 0.2	< 0.001
Electrocardiographic findings				
Right axis deviation, n (%)	10 (12.2)	2 (5)	8 (19)	0.089
Complete or incomplete RBBB, n (%)	18 (22)	5 (12.5)	13 (31)	0.044
Fragmented QRS, n (%)	20 (24.4)	9 (22.5)	11 (26.2)	0.697
T wave inversion on precordial leads, n (%)	33 (40.2)	14 (35)	19 (45.2)	0.345
ST segment depression, n (%)	16 (19.5)	7 (17.5)	9 (21.4)	0.654
ST segment elevation, n (%)	33 (40.2)	18 (45)	15 (35.7)	0.391
$S_1Q_3T_3$, n (%)	9 (11)	2 (5)	7 (16.7)	0.091
P wave duration (ms)	112 ± 48	100 ± 45	122 ± 52	0.004
P wave dispersion (ms)	106 ± 40	100 ± 34	116 ± 45	0.018
P wave duration of ≥ 120 ms, n (%)	23 (28)	6 (15)	17 (40.5)	0.001
P wave notching, n (%)	20 (24.4)	5 (12.5)	15 (35.7)	0.014
P wave maximum amplitude (mm)	1.39 ± 0.43	1.34 ± 0.34	1.43 ± 0.5	0.299

PTE: Pulmonary thromboembolism, LVEF: Left ventricle ejection fraction, TR: Tricuspid regurgitation, RBBB: Right bundle branch block.

Table 3. Comparison of electrocardiographic findings after exclusion of chronic obstructive lung disease

	All patients (n= 61)	PTE (-) (n= 31)	PTE (+) (n= 30)	p value
Heart rate (beat/min)	87 ± 20	79 ± 21	96 ± 16	0.001
Right axis deviation, n (%)	7 (11.5)	1 (3.2)	6 (20)	0.053
Complete or incomplete RBBB, n (%)	15 (24.6)	4 (12.9)	11 (36.7)	0.04
Fragmented QRS, n (%)	15 (24.6)	6 (19.4)	9 (30)	0.334
T wave inversion on precordial leads, n (%)	19 (31.1)	7 (22.6)	12 (40)	0.142
ST segment depression, n (%)	13 (21.3)	5 (16.1)	8 (26.7)	0.315
ST segment elevation, n (%)	25 (41)	14 (45.2)	11 (36.7)	0.5
S1Q3T3, n (%)	4 (6.6)	1 (3.2)	3 (10)	0.354
P wave duration (ms)	117 ± 28	105 ± 22	129 ± 28	< 0.001
P wave dispersion (ms)	110 ± 36	93 ± 30	126 ± 34	< 0.001
P wave duration of ≥ 120 ms, n (%)	16 (25.8)	3 (9.7)	13 (41.9)	0.004
P wave notching, n (%)	15 (24.2)	4 (12.9)	11 (35.5)	0.016
P wave maximum amplitude (mm)	1.38 ± 0.41	1.31 ± 0.33	1.44 ± 0.48	0.201

PTE: Pulmonary thromboembolism, RBBB: Right bundle branch block.

Table 4. Independent electrocardiographic predictors of pulmonary thromboembolism

	Univariable analysis			Multivariable analysis		
	OR	95% CI	p value	OR	95% CI	p value
Right bundle branch block	3.138	1.001-9.839	0.050	-	-	-
Heart rate	1.042	1.015-1.069	0.002	1.052	1.021-1.084	0.001
P wave dispersion	2.575	0.999-6.640	0.050	-	-	-
P wave duration of ≥ 120 ms	3.853	1.329-11.171	0.013	3.958	1.095-14.308	0.036

OR: Odds ratio, CI: Confidence interval.

DISCUSSION

Our study findings showed that the presence of IAB, namely P wave duration longer than 120 ms on the ECG, were significantly associated with APE, and it was found to be an independent predictor of APE. To the best of our knowledge, this was the first study demonstrating the potential effect of IAB for the presence of APE in patients with a preliminary diagnosis of APE.

The patients with APE may present with different clinical presentations, which may range from chest pain to cardiogenic shock[1,2]. Thus, it is a challenging disease based on the clinical presentations. Therefore, CTPA is performed in order to confirm or exclude the presence of APE. Similarly, the diagnosis of APE in our study was confirmed by CTPA in all patients.

In addition to being one of the first tests performed to the patients complaining of chest pain and shortness of breath, the ECG may aid in the diagnosis of APE when applied to the entire clinical situation. In previous studies, several ECG findings such as the $S_1Q_3T_3$ pattern, ST segment deviation on the precordial or inferior leads, T wave inversion on the precordial leads, and right bundle branch block have been shown as a marker for a main pulmonary trunk embolus[9,10]. In our study, we did not observe any significant difference in terms of $S_1Q_3T_3$ pattern, ST segment deviation on the precordial or inferior leads, and T wave inversion on the precordial leads between the groups even if we excluded the patients with chronic obstructive lung disease and chronic heart failure. These findings might be due to relatively small sample size of the study or low sensitivity of the above mentioned ECG parameters.

As possible explanations of the study findings, we thought that these ECG changes in APE are probably due to occlusion of the pulmonary artery by a massive embolus, which cause a rapid pressure overload to the right ventricle and the right atrium[11,12]. This rapid increase of pressure overload may lead to the dilatation and dysfunction of the right ventricle, thus resulting in decreased of blood flow through the right ventricle outflow tract, thereby reducing the left ventricle preload. Moreover, in an experimental study, Gold et al. demonstrated that acute pulmonary hypertension may cause right ventricle subendocardial ischemia, which may explain the disruption of the right-sided cardiac conduction and repolarization[13]. Furthermore, we hypothesized that decreased blood flow to the lung due to embolus may enhance the release of vasoconstrictive mediators such as histamine and catecholamines[10]. As a result, this release of vasoconstrictive mediators may cause ischemia of the right ventricle and right atrium as well as hypoxia of the Bachmann's bundle which is the equivalent of His-Purkinje system between the atria. Thus, the ischemic media can eventually result in deceleration of the conduction pathway of the right side of the heart, which may manifest itself as the prolongation of P wave on the ECG. In addition, P wave prolongation may reflect inhomogeneous atrial depolarization in response to various electrical and structural remodeling[8,14].

IAB, which is a newly introduced ECG parameter, is interpreted as the conduction time prolongation between the left and right atrium due to an impulse delay or blockage that is most often but not exclusively in the Bachmann's bundle. Several previous studies stated out that IAB had an association with the development of new-onset atrial fibrillation in patients with coronary artery disease and peripheral vascular disease[8,15,16]. Moreover, Senen et al. revealed that the left ventricular systolic dysfunction could lead to significant cardiac hemodynamic changes, which can alter the left atrium electrical properties resulting in a high prevalence of P wave dispersion and IAB in patients with dilated cardiomyopathy[17]. However, it is unknown whether there is any association between IAB and APE. This might be the first study to demonstrate that the prevalence of IAB, was significantly elevated in patients with APE. Moreover, the frequency of P wave dispersion was more common in patients with APE.

Our study findings may be useful and valuable in terms of clinical applicability. As a simple and easily obtained ECG parameter, IAB may have an additive diagnostic value in patients who present to emergency department due to APE signs and symptoms. However, as it was a retrospective case-control study, our study findings deserve further prospective and large scaled studies to clarify the exact role of IAB in patients with APE.

LIMITATIONS

Our study has some limitations. First of all, the sample size is relatively small. However, the power analysis of the study was found to be sufficient. Secondly, we were not able to observe whether there is any different in ECG findings during follow-up period. Finally, further studies with large sample size and longer follow-up time are required to increase the accuracy of the results.

CONCLUSION

In the present study, we demonstrated that IAB, namely P wave duration longer than 120 ms on the ECG, may be independently related with APE. As a simple, cheap, easy to obtain, and non-invasive ECG parameter, IAB may have an additive diagnostic value for predicting APE.

Ethics Committee Approval: The study was approved by the Kafkas University Faculty of Medicine Ethics Committee (Date: 30.01.2019; No: 80576354-050-99/31).

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer-reviewed.

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Conflict of Interest: The authors have no conflicts of interest to declare

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Vacuum-Assisted Closure for Sternal Wound Infection After Coronary Artery Bypass Surgery

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ABSTRACT

Introduction: Vacuum-assisted closure of sternal infected wounds has been reported to improve morbidity and mortality, besides decreasing duration of hospitalization. The aim of this study was to evaluate early outcomes of vacuum-assisted closure of infected sternal wounds after coronary bypass surgery in our clinic.

Patients and Methods: Sixty six patients who had sternal wound infection after coronary bypass surgery in our hospital between January 2016 and December 2019 were included in the study. After surgical debridement and removal of foreign materials, vacuum-assisted closure therapy was initiated at a mean postoperative 26.56 ± 5.5 days. After wound healing and negative cultures, treatment was terminated and sternal wounds were closed with appropriate procedures.

Results: Fifty six patients (84.84%) had deep sternal infection and 10 patients (15.15%) had superficial sternal infection. Early mortality was 13.63% (nine patients), all having deep sternal infections. The most common microorganisms cultured were *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Mean duration of hospitalization was 39.68 ± 2.48 days. No complications related with vacuum-assisted closure were detected. Recurrent sternal wound infection was not observed in any of the surviving patients.

Conclusion: Our results confirm that vacuum-assisted closure of wounds is a safe and effective treatment option for patients who are not candidates for primary closure or early muscle flap closure.

Key Words: Vacuum-assisted closure; sternal wound infection; coronary bypass surgery.

Koroner Baypas Cerrahisi Sonrası Sternal Yara İnfeksiyonunda Negatif Basınç Yardımlı Kapatma

ÖZ

Giriş: Vakum yardımlı kapama yönteminin morbidite ve mortaliteyi azalttığı, hastanede kalış süresini kısalttığı bildirilmiştir. Bu çalışmanın amacı, kliniğimizde koroner baypas cerrahisi sonrası gelişen sternal infeksiyonun vakum destekli kapama sistemi tedavisinin erken sonuçlarını değerlendirmektir.

Hastalar ve Yöntem: Hastanemizde Ocak 2016-Aralık 2019 tarihleri arasında, koroner baypas cerrahisi sonrası sternal yara infeksiyonu gelişen 66 hasta çalışmaya dahil edilmiştir. Hastalara cerrahi yara debridmanı ve yabancı cisimlerin uzaklaştırılmasından sonra, postoperatif ortalama 26.56 ± 5.5 günlerinde vakum yardımlı kapatma tedavisi başlanmıştır. Yara dokusunda yeterli kanlanma sağlanması, granülasyon dokusu oluşması ve negatif kültür sonuçları sağlandıktan sonra, uygun prosedür kullanılarak tedavi sonlandırılmıştır.

Bulgular: Elli altı hastada derin sternal, 10 hastada yüzeyel sternal infeksiyon tespit edilmiştir. Erken mortalite gelişen 9 (%13.63) hastanın tamamında derin sternal yara infeksiyonu mevcuttur. En sık üretilen mikroorganizmalar *Staphylococcus aureus* ve *Pseudomonas aeruginosa* olarak tespit edilmiştir. Ortalama hastanede kalış süresi 39.68 ± 2.48 gün olarak bulunmuştur. Vakum yardımlı kapatma tedavisi ile ilgili komplikasyon yaşanmamıştır. Yaşayan hastaların hiçbirisinde tekrarlayan sternal yara yeri infeksiyonu gözlenmemiştir.

Sonuç: Sonuçlarımız vakum yardımlı kapatma yönteminin, primer kapatma uygulanamayacak veya erken dönemde kas filebi ile tedavi edilemeyecek hastalarda güvenli ve etkili bir tedavi yöntemi olduğunu teyit etmiştir.

Anahtar Kelimeler: Vakum yardımlı kapama; sternal yara infeksiyonu; koroner baypas cerrahisi.

INTRODUCTION

Sternal wound infection (SWI) is a rare but life-threatening clinical condition after cardiac surgery. Incidence of sternal wound infection has decreased steadily in years but it is still related with increased morbidity, mortality, decreased survival and increased hospital costs[1-3]. There

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are several surgical treatment modalities for sternal infections including drainage of infective material, surgical debridement, primary sternal fixation with plates, sternal closure with muscle flaps. Vacuum-assisted closure (VAC) wound therapy was first reported as a new treatment option in 1997[4]. There is not still a consensus on the best treatment option for sternal infections. In 2016, recommendation guidelines for prevention and treatment of sternal wound infections was published by the American Association for Thoracic Surgery (AATS) to decrease SWI related morbidity and mortality after cardiac surgery and VAC therapy was recommended to enhance the treatment[5]. The aim of this study was to evaluate early outcomes of VAC therapy for SWI after coronary bypass surgery in our clinic.

PATIENTS and METHODS

Patient Population and Data Collection

Patients who underwent Coronary Bypass Grafting Surgery (CABG) in our hospital, between January 2016 and December 2019 were retrospectively reviewed. Among 4310 patients, 66 patients (1.53%) who had postoperative SWI and treated with vacuum-assisted closure (VAC) therapy were included in this study. Patients who had emergent surgical interventions and patients revascularized without use of mammarian arteries were excluded.

Patient data were collected from clinical records of the institution and laboratory results including blood and sternal wound cultures were retrieved from the electronic database of the hospital retrospectively, after approval of the study by the ethical committee of the hospital.

Definition of surgical site infection was made based on the criteria of Centers for Disease Control and Prevention[6,7]. Wound infection was defined as superficial if only subcutaneous and cutaneous layers were involved and defined as deep if the infection had reached sternal surface and/or involved the sternum. The patients with SWI were diagnosed as mediastinitis with isolation of the microorganism in sternal wound aspiration cultures or fluids and presence of symptoms as fever, angina and sternal instability besides the radiological findings of the CT scan.

Surgical Procedure and Treatment

All patients decided to be treated with VAC therapy were taken to operating room (Figure 1). Patients were covered with disposable drapes after being cleaned with chlorhexidine. General or local anesthesia was preferred depending on patient's clinical condition and the depth of surgical debridement. Surgical debridement was carried out under sterile conditions, all foreign materials, including the steel wires in patients with deep sternal infections were removed (Figure 2). Then

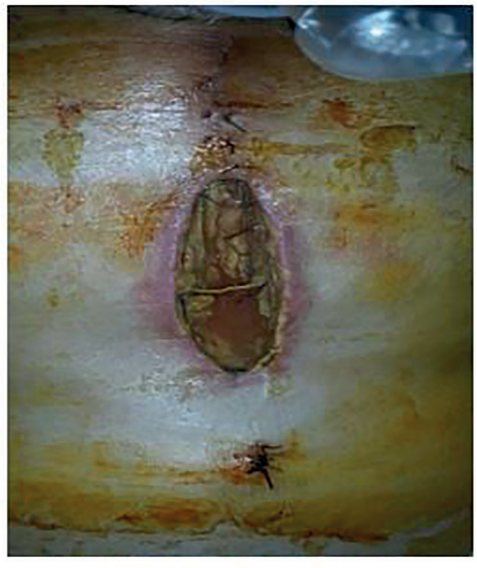

Figure 1. Shape of the wound at the time of initial diagnosis.

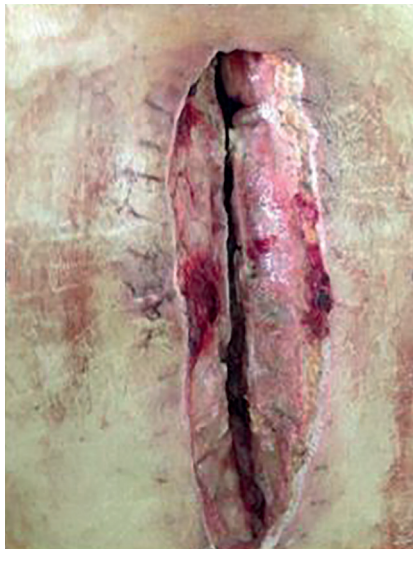

Figure 2. Surgical debridement and removal of foreign materials.

VAC treatment was started using V.A.C® Granufoam™, VeraT.R.A.C.™ Pad, V.A.C.Ulta™ (KCI USA, San Antanio, Inc., TX) System. The size of the foam was tailored depending on the size of the wound. Applied negative pressure was set to 25-75 mmHg depending on the depth of the wound and exposure of the heart to prevent iatrogenic injury. A dressing barrier was used between the heart and sponge if necessary. VAC was usually replaced every 48-72 hours depending on the amount of drainage and the planned surgical debridement. With each replacement wound cultures were sent to the laboratory. The wound closed by using the most appropriate closure method (Figure 3).

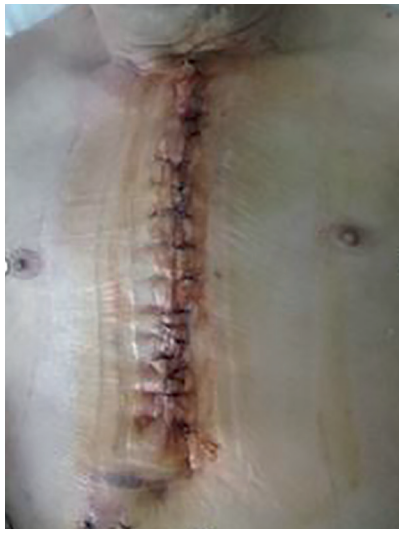

Figure 3. Final status of the wound subsequent the surgical closure.

Antibiotic administration was planned by the infection committee of the hospital. Treatment with antibiotics was started with the first positive culture and then modified depending on subsequent culture results.

Statistical Analysis

Statistical analysis were performed using statistical software (SPSS, version 23.0 for Windows; SPSS, Chicago, Illinois, United States). Numerical variables were given as mean and standard deviation (SD). Continuous random variables were presented as median and range (max-min values). Kolmogorov-Smirnov test was used in the distribution analysis of the data. Homogeneously distributed data were evaluated by the Student t-test, heterogeneous data were evaluated by the Mann-Whitney U test separately. To determine independent predictors for dependent variables; subsequently to univariate analysis test results the logistic regression analysis was applied to determine the ultimate risk factors and odds ratios of the factors foreseeing the mortality after VAC application subsequent to patients undergoing CABG surgery in our clinic.

Any difference with p value < 0.05 was regarded statistically significant.

RESULTS

Among 66 patients included in the study, 23 were females (33.8%) and 43 were males (63.2%). Mean age was 62.06 ± 9.37 years. The mean body mass index (BMI) of the patients was 26.5 ± 3.99 kg/m^2 and obesity was detected in 13 patients (19.6%). The frequency of patients with DM was 78.8% (n= 52) and 57.6% (n= 38) of patients had chronic obstructive pulmonary disease (COPD) as comorbidities. The preoperative demographics are shown in Table 1.

Table 1. Preoperative demographic data

Characteristics	Number (%)/Median
Age (years)	62.06 ± 9.37
BMI (kg/m^2)	26.5 ± 3.99
Gender	
Male	43 (63.2%)
Female	23 (33.8%)
COPD	38 (57.6%)
CVE	3 (4.5%)
PVD	1 (1.5%)
Hyperlipidemia (LDL > 150 mg/dL)	15 (22.7%)
DM (blood glucose level >140 mg/dL)	52 (78.8%)
AKI	12 (18.18%)
CKD	4 6.06%)

BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, CVE: Cerebrovascular event, PVD: Peripheral vascular disease, DM: Diabetes mellitus, AKI: Acute kidney injury, CKD: Chronic kidney disease.

Sternal dehiscence was found in 22 patients (33.3%) and the other 44 patients had only purulent flux (66,6%). Ten patients had superficial wound infections (15.2%) and 56 patients had deep sternal wound infections (DSWI) (84.8%). Twenty six patients had lesion size bigger than 10 cm (39.39%). Patients had their VAC treatment started at a mean of 26.56 days.

Prolonged intubation (more than 12 hours) was observed in 11 patients (16.66%). Postoperative mean albumin levels were 27.42 ± 5.35 g/dL and the blood albumin levels were found to be statistically significant for predicting prolonged hospital stay and mortality (p< 0.05). The mean hospital stay was 39.68 ± 2.48 days. Patients postoperative data were given in Table 2.

Table 2. Postoperative data

Variable	Number (%)/Median
Sternal dehiscence	22 (33.3%)
Lesion size (> 10 cm in longitudinal axis)	26 (39.39%)
Superficial wound infection	10 (15.2%)
Deep wound infection	56 (84,8%)
VAC application (mean day)	26.56 ± 6.5
Prolonged mechanical ventilation (> 12 h)	11 (16.66%)
Length of hospital stay (days)	39.68 ± 22.48

VAC: Vacuum-assisted closure.

Most common microorganisms cultured were *Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella aerogenes* were *Escherichia coli*. The microorganisms were detailed in Table 3.

Early mortality was seen nine patients (13.63%) all having deep sternal infections. Subsequently the separate analysis the logistic regression analysis was applied to find out independent risk factors of in hospital mortality. Postoperative hypoalbuminemia, prolonged mechanical ventilation, existence of preoperative respiratory insufficiency, acute and chronic renal dysfunction were found as significant risk factors for mortality ($p< 0.05$). *Pseudomonas, Klebsiella* and *Morganella* microorganisms were found to be significantly related with mortality in this study (Table 4).

Table 3. Microorganisms in mediastinal cultures

Microorganisms	Number (%)
Staphylococcus aureus	15 (n= 15, 22.7%)
Pseudomonas aeruginosa	14 (n= 14, 21.2%)
Klebsiella	10 (n= 10, 15.2%)
Escherichia coli	6 (n= 6, 9.1%)
Enterobacter	6 (n= 6, 9.1%)
Morganella morgagni	4 (n= 4, 6.06%)
Serratia	4 (n= 4, 6.06%)
Acinetobacter aerogenes	2 (n= 2, 3.03%)
Proteus mirabilis	2 (n= 2, 3.03%)

DISCUSSION

Deep sternal wound infections (DSWI) is a serious complication of cardiac surgery, increasing morbidity and mortality. It results in prolonged hospitalization, re-operations and increased costs[3,8]. In case of deep sternal infection, first step treatment principles are almost standard, including surgical debridement of all necrotic and infected tissues, removing foreign materials, drainage of purulent material under suitable antibiotic treatment. Techniques for closure of sternum vary; it can be closed immediately or delayed.

There are several therapeutic options for treatment of DSWI, including surgical revision with open or closed irrigation, surgical debridement followed by delayed closure with Robicsek technique, sternal plating, nitinol clips and muscle flap closure and VAC therapy but there is not still an exact consensus on the optimal approach for DSWI[9-11].

Durgun et al., reported sufficient results with rectus and pectoral muscle flaps for deep sternal infections[12]. Similarly a recent study by Pan et al., stated better short and long-term outcomes and unimpaired respiratory function with bilateral pectoralis muscle flaps compared with VAC therapy in a total of 132 post cardiac surgery patients[13].

On the contrary, Dohmen et al., in their consensus statement recommended prophylactic use of negative pressure wound therapy (NPWT) in patients with major risk factors (BMI < 15 or > 40 kg/m^2), insulin dependent diabetes mellitus, dialysis for chronic renal failure to prevent DSWI after cardiothoracic surgery[14]. VAC therapy helps to improve local blood flow, remove excessive effluent, protect superinfection with contamination and keep the edges of wound together[15-17]. Deniz and colleagues reported their comparative results of patients treated with conventional therapy and negative pressure

Table 4. Predictors of in-hospital mortality

	OR	95% CI Lower	UPPER	p value
Prolonged mechanical ventilation	13	2.61	64.607	0.003
Respiratory insufficiency	4.26	0.957	19.030	0.045
AKI	4.90	1.08	22.23	0.028
CKD	0.081	0.035	0.187	0.000
Postoperative hypoalbuminemia	0.804	0.668	0.968	0.019
Pseudomonas in cultures	6.80	1.42	32.47	0.008
Morganella in cultures	7.85	0.951	64.930	0.029
Klebsiella in cultures	7.85	0.951	64.930	0.029

OR: Odds ratio, AKI: Acute kidney injury, CKD: Chronic kidney disease.
$p< 0.05$ is statistically significant.

therapy and stated that NPWT provided better survival and low failure rate compared to conventional techniques[18].

Fuchs et al., reported that the VAC system helped to have negative wound cultures in a shorter time that resulted in reduced hospitalization period[19]. Similarly Raja and colleagues reported that VAC treatment reduces the time period between surgical debridement and sternal closure[20]. Negative pressure wound therapy is proposed in AATS guidelines as a class IIa recommendation in patients with deep sternal wound infections as a bridge for delayed sternal closure[5]. A recent study by Martino and colleagues, showed that VAC therapy had significantly improved outcomes of both deep and superficial wound infections with complete healing and without recurrence[21].

In this series, we reported our early experience with patients who had delayed closure and had VAC therapy before closure. Our patients had persistent infection even after debridement and we needed to drain mediastinal spaces due to purulent effluent with the VAC system. Our results confirmed effectiveness of VAC, with acceptable mortality rate and absence of recurrence in all cases.

Early mortality was found to be 13.6% in our series which is similar with the previous studies[22]. Risk factors for mortality were found to be respiratory insuffiency, prolonged ventilation, acute and chronic renal insufficiency and postoperative hypoalbuminemia in our study. Risk factors for deep sternal infections have been reported as obesity, advanced age, chronic obstructive lung disease, diabetes mellitus and use of mammarian arteries as conduits after CABG operations[15,23]. Patients in our series were high risk patients by means of these risk factors for infection, therefore the mortality observed was probably related with the preoperative comorbidities.

Duration of the VAC treatment seemed to affect the length of hospitalization (mean 39.6 days) but in fact these patients were our first group of patients and the decision making process for utilization of VAC system was prolonged. That is the probable reason for prolonged hospitalization. Depending on our early experience, we believe that early use of VAC with the onset of infection signs and symptoms, will contribute us for better results.

LIMITATIONS

Major limitation of the study is its retrospective design and relatively small number of patients. We did not have a control group treated with conventional methods to compare the effect of VAC treatment on morbidity and mortality in patients with mediastinitis, which we need to evaluate in a further study.

CONCLUSION

Despite adherence to all precautions to prevent sternal infections, postoperative superficial and deep infections may occur. Treatment options should be individualized, depending on patients clinical condition, risk factors, depth of the infection and microorganisms cultured. VAC of wounds is a safe and reliable treatment option for patients who are not candidates for primary closure or early muscle flap closure.

Ethics Committee Approval: The study was approved by the Non-Invasive Clinical Research Ethics Committee of Health Sciences University Kartal Koşuyolu High Specialization Training and Research Hospital (Date: 23.05.2019; Number: 2019.4/19-196).

Informed Consent: Due to the design of the study, consent to volunteer could not be obtained from the patients.

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Author Contributions: Concept/Design - HE, AA; Analysis/Interpretation - AK; Data Collection - SK, YK; Writing - AA, AK, HE; Critical Revision - AA, AK, HS; Final Approval - HS; Statistical Analysis - AK; Overall Responsibility - HE, AK, SK, YK, AA, HS.

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Inferior Vena Cava Collapsibility Index in Severe Acute Decompensated Heart Failure as Predictor of In-Hospital Mortality

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ABSTRACT

Introduction: The aim of this study was to assess the relation between the diameter and collapsibility of the inferior vena cava (IVC), other markers, clinical variables and in-hospital mortality in patients hospitalized with severe acute decompensated heart failure (ADHF).

Patients and Methods: An observational prospective study was conducted that included patients hospitalized with severe ADHF from April 2019 to March 2020. Inferior vena cava collapsibility index (IVCCI) was measured during the first 12 hours at admission. The endpoint was in-hospital mortality.

Results: Two hundred thirty one patients hospitalized for ADHF, 28 (12.1%) of them died during hospitalization and formed non-survivors group. There were significant difference between non-survivors and survivors in case of IVVCI (21.25 ± 5.6 vs. 36.2 ± 18.3; p= 0.01 respectively). According to multivariate analysis IVCCI remained independent predictor of in-hospital mortality (p< 0.05). An IVCCI less than 23 predicted in-hospital mortality with 69% sensitivity and 75% specificity.

Conclusion: In patients hospitalized with acute decompensated heart failure, a low IVCCI by 2D echocardiography at the time of admission is associated with a higher in-hospital mortality.

Key Words: Inferior vena cava collapsibility; heart failure; hospitalization; mortality.

Şiddetli Akut Dekompanse Kalp Yetmezliğinde Hastane İçi Mortalitenin Prediktörü Olarak İnferior Vena Kava Kollapsibilite İndeksi

ÖZET

Giriş: Bu çalışmanın amacı, şiddetli akut dekompanse kalp yetmezliği olan hastalarda inferior vena kava çapı ve kollapsibilitesi, diğer belirteçler, klinik değişkenler ve hastane içi mortalite arasındaki ilişkiyi değerlendirmektir.

Hastalar ve Yöntem: Nisan 2019 tarihinden Mart 2020 tarihine kadar şiddetli akut dekompanse kalp yetmezliği ile hastaneye yatırılan hastaları içeren gözlemsel prospektif bir çalışma yürütülmüştür. İnferior vena kava kollapsibilite indeksi hastaneye yatışta ilk 12 saat içinde ölçülmüştür. Sonlanım hastane içi mortalitedir.

Bulgular: Akut dekompanse kalp yetmezliği nedeniyle 231 hasta hastaneye yatırılmış, 28 (%12.1)'i hastanede yatarken ölmüş ve hayatta kalmayanlar grubunu oluşturmuştur. İnferior vena kava kollapsibilite indeksi durumunda (21.25 ± 5.6 vs. 36.2 ± 18.3; p= 0.01) hayatta kalmayanlar ve hayatta kalanlar arasında önemli fark bulunmuştur. Multivariate analize göre inferior vena kava kollapsibilite indeksi hastane içi mortalitenin bağımsız prediktörü olarak tespit edilmiştir (p< 0.05). Değeri 23'ten düşük inferior vena kava kollapsibilite indeksi, %69 duyarlılık ve %75 özgüllük ile hastane içi mortaliteyi öngörmüştür.

Sonuç: Akut dekompanse kalp yetmezliği ile hastaneye yatırılan hastalarda, başvuru sırasında iki boyutlu ekokardiyografi ile ölçülen düşük inferior vena kava kollapsibilite indeksi daha yüksek hastane içi mortalite ile ilişkilidir.

Anahtar Kelimeler: İnferior vena kava kollapsibilite; kalp yetmezliği; hastanede yatış; mortalite.

INTRODUCTION

Acute decompensated heart failure (ADHF) is a sudden and progressive worsening syndrome of heart failure (HF), which is characterized by exacerbation of HF signs and symptoms resulting in the need for urgent treatment with hospitalization. ADHF constitutes

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a complex clinical syndrome, representing a broad spectrum of diseases and statuses with heterogeneous clinical presentations. ADHF poses a unique medical burden of high morbidity and mortality. The continued high mortality rate for patients hospitalized with ADHF provides a compelling indication for accurate risk stratification for potentially improving individual management and hospital outcome.

In patients admitted due to ADHF, the degree of congestion is of prognostic relevance[1]. Congestion is defined as elevated left ventricular filling pressure and further subclassified in hemodynamic and clinical congestion depending on the absence or presence of clinical signs and symptoms of congestion[2]. According to a scientific statement of the European Society of Cardiology, the reference standard for evaluation of hemodynamic congestion is cardiac catheterization to measure right atrial pressure (RAP) and pulmonary capillary wedge pressure (PCWP)[2]. However, the routine use of cardiac catheterization is limited due to its invasive nature, other markers of decongestion are needed in order to guide physicians during decongesting therapy. Based on this, echocardiography guidelines recommend ultrasound assessment of the inferior vena cava (IVC) to estimate RAP[3]. Considerable efforts have been made to stratify patient risk in order to identify patients with a poor prognosis in whom closer surveillance or more intense treatment might improve outcome or to identify potential mechanisms driving outcome that might be targets for therapy. Published data from studies indicate that IVC dilation and collapsibility may be associated with early readmission and all cause mortality after hospitalization in patients with ADHF[4-6]. In this study we assessed the importance of IVC measurements as a marker for in-hospital mortality other than all cause mortality in severe ADHF patients.

PATIENTS and METHODS

A prospective and observational study included patients from April 2019 to March 2020. We enrolled 231 patients for acute decompensated chronic HF or new onset ADHF, functional class per New York Heart Association (NYHA) classification grade III or IV and without signs of acute coronary syndrome. The study was approved by the institutional ethical board and informed consent was obtained from all patients. The diagnosis of ADHF was performed by medical history and physical examination, in addition to NT-proBNP assay[7]. The exclusion criteria were; need for non-invasive positive pressure ventilation or intubation, cardiogenic shock with end-organ hypoperfusion plus systolic blood pressure < 90 mmHg, inability to undergo echocardiography in 12 hours of admission, presenting predominantly as right-side HF, ADHF due to significant arrhythmias, acute pulmonary embolism, acute exacerbation of chronic pulmonary disease, advanced renal failure (glomerular filtration rate < 30 mL/min/1.73 m^2), pregnancy, myocarditis, constrictive pericarditis, pericardial effusion, chronic hepatitis. Primary end point was in-hospital mortality.

On admission, the following data were recorded: age, gender, blood pressure, heart rate, oxygen saturation, medications, electrocardiogram, NT-terminal pro-BNP, hemoglobin, albumin, creatinine, sodium. Glomerular filtration rate was calculated according to the Modification of Diet of Renal Disease (MDRD-4) formula. The presence of diabetes mellitus, hypertension, coronary artery disease, valvular heart disease were also noted.

A comprehensive echocardiography was performed during the first 12 hours of admission by an expert cardiologists who were not involved in the treatment of the patients. Conventional two-dimensional echocardiography was performed using commercially available equipment (Vivid 7, General Electric Vingmed Ultrasound, Horten, Norway) with a 2.5 MHz transducer. Left ventricular ejection fraction (LVEF) was determined by the biplane Simpson's method. The measurement of IVC diameters were performed with the patient in the supine position head elevated 30 degrees[8]. The transducer was placed in the subxiphoidal region, and long and short axis views of the IVC were obtained just below the diaphragm in the hepatic segment. IVC diameters were measured within 2 cm from the right atrium; the minimum diameter was obtained during full forced inspiration, whereas the maximum diameter was obtained during expiration. The inferior vena cava collapsibility index (IVCCI) was determined by the ratio of the minimum and maximum diameters of the IVC according to the following formula[9]: IVCCI= (maximum diameter of the IVC-minimum diameter of the IVC)/(maximum diameter of the IVC).

Inpatient medical management by the primary medical team was guided by protocols from the ESC guidelines on the treatment of ADHF[10]. The patients who did not respond to medical management and died formed the non-survivor group, the patients who responded to medical treatment and were discharged formed the survivor group.

Statistical analyses were performed using SPSS 20.0 statistical package (SPSS Inc., Chicago, IL). Categorical variables (demographics and comorbidities) were given as counts and percentages. Continuous variables and IVC measurements were given as means with standard deviations, Kolmogorov-Smirnov tests were used to compare continuous variables

between groups. The Student's t-test and Mann-Whitney U test was employed to compare continuous variables, the chi-square or Fisher's exact test was employed to compare categorical variables, and Pearson's correlation test was employed to evaluate the relationship between pairs of continuous variables. Cox proportional hazards analysis was conducted to assign the independent risk factors for in-hospital mortality. Optimal cut off values for IVCCI for in hospital mortality prediction were determined by establishing receiver operating characteristic (ROC) curves and calculating the area under the curve (AUC) for distinct IVCCI diameters. Survival was analyzed using the Kaplan-Meier (K-M) method using cumulative survival curves with the log-rank (Mantel-Cox) test. $p< 0.05$ was considered to be statistically significant.

RESULTS

Two hundred thirty one patients admitted with severe ADHF were included in the study. Baseline demographic, clinical, laboratory and comprehensive echocardiographic characteristics of in hospital survivors and non-survivors are demonstrated in Table 1. All patients were NYHA class III or IV with a mean age of 70.3 ± 12.1 years. Some 28.5% of the patients had LVEF ≥ 50% as preserved LVEF (68 patients, data not shown). Twenty eight (12.1%) patients died in hospital formed non-survivors group and they were older (74.3 ± 10 vs. 69.7 ± 12.2 years; p= 0.05). The prevalence of diabetes mellitus, hypertension, coronary artery disease and valvular heart disease did not differ between the groups. There were significant difference between the clinical characteristics

Table 1. Baseline characteristics of the study population

	All patients (n= 231)	Survivals (n= 203)	Non-survivals (n= 28)	p value
Age (years)	70.3 ± 12.1	69.7 ± 12.2	74.3 ± 10	0.05
Gender, n (%)	119 (51.5)	105 (51.7)	14 (50)	0.8
Diabetes mellitus, n (%)	140 (60.6)	124 (61)	16 (57)	0.5
Hypertension, n (%)	162 (70.1)	144 (70.9)	18 (64.2)	0.4
Coronary artery disease, n (%)	77 (33.3)	68 (33.5)	9 (32.1)	0.7
Valvular heart disease, n (%)	28 (12)	25 (12.3)	3 (10.8)	0.4
Systolic blood pressure (mmHg)	127 ± 30.2	129.4 ± 29.9	113.75 ± 27.2	0.01
Mean arterial pressure (mmHg)	97.4 ± 22	97.9 ± 22.4	93.75 ± 19.8	0.3
Saturation O_2 (%)	93.4 ± 6.4	93.8 ± 5.2	90.2 ± 12	0.006
Heart rate (minutes)	94 ± 14	92.6 ± 14.3	101 ± 6.9	0.03
NT-proBNP	8199.2 ± 895.7	8037.9 ± 793.8	9368.7 ± 712.2	0.01
Hemoglobin (g/dL)	11.2 ± 2.38	11.1 ± 2.4	11.85 ± 2.2	0.1
Albumin (g/L)	35.1 ± 4.2	34.8 ± 4.4	35.4 ± 1.3	0.7
eGFR (%)	54.1 ± 26.6	56.1 ± 27.7	39.2 ± 14	0.02
Sodium (mmol/L)	133.7 ± 6.5	134.4 ± 6.5	128.5 ± 6.4	0.01
Left ventricle ejection fraction (%)	35.3 ± 12.9	36.2 ± 12.4	30 ± 14.8	0.01
Left atrium diameter (cm)	4.59 ± 0.54	4.5 ± 0.5	4.8 ± 0.6	0.03
Pulmonary artery systolic pressure (mmHg)	40.9 ± 11.6	39.8 ± 11.2	48.75 ± 11.6	0.01
IVC diameter, expiration (cm)	2.43 ± 0.5	2.4 ± 0.5	2.5 ± 0.3	0.3
IVC diameter, inspiration (cm)	1.61 ± 0.63	1.5 ± 0.6	1.9 ± 0.3	0.02
IVC collapsibility index (%)	34.3 ± 0.63	36.2 ± 18.3	21.25 ± 5.6	0.01

eGFR: Estimated glomerular filtration rate, IVC: Inferior vena cava.

Table 2. Multivariate analysis of in hospital mortality

	Hazard ratio	95% CI	p value
Left ventricle ejection fraction (%)	1.003	0.962-1.003	0.8
Age (years)	1.028	0.976-1.083	0.3
NT-proBNP (pg/mL)	1.002	1.001-1.003	0.001
IVC collapsibility index (cm)	0.892	0.824-0.964	0.004

IVC: Inferior vena cava, CI: Confidence interval.

of survivors and non-survivors groups. On admission, non-survivors had higher NT-proBNP levels (9368.7 ± 712.2 vs. 8037.9 ± 793.8; p= 0.01), lower sodium levels (128.5 ± 6.4 vs. 134.4 ± 6.5; p= 0.01) and lower LVEF (30 ± 14.8 vs. 36.2 ± 12.4). Mean IVC diameters were 2.43 ± 0.5 cm for expiration and 1.61 ± 0.63 cm for inspiration, mean IVCCI was 34.3% ± 0.63. There were significant difference between non-survivors and survivors in case of IVVCI (21.25 ± 5.6 vs. 36.2 ± 18.3; p= 0.01 respectively). To determine the independent predictors of in-hospital mortality, we performed multivariable logistic regression analysis by using variables age, LVEF, NT-proBNP and IVCCI (Table 2). These variables are also statistically significant in previous studies for predicting prognosis. Only NT-proBNP (HR: 1.002, 95% CI: 1.001-1.003, p= 0.001) and IVCCI (HR: 0.892, 95% CI: 0.824-0.964, p= 0.004) were independent predictors of in-hospital mortality. We performed a ROC analysis and determined a cutoff value for IVCCI of < 23% (69% sensitivity and 75% specificity) with area under the curve (AUC) value 0.733 (95% CI: 0.661-0.804; p< 0.001) for predicting in hospital mortality (Figure 1). Kaplan-Meier test resulted shorter survival in patients with IVCCI < 23% (log-rank, p< 0.001) (Figure 2).

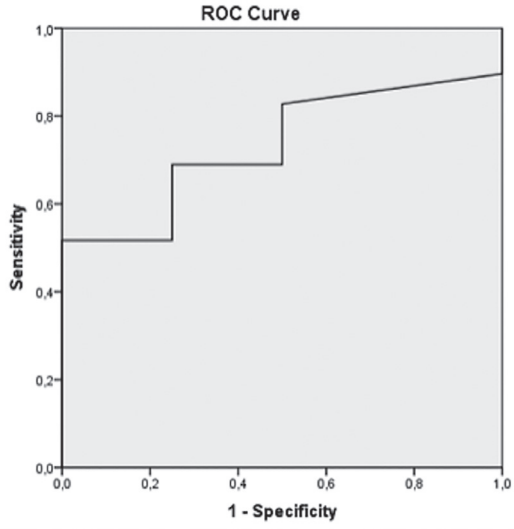

Figure 1. Receiver operator characteristic (ROC) curve analysis of inferior vena cava collapsibility index (IVCCI) determined a cut-off value for IVCCI of 23% for predicting in-hospital mortality with 69% sensitivity and 75% specificity.

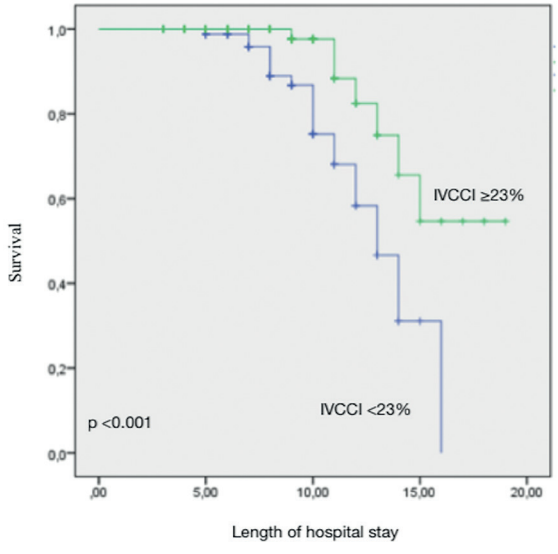

Figure 2. Kaplan-Meier analysis of inferior vena cava collapsibility index (IVCCI) < 23% and ≥ 23% on in-hospital mortality. Log Rank (Mantel-Cox), p< 0.001.

DISCUSSION

Our study found that a depressed IVCCI at admission is associated with a poor prognosis after hospitalization for severe ADHF. Patients with an IVCCI less than 23% at admission had higher in-hospital mortality.

The IVC diameter is a brief assessment of cardiac function, also a sign of venous congestion. Systolic or diastolic left ventricular dysfunction ends up left atrial hypertension, the pressure is delivered back across the pulmonary circulation to result in pulmonary arterial hypertension that combines any preexisting dysfunction of right ventricle and aggravates tricuspid regurgitation[11]. RAP and IVC distension increases as consequence of these stresses. If congestion is the hallmark of ADHF, then distension of the great veins may be the best indication on imaging. IVCCI can appropriately be used to estimate RAP semiquantitatively[3]. We have shown that IVC dilated and the attenuated IVCCI is incorporated with a worse prognosis of in-hospital mortality in ADHF patients.

Despite the crucial role of physical examination, physicians are becoming less skilled at physical examination and dependent on modern technology[12]. It is noteworthy that the IVC status

can be accurately evaluated by a novice in imaging, whereas elevated jugular venous pressure (JVP) is not easily identified even by experienced cardiologists[13-15]. Therefore, IVCCI assessment may be a plausible alternative for JVP in estimating RAP, treatment inducement, and prediction of outcomes, and for patients two-dimensional echocardiography performed routine measurement of IVCCI is legitimate.

The IVC assessments is usually simple to perform in patients with HF and has low inter-observer alteration. Instead of invasive catheterization and complications such as air embolism, pneumothorax, or injury of great vessels, when echocardiography is available, IVC measurements may supply similar data in HF patients[16,17]. Of note, IVCCI assessment can be a reasonable representative for jugular venous pressure regardless of the presence of ADHF in the diagnosis and prognosis.

In patients with HF, RAP elevation as predicted by the IVCCI was outstandingly associated with poor clinical outcomes, the IVCCI estimated the regulation of diuretics more precisely than clinical examination[18,19]. Also, a recent study showed IVCCI could be used for selection of diuretic strategy[20]. These point out the clinical practicality of the IVCCI regardless of its relationship with RAP in HF.

There is no research directly examining in-hospital mortality and IVCCI correlation in ADHF patients. Ours is the first study to investigate the relationship between IVC measurements and other markers of in-hospital mortality in patients with ADHF. Two recent studies evaluated IVCCI and mortality in hospitalized ADHF patients but as a prognostic marker of combined event of mortality and HF readmission during the 180 days of follow up[6,21]. Both concluded a low IVCCI indicative of IVC congestion, as a basic and helpful tool that helps to rapidly and non-invasively stratify the prognosis of these patients in the onset of medical care, and consolidate with adverse outcomes in patients with a wide spectrum of cardiovascular diseases.

Our study demonstrated that in terms of prognosis, the IVCCI < 23% at admission as a response of systemic congestion was associated with an increased possibility of mortality at initial hospitalization. The lack of IVC collapse appears to be more significant than the degree of maximum diameter. Also in our study plasma NT-proBNP levels were predictive of death after hospitalization for ADHF like in previous studies[22]. NT-proBNP level is predictive of in-hospital mortality in patients with either reduced or preserved LVEF independent of other clinical and laboratory variables.

There are few important differences with current study and the above mentioned ADHF studies which reinforced the relationship between congestion and the prognosis[6,21]. First, all of the present study patients were hospitalized with NYHA functional class III or IV, higher than 47% of Romano et al. and 19% of Laorden et al.[6,21]. Second, the predominant HF type in our study was heart failure with reduced ejection fraction, however both of other studies had predominantly patients with preserved ejection fractions. Third our sample size is more than the above mentioned hospitalized ADHF and prognosis IVCCI studies. Consequently relatively high event rate, low IVCCI in outcome patients and predictive levels of NT-proBNP which is inconsistent with prior studies may be explained by these differences.

In our study, in-hospital mortality rate was 12.1% which is higher than studies including hospitalized ADHF patients; 6.7% and 7.6% in the most recent ones, and 3.8% in two well known researches[23-26]. In a multi-center, prospective in-hospital mortality assessed study, indicators of outcome included advanced age, low admission SBP and sodium levels, high heart rate, and elevated creatinine levels[26]. The higher mortality rates in our study may be because of all hospitalized patients possessed most of these indicators and additionally all being severe ADHF (NYHA functional class III or IV). Esc-HF Pilot study patients had mean 133 mmHg SBP and 88/min HR (127 mmHg SBP and 94/min in our cohort) with only 28% severe ADHF[25]. A newly published study reported 7.6% in-hospital mortality having 70% severe ADHF patients with 88/min HR still lower indicator values than our cohort. As a result more tachycardia and symptomatic patients in our study eventuated poor in-hospital prognosis. In addition, lower mean LVEF value and low usage of HF medications in our patients might be other reasons for high in-hospital mortality.

STUDY LIMITATIONS

Our study has some limitations. The research was conducted at a tertiary referral high volume hospital where excessive rate of severe and complicated patients referred which may limit the generalization of its conclusions. Our study was not a prospective randomized study, unmeasured variables if might have been available could effect the findings. Additionally, we report only in-hospital mortality and our results did not approve for post discharge conclusions. Furthermore, our registry data identify relationships between patient versatility and in-hospital mortality and did not describe cause and effect correlations.

CONCLUSION

The current study's findings suggests that determining IVCCI < 23% during the frirst 12 hours of admission is an independent risk factor for in-hospital mortality of severe ADHF. The IVC measurements are easy to perform and ensures similar prognostic data as plasma concentrations of NT-proBNP. By contrast, measurement of LVEF did not contribute to prognostic information. Further studies needed to evaluate IVC characteristics with signs of severe ADHF in order to stratify the other risk factors for these patients.

Ethics Committee Approval: This study was approved by Health Sciences University, Kartal Kosuyolu High Specialization Training and Research Hospital, Clinical Research Ethics Committee (22.09.2020, 2020/7/349).

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Outcomes of Operated Partial-Intermediate Atrioventricular Septal Defect Patients

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ABSTRACT

Introduction: Follow-up results of patients with partial-intermediate atrioventricular septal defect (AVSD) operated in 1996-2016 at Baskent University are presented.

Patients and Methods: Data obtained from hospital records consists of echocardiographic and angiographic details before surgery, age and weight at surgery, operative details, presence of Down's syndrome, details of postoperative care, early postoperative and latest echocardiographic findings and hospitalization for reintervention.

Results: One hundred seventy eight patient-files were reviewed including 41.6% (n= 74) male, 58.4% (n= 104) female patients. The mean age of patients were 47.09 ± 44.25 (median, 30; 25 and 75 percentiles, 17 and 66.5, respectively) months. The mean body weight during the operation was 15.00 ± 11.22 (median, 11; 25 and 75 percentiles, 8.27 and 17, respectively) kg. Study group included 152 patients (85.3%) with partial AVSD and 26 of patients (14.7%) with partial AVSD. A total of 39 patients (19.1%) were diagnosed with down syndrome. Associated cardiac anomalies were present in 21.3% of patients. Operative technique was modified single-patch technique (Wilcox) in 14.6% (26 patients), pericardial patch in 25.8% (128 patients) and pericardial patch and annuloplasty in 13.5% (24 patients). The cleft in the left atrioventricular (AV) valve was closed in 92.1% all of patients.The early mortality and morbidity in the postoperative first month were calculated as 5.6 and 21.2% and the late mortality (> 1 month) and morbidity rates were calculated as 1.2% and 17%, respectively. The most common cause of late morbidity was left AV valve insufficiency, left ventricular outflow tract obstruction and therefore reoperations (15.2%).

Conclusion: Although the mortality and morbidity rates are low in partial AVSD operations, the rate of reoperations for left AV valve insufficiency and left ventricular outflow tract obstruction are still high. Patients should be done corrective surgery around age two and follow up should be performed in terms of reoperating requirement.

Key Words: Partial atrioventricular septal defect; left atrioventricular valve insufficiency; left outflow tract obstruction; reoperation.

Ameliyat Edilmiş Parsiyel-İntermediate Tip Atriyoventriküler Septal Defektli Hastalarımızın Sonuçları

ÖZ

Giriş: Bu çalışmada, Başkent Üniversitesi Tıp Fakültesinde 1996-2016 yılları arasında ameliyat edilen parsiyel ve intermediate tip atriyoventriküler septal defektli (AVSD) hastaların sonuçları değerlendirilmiştir.

Hastalar ve Yöntem: Hastane dosyaları incelenerek hastaların ameliyat öncesi ekokardiyografi ve anjiyografi bulguları, ameliyat yaşları ve ağırlıkları, ameliyat teknikleri ve süreleri, down sendromu varlığı, postoperatif dönemdeki takip ve ekokardiyografi bilgileri kaydedilmiştir.

Bulgular: Ameliyat edilen toplam 178 hastanın %41.6 (n= 74)'sı erkek, %58.4 (n= 104)'ü kızlardan oluşmuştur. Ameliyat sırasındaki yaş ortalamaları 47.09 ± 44.25 ay (median yaş 30 ay, 25. persentil 17 ay, 75. persentil 66.5 ay), ortalama vücut ağırlıkları 15.00 ± 11.22 kg (median 11 kg, 25. persentil 8.27 kg, 75. persentil 17 kg) olarak hesaplanmıştır. Hastalardan 152 (%85.3)'sinin parsiyel, 26 (%14.7)'sının intermediate tip AVSD hastaları olduğu belirlenmiştir. Hastaların %19.1 (34 hasta)'ini down sendromlu hastalar oluşturmuştur. %21.3'ünde ek kardiyak anomali tespit edilmiştir. Hastaların %14.6 (intermediate tip olan 26 hasta)'sı modifiye tek yama tekniği (wilcox) ile, %71.9 (128 hasta)'u perikard yama, %13.5 (24 hasta)'i perikard yama + annuloplasti yapılarak ameliyat edilmiştir. Hastaların %92.1'inin mevcut klefti kapatılmıştır.

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Hastaların ilk bir ay içindeki erken morbidite oranı %21.2 (35 hasta), erken mortalite oranı ise %5.6 (10 hasta) olarak hesaplanmıştır. Geç morbidite (> 1 ay) %17 (27 hasta), geç mortalite ise %1.2 (2 hasta) olarak hesaplanmıştır. En sık geç morbidite nedeni sol atriyoventriküler kapak yetersizliği, sol ventrikül çıkış yolu darlığı ve bu nedenle yapılan reoperasyonlardır (%15.2).

Sonuç: Parsiyel AVSD'lerin ameliyat sonrası erken mortalite ve morbiditesi düşük olmasına rağmen sol atriyoventriküler kapak yetersizliği ve sol ventrikül çıkış yolu darlığı nedeniyle reoperasyon oranı hala yüksektir. Hastalara çok geciktirmeden iki yaş civarında tüm düzeltme ameliyatı yapılmalı ve reoperasyon gereksinimi açısından yakın izlem yapılmalıdır.

Anahtar Kelimeler: Parsiyel atriyoventriküler septal defekt; sol atriyoventriküler kapak yetersizliği; sol ventrikül çıkış yolu darlığı; reoperasyon.

INTRODUCTION

Atrioventricular septal defect (AVSD) is a congenital heart disease involving the atrioventricular valves, the inlet part of the interventricular septum and the primum part of the atrial septum to varying degrees. Among congenital heart diseases, AVSD is seen with a frequency of 2.9% and approximately 25% of them are partial type AVSD[1]. If there is no symptom in partial AVSD, corrective surgery at an early age is recommended at preschool age but if there are signs of congestive heart failure due to severe left atrioventricular valve insufficiency and atrial shunt[1-3]. Atrioventricular block requiring pacemaker, significant mitral valve insufficiency (MR), left ventricular outflow tract obstruction (LVOTO) may occur after surgery, and patients may need to be operated again[3].

In our study, we aimed to present long-term results by evaluating the data of patients with partial and intermediate type AVSD who were operated at Baskent University Medical Faculty Hospital between 1996 and 2016.

PATIENTS and METHODS

The data of 178 patients with partial and intermediate type AVSD who were operated at Baskent University Medical Faculty Hospital between 1996 and 2016 were retrospectively reviewed. This study was certified by Baskent University Medical and Health Sciences Research Board (Project number: KA19/163). Patients' surgical age, intraoperative weight, preoperative echocardiography findings (especially AV valve insufficiency), presence of down syndrome, pulmonary artery pressures and pulmonary vascular resistance (PVR) determined in preoperative catheter angiography, technique used in surgery, cardiopulmonary bypass and aortic clamp times were examined. Postoperative mechanical ventilation times, inotropic agent administration times, inotrope scores, length of stay in intensive care, presence of infection, postoperative AV block and arrhythmia, early mortality and morbidity, discharge time, postoperative early echocardiography findings, follow-up times, and the last echocardiographic findings, late mortality and morbidity during follow-up were recorded. The inotrop score was calculated as follows[4,5]; dopamine μg/kg/min x 1 + dobutamine μg/kg/min x 1 + adrenaline μg/kg/min x 100 + milrinone μg/kg/min x 10.

Statistical Analysis

Statistical analysis were performed using the "Statistical Package for the Social Sciences software (version 20 for Windows; SPSS, Chicago, IL, USA)" program. T test and analysis of variance (ANOVA) were used for comparisons of mean between groups, and Chi-square test was used to compare categorical variables. For the reoperation risk factor significance, cox regression analysis was used. Statistically, a p value of < 0.05 was considered significant.

RESULTS

Of the 178 operated patients, 41.6% (n= 74) were male and 58.4% (n= 104) were female. Mean age at surgery 47.09 ± 44.25 months (median age 30 months, 25th percentile 17 months, 75th percentile 66.5 months), mean body weight 15.00 ± 11.22 kilograms (kg) (median 11 kg, 25th percentile 8.27 kg, 75th percentile 17 kg). One hundred fifty two of the patients were partial and 26 were intermediate type AVSD. 19.1% of the patients (34 patients) were diagnosed with down syndrome. 21.3% had additional cardiac anomaly. The most common additional cardiac anomalies were secundum atrial septal defect (ASD) and patent ductus arteriosus (PDA). General characteristics of the patients are shown in Table 1. 14.6% of the patients were operated with modified single patch technique (wilcox), 71.9% (128 patients) pericardial patch, 13.5% (24 patients) pericardial patch + annuloplasty. The cleft was closed in 92.1% of the patients.

The early morbidity of the patients in the first month was 21.2% (35 patients), the most common cause of morbidity was pericardial effusion and infection. Early mortality was calculated as 5.6% (10 patients). When early mortality is calculated separately; It was found that 15.3% (four patients) for the intermediate type and 3.6% (six patients) for the partial type. Five of the patients died in the first 48 hours postoperatively due to hemodynamic instability (four patients partial, one patient intermediate type), four patients sepsis (one partial, three intermediate type), one patient died on the 13th postoperative day due to sudden arrhythmia and cardiac arrest (partial type). In 36% of the patients, in the preoperative period, in 27.6% in the postoperative period, and in 48% of

Table 1. General characteristics of patients

	Mean ± SD (min-max)
Age (month)	47.09 ± 44.25 (3-240)
Weight (kg)	15.00 ± 11.22 (3-64)
Pulmonary artery pressure (mmHg)	22.83 ± 8.54 (9-62)
Pulmonary vascular resistance	1.51 ± 1.19 (0.1-7.9)
Cardiopulmonary bypass time (min)	71.93 ± 24.59 (36-185)
Aortic clamp time (min)	48.48 ± 19.32 (22-141)
Inotrop time (day)	2.65 ± 5.10 (0.2-53)
Inotrop score	7.61 ± 12.38 (2-122)
Mechanical ventilator duration (hour)	20.40 ± 19.32 (4-456)
Intensive care unit stay (day)	3.97 ± 9.22 (1-110)
Time to discharge (day)	6.58 ± 4.59 (3-24)
AV valve reoperation time (year)	4.51 ± 2.73 (1-10)
LVOTO reoperation time (year)	2.62 ± 1.88 (0.5-5)

AV: Atrioventricular, LVOTO: Left ventricular outflow tract obstruction, SD: Standard deviation.

the patients, 3rd and 4th degree mitral insufficiency (MR) were detected in the last echocardiography. No significant difference was found between the surgical techniques in terms of the degree of MR in the postoperative period (p= 0.135). There was no significant difference between preoperative MR (p= 0.640) and postoperative MR (p= 0.639) in patients with partial and intermediate defects.

Postoperative infections, confirmed by blood, urine, or tracheal aspirate cultures, were seen in 7.8% of the patients. Postoperative complete AV block developed in 21 patients (11.8%), of which only five patients had permanent AV block and pacemaker was implanted. Late morbidity (> 1 month) was 17% (27 patients), and late mortality was 1.2% (two patients). The most common late morbidity reasons were MR, left ventricular outflow tract obstruction (LVOTO) and reoperations performed for this reason (15.2%).

Reoperations

Valve surgery was performed in 21 patients (11.8%) due to significant MR. Mitral valve repair was performed in 7 patients (3.9%) and mitral valve replacement in 14 patients (7.9%). Nineteen of these patients had partial defects and two of them were intermediate type. Postoperative LVOTO developed in nine patients and 4 (2.2%) of these were operated. All of these patients were those who were repaired with partial type and pericardial patch. It was observed that two patients had undergone reoperation for both valve and LVOTO. The mean time for reoperation for MR was 4.48 ± 2.65 (1-10) years, and for LVOTO was 2.62 ± 1.88 (0.5-5) years.

In terms of reoperation for left AV valve and LVOTO, no significant risk factor was found for reoperation in the analysis performed by determining the absence of down syndrome, surgery age and weight, mitral insufficiency before and after surgery, type of AVSD, surgical technique, not closing the cleft, as risk factors.

Comparison of Patients with and Without Down Syndrome

Patients with and without Down's syndrome, gender, age of surgery, body weight during surgery, AVSD type, preoperative pulmonary artery pressure (PAP), preoperative and postoperative MR degrees, cardiopulmonary bypass (CPB), aortic clamp times, intensive care inotrope score, the durations of mechanical ventilation were compared in duration of stay in the intensive care unit, duration of discharge, postoperative AV block and infection, early mortality and morbidity, late mortality and morbidity, reoperations due to valve or LVOTO (Table 2). It was observed that patients with down syndrome had more postoperative infections (p= 0.038). While reoperation was required in patients who did not have down syndrome due to MR and LVOTO, it was determined that patients with down syndrome did not undergo reoperation (p= 0.013). There was no significant difference between the groups in terms of other parameters.

Comparison of Surgical Techniques

Patients were grouped according to the surgical techniques and compared according to the same parameters. Preoperative MR of the patients who underwent annuloplasty was higher than the others (p= 0.008) and the discharge time of these patients was shorter (p= 0.008). Intermediate type AVSD was operated with the Wilcox technique, these patients were found to have higher preoperative PAP (p= 0.001) and PVR (p= 0.001), early morbidity higher in this group (p= 0.003), and more hospital stay (p= 0.008). There was no significant difference between groups in terms of other parameters (Table 3).

Early Mortality

In terms of early mortality, the presence of down syndrome, AVSD type, surgery age and weight, surgery technique, CPB, aortic clamp time, postoperative AV block development and infection were compared. It was found that early mortality was higher in the intermediate type (p= 0.019), in patients with lower age (p= 0.011) and lower weight during surgery (p= 0.013), higher preoperative PAP (p= 0.019), longer CPB duration (p= 0.016), and long aortic clamp time (p= 0.001).

Table 2. Comparison of down and not affected by down syndromes patients

	Down syndrome (n= 34) (mean ± SD)	Not affected by down syndrome (n= 144) (mean ± SD)	p value
Age (month)	47.20 ± 42.47	47.06 ± 44.81	0.987
Weight (kg)	14.81 ± 13.09	15.05 ± 10.78	0.923
Pulmonary artery pressure (mmHg)	24.75 ± 9.85	22.41 ± 8.18	0.702
Pulmonary vascular resistance	1.76 ± 1.44	1.44 ± 1.12	0.231
Cardiopulmonary bypass time (min)	73.41 ± 24.98	71.58 ± 24.57	0.702
Aortic clamp time (min)	48.12 ± 16.87	48.57 ± 19.91	0.893
Inotrop time (day)	1.71 ± 1.05	2.89 ± 5.69	0.269
Inotrop score	6.04 ± 4.42	8.02 ± 13.70	0.206
Mechanical ventilator duration (hour)	15.21 ± 12.59	21.52 ± 49.22	0.195
Intensive care unit stay (day)	3.28 ± 2.05	4.12 ± 10.11	0.375
Time to discharge (day)	7.75 ± 5.73	6.19 ± 4.17	0.400
AV valve reoperation time (year)	-	4.15 ± 2.66	
LVOTO reoperation time (year)	-	2.62 ± 1.88	

AV: Atrioventricular, LVOTO: Left ventricular outflow tract obstruction, SD: Standard deviation.

Table 3. Comparison of surgical techniques

	Modified single patch (Wilcox) (mean ± SD)	Pericardium patch (mean ± SD)	Pericardium patch + annuloplasty (mean ± SD)	p value
Age (month)	29.51 ± 33.73	50.99 ± 44.90	46.20 ± 47.90	0.978
Weight (kg)	10.35 ± 6.18	15.80 ± 11.57	16.03 ± 12.76	0.655
Pulmonary artery pressure (mmHg)	28.85 ± 10.68	21.92 ± 7.71	20.14 ± 6.56	**0.001**
Pulmonary vascular resistance	2.31 ± 1.98	1.44 ± 0.95	0.94 ± 0.62	**0.001**
Cardiopulmonary bypass time (min)	74.81 ± 18.99	69.41 ± 25.23	82.04 ± 24.61	0.384
Aortic clamp time (min)	53.70 ± 13.49	46.43 ± 20.98	53.46 ± 13.20	0.278
Inotrop time (day)	4.34 ± 5.67	2.56 ± 5.52	1.45 ± 0.94	0.154
Inotrop score	6.76 ± 12.82	7.67 ± 13.47	8.13 ± 6.23	0.847
Mechanical ventilator duration (hour)	29.20 ± 52.19	20.07 ± 47.78	12.79 ± 6.23	0.072
Intensive care unit stay (day)	4.81 ± 5.25	4.12 ± 10.73	2.33 ± 1.09	0.096
Time to discharge (day)	11.60 ± 6.02	5.08 ± 2.01	7.28 ± 5.73	**0.008**
AV valve reoperation time (year)	4.95 ± 2.89	4.23 ± 2.77	3.16 ± 2.56	0.757
LVOTO reoperation time (year)	-	2.62 ± 1.88	-	

AV: Atrioventricular, LVOTO: Left ventricular outflow tract obstruction, SD: Standard deviation.

DISCUSSION

In the previous years in partial type AVSD, if there are no signs of heart failure, it was recommended to perform all correction surgery at preschool ages, but nowadays, it has been shown that the results of surgery are better at earlier ages[2,6-9]. Many centers prefer the age of three to four years as the age of surgery due to lower surgical complications. However, Devlin et al. did not find an increase in early mortality, left AV insufficiency or stenosis, pacemaker need, need for reoperation for AV valve or LVOTO in patients who underwent early repair around the median 1.5 years in their series, and they recommended surgery around the age of two years[8].

The early mortality of partial AVSDs in the first 1 month postoperatively has decreased from 10% to 1-5% in the last 20 years[2,3,7,8]. In our study, early mortality was 5.6% in all patients, 3.6% in the partial type, and the median age at surgery was 30 months.

Although early mortality is low in atrioventricular septal defects, the main problem is the high rate of reoperation due to left AV valve insufficiency and/or LVOTO. The reoperation rate for AVSD has been reported as 6-28%[2,7,8,10]. The most common cause of reoperation is AV valve insufficiency and its frequency is 5-19%[2,11]. Moderate or severe left AV valve insufficiency in the early postoperative period causes reoperation[2,7,11-14]. Bove et al., stated that left AV valve insufficiency was caused by technical deficiencies such as separation of the cleft suture or incomplete cleft closure, or insufficient repair caused by not clear recognition of the morphological anomalies of the valve[11]. Anatomic residual lesions of the left AV valve are common causes of reoperation in children with partial AVSD. The most common anomalies; anomaly adhering chordae and/or additional papillary muscle anomalies are asymmetric development of one of the superior leaflets. Subvalvular apparatus anomalies of the valve are also common in partial AVSD[11,13]. Therefore, surgery in partial AVSD should be performed before these secondary fibrotic changes begin, and it is preferably recommended before two years of age[8,11]. Failure to close the cleft in the left AV valve causes significant valve insufficiency in the postoperative period[2,14,15]. Kleft closure and postoperative annular dilatation are the most important factors affecting the results of valve repair[14,15]. Palada et al. recommended ring-shaped reduction with cleft repair to reduce reoperation rates and prevent long-term valve insufficiency[15]. The reoperation rate was 11.8% in our patients due to left AV valve insufficiency. It was observed that 92.1% of the patients had cleft closed during surgery. However, no difference was found between surgical techniques in terms of postoperative mitral insufficiency and reoperation. In our patient group, preoperative and postoperative MR, keeping the cleft open were not found as risk factors for reoperation for the left AV valve. Left ventricular outflow tract obstruction is the second most common cause of operation in AVSD and its frequency is reported as 1-10%[3,8,16-19]. Since the aortic valve is located in front and to the right in AVSDs, it cannot be placed between the AV valves normally. The LVOT is longer and its distal part is narrower. Elonge and abnormal angled LVOT and various intrinsic anomalies facilitate the formation of stenosis. The abnormal AV valve and subvalvar apparatus anatomy also greatly affects the LVOT geometry. Abnormal adhering AV valve chordates and accessory fibrous bands also cause stenosis. Due to these anatomical features in AVSD, LVOT stenosis may develop at many different levels after surgery[3,8,16-19].

Although the modified single patch technique was held responsible for LVOTO in the past, many publications have shown that it is not related[16-20]. In this study, we compared surgical techniques and types of AVSD in terms of LVOTO development, and we found no statistically significant difference. Again, there was no statistically significant difference between surgical techniques and types of AVSD between reoperation for AV valve and LVOTO. In previous studies, it was reported that there was no difference between AVSD types in terms of reoperation frequency due to AV valve and LVOTO[13,15]. However, in our study in which we compared partial and complete AVSD, we reported that postoperative valve insufficiency and therefore the rate of reoperation were high in partial AVSD[21]. Since patients with down syndrome have a higher tendency to pulmonary vascular reactivity and respiratory complications, the postoperative period of mechanical ventilation is longer, the risk of infection is higher, and the duration of intensive care stay is longer[22,23]. However, in many studies, down syndrome was not found as a risk factor for operative mortality. Mortality rates are the same as patients without down syndrome, reoperation rates were lower[23-25]. We also found that patients with down syndrome had significantly more infections in the postoperative period. However, no difference was found between inotrope score, mechanical ventilator, intensive care and discharge times. There was no reoperation in down syndrome patients due to AV valve insufficiency or LVOTO.

CONCLUSION

Postoperative early mortality of partial AVSDs is low, but the reoperation rate is high in the late period due to left AV valve insufficiency and LVOTO. All correction surgery should be performed at the age of two years without delay and close monitoring should be performed in terms of the need for reoperation.

Ethics Committee Approval: This study was approved by Baskent University Medical and Health Sciences Research Board (Date: 07.05.2019 - Project Number: KA19/163).

Informed Consent: Informed consent was obtained.

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Initial Experience with Cadaveric Lobar Lung Transplantation in Turkey

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ABSTRACT

Introduction: Lung transplantation is the final treatment option for end-stage lung diseases. A scarce donor pool is the primary cause of waiting list mortality. Lobar lung transplantation has been proposed to overcome the donor pool shortage. Herein we present our initial experience with patients who underwent lobar lung transplantation.

Patients and Methods: This single-center retrospective study included patients who underwent cadaveric lobar lung transplantation between December 2016 and December 2018 at our Lung Transplant Center. The procedure was performed only in patients with an emergency status.

Results: Of the 55 lung transplants during the study period, six [10.9%; four female, two male; median age, 35.3 years (range, 22-42 years)] were lobar lung transplants. The indications were bronchiectasis (three patients), chronic obstructive pulmonary disease (one patient), cystic lung disease (one patient), and lepidic type adenocarcinoma (one patient). The transplantations included bilateral lobar lung in two patients, the right single lung and the left lower lobe in two patients, and the left single lung and the right lower lobe in two patients. One-year mortality was 16.6% (1/6). Two patients died 23 and 24 months after lung transplantation. Three patients were alive at the last follow-up (at 24, 25, 47 months).

Conclusion: Lobar lung transplantation can be a life-saving treatment option in critically ill patients with small thoracic cavities to overcome donor shortage. Furthermore, it is a feasible operative technique in recipients with a reduced unilateral thoracic cavity.

Key Words: Cadaveric donor; donor-recipient size matching; lobar lung transplantation.

Kadavradan Lober Akciğer Nakli: Türkiye'de İlk Deneyimler

ÖZ

Giriş: Akciğer nakli, son dönem akciğer hastalıkları için son tedavi seçeneğidir. Donör havuzunun azlığı, bekleme listesi ölümlerinin başlıca nedenidir. Donör havuzu azlığının üstesinden gelmek için lober akciğer nakli önerilmiştir. Bu çalışmada, lober akciğer nakli yapılan hastalar ile ilgili ilk deneyimimiz sunulmuştur.

Hastalar ve Yöntem: Bu tek merkezli retrospektif çalışma, akciğer nakli merkezimizde Aralık 2016-Aralık 2018 tarihleri arasında kadavra lober akciğer nakli yapılan hastaları içermektedir. Bu prosedür sadece acil durumu olan hastalarda uygulanmıştır.

Bulgular: Çalışma dönemindeki 55 akciğer naklinden altısı [%10.9; dördü kadın, ikisi erkek; medyan yaş 35.3 yıl (aralık, 22-42 yaş)] lober akciğer nakli idi. Endikasyonlar bronşektazi (üç hasta), kronik obstrüktif akciğer hastalığı (bir hasta), kistik akciğer hastalığı (bir hasta) ve lepidik tip adenokarsinom (bir hasta) idi. İki hastada bilateral lober akciğer, iki hastada sağ tek akciğer ve sol alt lob, iki hastada sol tek akciğer ve sağ alt lob akciğer nakli idi. Bir yıllık mortalite %16.6 (1/6) idi. Akciğer naklinden sonra 23. ve 24. ayda iki hasta ölmüştür. Üç hasta halen hayattadır (24, 25 ve 47. aylarda).

Sonuç: Lober akciğer nakli, donör eksikliğinin üstesinden gelmek için küçük göğüs boşlukları olan kritik hastalarda hayat kurtarıcı bir tedavi seçeneği olabilir. Aynı zamanda, tek taraflı göğüs boşluğu azalmış alıcılarda uygulanabilir bir ameliyat tekniğidir.

Anahtar Kelimeler: Kadavra donör; donör-alıcı boyutu eşleştirme; lober akciğer nakli.

INTRODUCTION

Lung transplantation has emerged as a life-saving treatment option for end-stage lung diseases with accumulating surgical experience and improved immunosuppressive therapy, donor care and protection, infection treatment, postoperative follow-up, and medical

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technology. Survival outcomes have also improved with increasing lung transplants in the recent years. Because of the disproportionate increase in the number of transplant candidates vs. cadaver donor lungs, availability of feasible donors is a challenge. In particular, patients with a small thoracic cavity and end-stage lung disease, such as pulmonary fibrosis and cystic fibrosis, experience long waiting times for appropriately sized donor lungs. Cadaveric lobar lung transplantation can be a life-saving option for such patients with worsening or critical conditions.

In 1994, Bisson et al. reported the first cadaveric bilateral lobar lung transplantation in two recipients with a diagnosis of cystic fibrosis[1]. Subsequently, several centers have published their outcomes with cadaveric lobar lung transplantation[2-4]. Lobar lung transplantation is not performed routinely; owing to the difficulty of donor and recipient lung size matching, only a few experienced centers perform this procedure. Small grafts cause lung hyperextension and limit exercise tolerance because of hemodynamic deterioration, whereas oversized grafts cause atelectasis, diaphragm dysfunction, high pulmonary vascular resistance, and poor gas exchange.

Further challenges with lobar lung transplantation include unexpectedly large donor organs, pathology localized in a single lobe, and the small size of the unilateral thoracic cavity. We aimed to present the outcomes of cadaveric lobar lung transplantation at our institution.

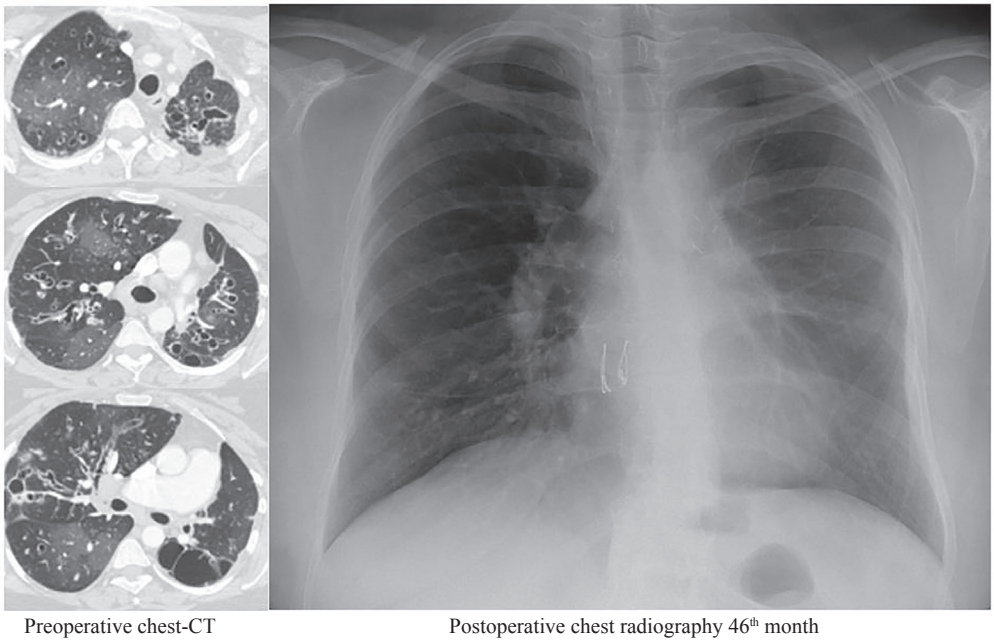
PATIENTS and METHODS

This single-center retrospective study included cadaveric lobar lung transplants performed between December 2016 and December 2018 at Kartal Kosuyolu High Specialization Training and Research Hospital, Istanbul, Turkey. Lobar lung transplantation was performed in patients with a small chest wall cavity with a deteriorating condition that precluded waiting for an appropriately sized donor lung. Furthermore, it was performed unilaterally owing to a decreased thoracic cavity volume because of underlying disease or previous lobectomy (Figure 1).

Patients with end-stage lung disease were listed for lung transplantation according to the consensus document for the selection of lung transplant candidates of the Pulmonary Transplantation Council of the International Society for Heart and Lung Transplantation[5]. Demographic characteristics, preoperative patient data, intraoperative data, length of intensive care unit stay, and primary graft dysfunction (PGD) and survival data of the patients were recorded. All data were recorded prospectively and retrospectively analyzed. PGD was defined according to the 2016 report of the International Society for Heart and Lung Transplantation Working Group on PGD[6].

Donor Selection

The predicted total lung capacities (pTLC) of the donor and the recipient were calculated using a formula considering donor



Preoperative chest-CT examination

Postoperative chest radiography 46th month

Figure 1. Right lung and left lower lobe lung transplantation.

height and sex[7]. The pTLC of the donors ranged between 75% and 125% of the pTLC of the recipients. The final decision was made by visual examination in the operating room.

The estimated donor total lung capacity (L) was calculated as follows:

pTLC (male)= 7.99 x height in meters - 7.08

pTLC (female)= 6.6 x height in meters - 5.79.

The total lung capacity (sr-TLC) of the transplanted lung was calculated as follows:

sr-TLC = donor TLC x (1 - S x 0.0526)

Where, S is the number of resected segments.

Surgery Procedure

Donor lobectomy was performed on the back table. On the right, an upper lobectomy was performed to transplant the middle and lower lobes. The oblique fissure was dissected, and the interlobar pulmonary artery was prepared. The upper lobe vein was cut to preserve the atrial cuff covering both the right upper and lower veins. The upper part of the oblique fissure between the upper and lower lobes and the horizontal fissure between the upper and middle lobes were separated using a stapler. The branches of the upper lobe of the pulmonary artery were dissected and cut. Bronchial transection was performed on only one ring of the middle lobe and the apical segment bronchus of the lower lobe in the distal part of the intermediary bronchus. Care was taken to protect the peribronchial connective tissue. An aortic graft obtained from the donor was used when atrial anastomosis was required to expand and preserve venous flow from the middle lobe in the donor. A sufficient length of the proximal donor pulmonary artery was maintained sufficiently to allow anastomosis without any tension.

An upper lobectomy was performed to transplant the left lower lobe. The fissure was prepared, and the bridge between the upper and lower lobes was cut with a stapler. The interlobar pulmonary artery was dissected. The lingula artery and the branches of the upper lobe were dissected and cut. The upper pulmonary vein was ligated and cut. The atrial cuff was preserved. The left lower lobe bronchus was cut at the bronchial bifurcation level, and the apical segment bronchus of the lower lobe was preserved to allow anastomosis.

In our clinic, indications for the use of intraoperative central venoarterial extracorporeal membrane oxygenation (C-VA-ECMO) were hypercapnia ($PaCO_2$ > 55 mmHg), arterial saturation < 85%, cardiac index < 2 L/min/m^2, and mPAP > 40 mmHg. C-VA-ECMO was used for intraoperative cardiopulmonary support by cannulating the right atrial auricle and the ascending aorta. A 15-19 French (Fr) arterial cannula was used for the aorta, and a 2-stage venous cannula or a 36 Fr curved-tip cannula was used for the right atrium. C-VA-ECMO was performed after unilateral pneumonectomy, without considering the aforementioned criteria, during bilateral lower lobe transplantation. Whole-lung and unilateral lobar transplantation were performed in cases with a unilateral small thoracic cavity. In the case of unbalanced lung perfusion, pneumonectomy of the less-perfused lung was first performed. After strict bleeding control, C-VA-ECMO support was initiated. C-VA-ECMO was gradually weaned and terminated after the implantation of both lungs. C-VA-ECMO support was discontinued in patients who were hemodynamically stable and had the following arterial blood measures: PaO_2 > 70 mmHg, $PaCO_2$ of 35-50 mmHg, tidal volume of 6-10 mL/kg, positive end-expiratory pressure within acceptable limits (10 cmH_2O), and low pulmonary artery pressure without right ventricular failure.

The study was approved by the Kartal Kosuyolu High Specialization Training and Research Hospital Local Ethics Committee (ID: 2020/8/355).

RESULTS

Between December 2016 and December 2019, 55 patients underwent lung transplantation, of which 6 (10.9%) underwent lobar transplantation from deceased donors. Of the six patients, four were female and two were male; their median age was 35.3 years (range, 22-42 years). The primary diagnoses among the patients were bronchiectasis (three patients), chronic obstructive pulmonary disease (one patient), cystic lung disease (one patient), and lepidic type adenocarcinoma (one patient). ECMO was used a bridge to lung transplantation in one patient. The mean resting O_2 flow rate was 5.6 L/min (range, 4-10 L/min) during the pre-transplant examination for lung transplantation feasibility. Hypoxemia (PaO_2 < 60 mmHg) and hypercarbia ($PaCO_2$ > 45 mmHg) were observed in all and four patients, respectively, on blood arterial gas analyses. Pulmonary function tests could not be performed in four patients. Four patients did not achieve maximal exercise capacity during the 6-minute walk test (6MWT). Right ventricular dilatation was seen in three patients; the mean tricuspid annular plane systolic excursion value was 20 mm (range, 15-26 mm) on echocardiographic examination. Pulmonary hypertension was observed in three patients, as measured using right heart catheterization with the patient supine and at rest (Table 1).

The cause of donor brain death was intracranial hemorrhage in two patients and head trauma in four patients. The mean oxygenation index [partial pressure of oxygen (PaO_2) at a

Table 1. Clinical characteristics of patients

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age	42	35	58	27	28	22
Gender	Male	Female	Female	Female	Female	Male
Height	175	157	157	158	159	180
Diagnosis	Adenocarcinoma lepidic type	Bronchiectasis	COPD	Cystic lung disease	Bronchiectasis	Bronchiectasis
Waiting list time days	4	36	54	181	363	194
BMI (kg/m^2)	29.3	25.6	24.1	16.2	16.1	28
O_2-therapy (L/min)	ECMO (bridge to lung transplantaion)	5	4	5	10	4
Arterial blood gas						
pH	None	7.34	7.4	7.42	7.4	7.33
PaO_2		42.5	50.6	42.6	52.4	46.7
$PaCO_2$		60.9	52.5	56.7	38	66.1
Sat %		79.9	86	89.8	69.2	78.5
Pulmonary function test						
FVC (% of predicted)	Unperformed	23	91	24	34	35
FEV_1 (% of predicted)		18	28	22	27	23
DLCO (% of predicted)		Unperformed	Unperformed	Unperformed	24	38
6MWT						
Distance m	Unperformed	Unperformed	66	290	Unperformed	266
Final SpO_2 (%)			75	83		85
Echocardiogram						
RV dilation	+	-	-	-	+	+
TAPSE mm	18	16	26	26	15	21
Right heart catheterization						
PABs (mmHg)	None	41	28	25	70	44
PABm (mmHg)		26	17	13	49	30
CO (mL/min)		5.54	3.4	5	4.4	6.5
PAWP (mmHg)		-	-	6	8	12

COPD: Chronic obstructive pulmonary disease, BMI: Body mass index, ECMO: Extracorporeal membrane oxygenation, FVC: Forced vital capacity, FEV_1: Expiratory volume in one second, DLCO: Diffusing capacity for carbon monoxide, 6-MWT: 6 minute walk test, RV: Right ventricle, RHC: Right heart catheterization, PAPs: Systolic pulmonary arterial pressure, PAPm: Mean pulmonary arterial pressure, CO: Cardiac output, PAWP: Pulmonary artery wedge pressure.

positive end-expiratory pressure (PEEP) of 5 mmHg and fraction of inspired oxygen (FiO_2) of 1.0] at the time of organ offer was 384 (range, 269-480). The mean mechanical ventilation time was 4.16 days (range, 2-9 days). Three donors had a history of smoking (> 20 packs/year; Table 2). The pTLC of the donor was between 76% and 114% of the pTLC of the recipient. The donor-recipient sex match was male to female in three patients, female to female in one patient, female to male in one patient, and male to male in one patient (Table 3).

The mean waiting time was 139 days (range, 4-363 days). The lobar lung transplantations performed were bilateral in two patients, whereas two patients received the right single lung and left lower lobe and two patients received the left single lung and right lower lobe transplant. All transplantation was performed with C-VA-ECMO support. ECMO as a bridge to lung transplantation was used in one patient. The mean mechanical ventilation duration and intensive care unit stay were 4.5 days (range, 1-4 days) and 7.8 days (range, 4-20 days), respectively. The mean red blood cell, fresh frozen plasma, and pooled platelet units transfused peri- and post-operatively were 11.3 units (range, 6-21 units), 9.5 units (6-11 units), and 1.3 units (0-3 units), respectively (Table 4).

One-year mortality was 16.6% (1/6). The causes of death included multiorgan failure on postoperative day 85, relapse of lepidic type adenocarcinoma on postoperative month 23, and chronic lung allograft dysfunction on postoperative month 24. The second patient and two patients who underwent bilateral lower lobe transplantation are alive without any complaints on follow-up at postoperative months 24, 25, and 47 (Figure 2).

Table 2. Donor characteristics

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Cause of death	Intracranial hemorrhage	Head trauma	Intracranial hemorrhage	Head trauma	Head trauma	Head trauma
Gender	Female	Male	Female	Male	Male	Male
Age	21	19	51	39	52	37
Height (cm)	170	172	160	182	180	181
Heavy smoker (> 20 pack/year)	-	-	+	+	+	-
PaO_2 mmHg on FiO_2 of 1.0	351	394	473	480	341	269
Intubation time (day)	2	2	4	3	5	9

FiO_2: Fraction of inspired oxygen, pTLC: Predicted total lung capacity.

Table 3. Gender and pTLC mismatch

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Donor to recipent	F/M	M/F	F/F	M/F	M/F	M/M
Recipent pTLC (Liter)	5.08	4.57	4.57	4.63	4.70	7.30
Donor pTLC (Liter)	5.79	6.66	4.77	7.46	7.30	7.38
Sr-TLC	4.26	5.25	3.51	4.71	3.84	5.84
Calculated range in D/R TLC ratio	-0.83	+1.14	-0.76	+1.01	-0.81	-0.8

pTLC: Predicted total lung capacity, M: Male, F: Female, Sr-TLC: Total lung capacity in the transplanted lung, D/R: Donor/recipent.

DISCUSSION

Despite the recommendations of the Pulmonary Transplantation Council of the International Society for Heart and Lung Transplantation, in our experience, patients with end-stage lung disease were not referred at the optimal time and were listed for lung transplantation despite significant deterioration in respiratory function. Most patients were already on long-term oxygen therapy, had pulmonary hypertension, and were unable to perform pulmonary function tests and the 6MWT[5]. Owing to the deteriorating condition, insufficient time to identify a suitable donor was available in all patients, leaving the use of an oversized lung graft by lobectomy as the only option to prevent waiting list mortality. The Toronto Lung Transplant Group, one of the most experienced teams, has performed lobar lung transplantation in 4.5% of all standard lung transplantations[8]. In our study, the ratio of lobar lung transplantation was 10.9%. This high ratio could be attributed to a high number of critically ill patients and the small number of waitlisted patients. Another reason could be that most patients had underlying diseases, such as bronchiectasis, that caused unilateral lung volume loss.

Selecting between wedge resection or anatomic lobectomy in case of unexpected size mismatch during the procedure is challenging. Loizzi et al. compared patients who underwent standard lung transplant with those who underwent lobar lung transplant. They concluded that the upper limit for the donor to recipient pTLC ratio should be 1.15-1.20, with a definite preference for lobar transplantation when the ratio is > 1.20[9]. Lobectomy can be performed on the back-table or after implantation to reduce size. Using back-table lobectomy can help reduce ischemia time as it can be performed by a separate surgeon concurrently with recipient preparation and prevents impaired visibility of the hilum because of the large lung thoracic cavity, this preventing mismatch. Another benefit of back-table lobectomy over post-implant lobectomy

Table 4. Intraoperative data and outcomes

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Transplantation type	Left lung Right lower lob	Right lung Left lower lob	Left lung Right lower lob	Right middle + lower lob left lower lob	Bilateral lower lob	Right lung Left lower lob
Intraoperative ECMO	+	+	+	+	+	+
Number of transfusions on first postoperative day, units						
RBC	21	6	15	10	6	10
FFP	11	6	11	9	11	9
Pooled platelet	1	2	3	3	1	1
Severe PGD	+	-	+	-	+	-
Mechanical ventilation (days)	14	1	3	2	3	4
ICU stay (days)	20	4	10	4	5	4
Hospital stay (day)	52	22	44	17	34	39
Mortality	Died	Alive	Died	Alive	Alive	Died
Survival (month)	23	47	3	25	24	23
Cause of death	Relapse		Multi-organ failure progression			CLAD

ECMO: Extracorporeal membrane oxygenation, FFP: Fresh frozen plasma, RBC: Red blood cells, PGD: Primary graft dysfunction, ICU: Intensive care unit.

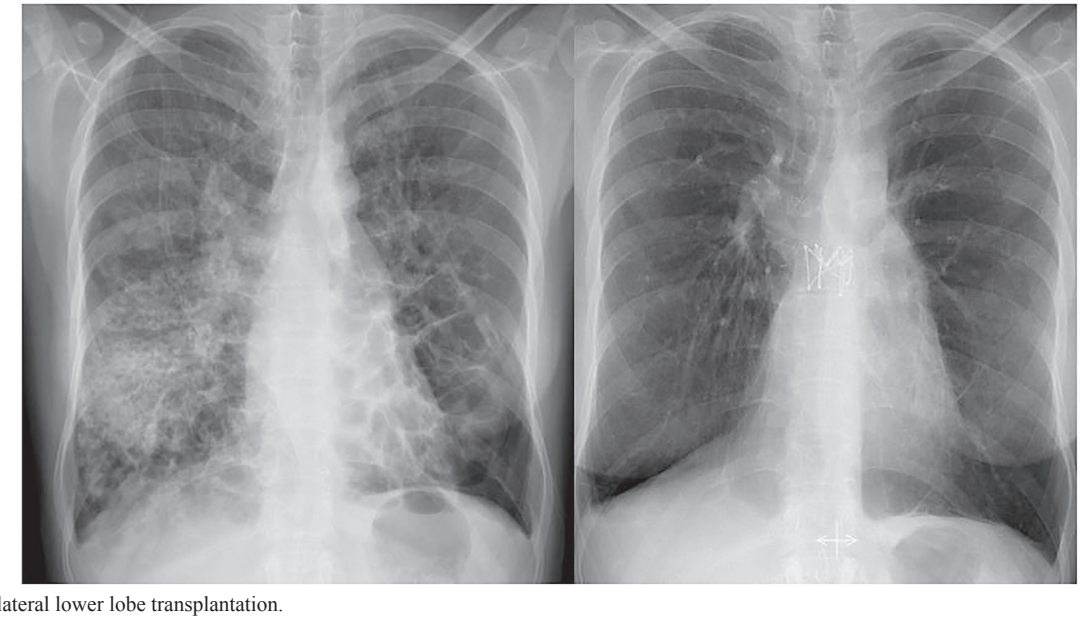


Figure 2. Bilateral lower lobe transplantation.

is that a bronchial stump is not required. However, performing back-table lobectomy poses technical challenges as dissection becomes difficult owing to the lack of blood circulation in the vessels, whereas post-transplant lobectomy may be challenging because of the large size of the lung within a small chest cavity. Another disadvantage of post-implantation lobectomy is that the manipulation of the recently perfused lung may cause reperfusion injury, which may cause further damage to the transplanted lung.

Lobar lung transplantation candidates are at higher risk owing to hemodynamic instability because of their poor general condition during the perioperative reperfusion phase.

Perioperative management for lobar lung transplant recipients differs from that for standard lung transplant recipients. After implantation, the implanted lobe receives almost all the cardiac output during the remnant native lung pneumonectomy. This excessive increase in pulmonary circulation causes increased pulmonary pressure and extravascular fluid leakage and eventually, pulmonary edema. Cardiopulmonary bypass or ECMO support is recommended during the procedure to prevent overloading of the pulmonary vascular bed[10]. Peripheral or central venoarterial ECMO, which requires less heparin and provides thoracic epidural analgesia, has replaced CPB[11].

Cadaveric lobar lung transplantation is increasingly being performed to expand the donor pool for critically ill patients and patients with a deteriorating condition while waiting. However, although lobectomy is a standard and simple technique, lobar lung transplantation is not performed routinely. Only a few centers have reported their short- and long-term results with lobar lung transplantation in the last decade[2,3,8,12]. In a report published by the Toronto Lung Transplant Team that included 75 patients, the 1-, 3-, and 5-year survival rates did not differ significantly between lobar lung transplantation and standard lung transplantation recipients (73.2% vs. 84.4%, 56.9% vs. 68.4%, and 50.4% vs. 55.8%, respectively)[8]. We experienced only one in-hospital mortality; while two patients died at 23 and 24 months postoperatively, these deaths directly related to the lobar transplantation.

Early postoperative mortality among transplant recipients ranges from 0% to 28%[2,3,13,14]. Reportedly, mortality is higher among lobar lung transplants than among standard lung transplants[4]. However, most studies have reported no significant differences in long-term survival among both groups[15]. Lobar lung transplantations are performed mostly urgently owing to patient condition deterioration[16]. In our study, two patients who underwent lower lobar transplantation had an urgent status and both survived. No complications were seen within two years postoperatively. Whether to perform lobar lung transplantation instead of standard lung transplantation in case of an available appropriately sized recipient remains unclear. Although the two urgent patients survived with acceptable outcomes, lobar lung transplantation is not routinely performed at our clinic. However, given the increase in the number of transplant candidates with small thoracic cavities, such as those with cystic fibrosis, it is poised to become routine practice owing to donor unavailability. Future case series evidence would better our understanding of technical feasibility and outcomes.

This study has several limitations. This was a retrospective, single-center study. A control group was absent. Owing to our limited experience with patients undergoing lobar lung transplantation in Turkey, our sample size was limited. Regardless of the limitations, in our experience, lobar lung transplantation is a life-saving treatment option for critically ill recipients with small thoracic cavities, particularly those with cystic fibrosis and pulmonary fibrosis. Furthermore, it is a feasible surgical technique in recipients with a reduced unilateral thoracic cavity.

Ethics Committee Approval: The study was approved by Kartal Kosuyolu High Specialization Training and Research Hospital Local Ethics Committee (ID: 2020/8/355).

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Renal Artery Embolism: A Salvage Therapy with Catheter-Directed Intra Arterial Ultraslow Thrombolytic Infusion

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ABSTRACT

Renal artery thrombosis is an uncommon but threatening condition. Although percutaneous interventions and thrombolytic treatments have proven beneficial, there is no clear treatment strategy. We present a patient that was diagnosed with right renal artery thrombosis, and nephrectomy was suggested at the referred hospital. In this case, catheter-directed intra arterial ultraslow thrombolytic infusion secured the patency of the renal artery as a salvage therapy. The aim of this case report is to draw attention to catheter-directed intra arterial thrombolytic infusion in renal artery thrombosis treatment options.

Key Words: Renal artery thrombosis; catheter directed thrombolysis; thrombolysis.

Renal Arter Embolisi: Kateter Aracılı İntraarteriyel Ultra Yavaş Trombolitik İnfüzyon ile Kurtarma Tedavisi

ÖZ

Renal arter trombozu nadir fakat tehdit edici bir durumdur. Perkütan girişimler ve trombolitik tedavilerin yararlı olduğu kanıtlanmış olsa da net bir tedavi stratejisi yoktur. Burada dış merkezde sağ renal arter trombozu tanısı alan ve nefrektomi önerilen bir hasta sunulmuştur. Bu olguda kateter aracılı intraarteriyel ultra yavaş trombolitik infüzyonu, bir kurtarma tedavisi olarak renal arter açıklığını sağlamıştır. Bu olgu sunumunun amacı, renal arter trombozu tedavi seçeneklerinde kateter aracılı intraarteriyel trombolitik infüzyona dikkat çekmektir.

Anahtar Kelimeler: Renal arter trombozu; kateter aracılı tromboliz; tromboliz.

INTRODUCTION

Thrombosis of the renal artery is an uncommon condition that results from obstruction or decrease of renal arterial flow by a thrombus. That may result in irreversible damage to the renal parenchyma and leads to renal infarction.

Many risk factors are known to favor but atrial fibrillation is currently considered the most important risk factor for this condition[(1)]. Patients mostly present with abdominal and/or flank pain, uncontrolled hypertension[(2)]. Laboratory findings include an increase in lactate dehydrogenase level, an increase in C-reactive protein level, and renal impairment.

Thrombosis of the renal artery can mimic many other pathological conditions, including acute abdomen, renal colic, pyelonephritis, rupture of aortic aneurysm, pulmonary embolism, and more[(3)]. It is important to make a differential diagnosis and proceed with an optimal diagnostic workup for preventing kidney damage. Although percutaneous interventions and thrombolytic treatments have proven beneficial, there is no clear treatment strategy. In this report, we reported a patient that was suggested nephrectomy at the referred hospital was diagnosed with right renal artery embolism. We applied thrombolytic treatment with percutaneous intervention as a salvage therapy.

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CASE REPORT

A 63-year-old man was referred from another hospital to our hospital. The patient was admitted with right flank pain and nausea. Physical examination revealed tenderness and side pain in the right abdomen. He had elevated blood pressure that was resistant to anti-hypertension drugs. The patient had atrial fibrillation and was not using oral anti-coagulation drugs. The patient had diabetes mellitus using subcutaneous insulin. Laboratory tests revealed an increase in creatinine value, C-reactive protein level, lactate dehydrogenase level. His blood count test was revealed elevated white blood cells with neutrophils dominance. The patient has performed a computed tomography (CT) with an intravenous contrast agent at the referred hospital. The CT was showed that the left renal hypoperfusion and a suggestive image of thrombus in the left renal artery (Figure 1). The echocardiography revealed normal left ventricle functions with no sign of intracardiac thrombus. Nephrectomy was suggested to the patient at the referred hospital. Because of the persistent pain and worsening of renal functions, we decided to do a renal angiography for considering percutaneous therapeutic options. Renal angiography showed that the left mid segmentary artery was occluded. The right main renal artery was obstructed and dense thrombus filled (Figure 2A). Percutaneous intervention and a thrombolytic decision were taken.

We planned to apply intraarterial thrombolytic into a dense thrombus filled with the right main renal artery. For engagement to the right main renal artery internal mammary, right, and a renal catheter was used respectively. 8 Fr renal catheter was engaged to the right main renal artery. Then the obstructed segment was passed with a soft guidewire (Asahi-Japan). The catheter engagement wasn't enough. To evaluate the distal run-off and for better catheter engagement, a Corsair Pro microcatheter (Asahi-Japan) was inserted through the renal catheter. An adequate distal run-off was observed (Figure 2B). The guidewire was changed with Grand Slam guidewire (Asahi-Japan) for better engagement. Besides a second Grand Slam guidewire was inserted into distal to support for engagement. With 2.0 x 20 mm and 3.0 x 20 mm percutaneous transluminal coronary angioplasty (PTCA) balloon catheter, the obstructed lesion was pre dilated. Because of the distal flow was decreased, 5.0 x 20 and 5.0 x 30 mm balloon catheter was also inflated. For better catheter engagement, we decided to implant a stent in the renal artery. With that, we could insert the catheter into the mid renal artery via stent support. 5.0 x 18 renal stent (Boston Scientific-USA) was implanted into the distal region (Figure 2C). A second 5.0 x 18 mm renal stent (Boston Scientific-USA) was implanted into the proximal with overlapping to the first one. Upon no re-flow was observed, the in-stent regions were dilated with balloons again. A weak distal flow filled with thrombus was observed. As the 5.0 x 20 mm balloon was inflated into the distal stent, A 4 Fr Pigtail catheter was inserted into the mid renal artery region on through the second Grand Slam guidewire (Figure 2D). There were no contraindications for applying a thrombolytic agent. Bolus 10 mg tPA (Tissue Plasminogen Activator-Alteplaz) was applied then 1 mg per hour slow infusion was started through the Pigtail catheter.

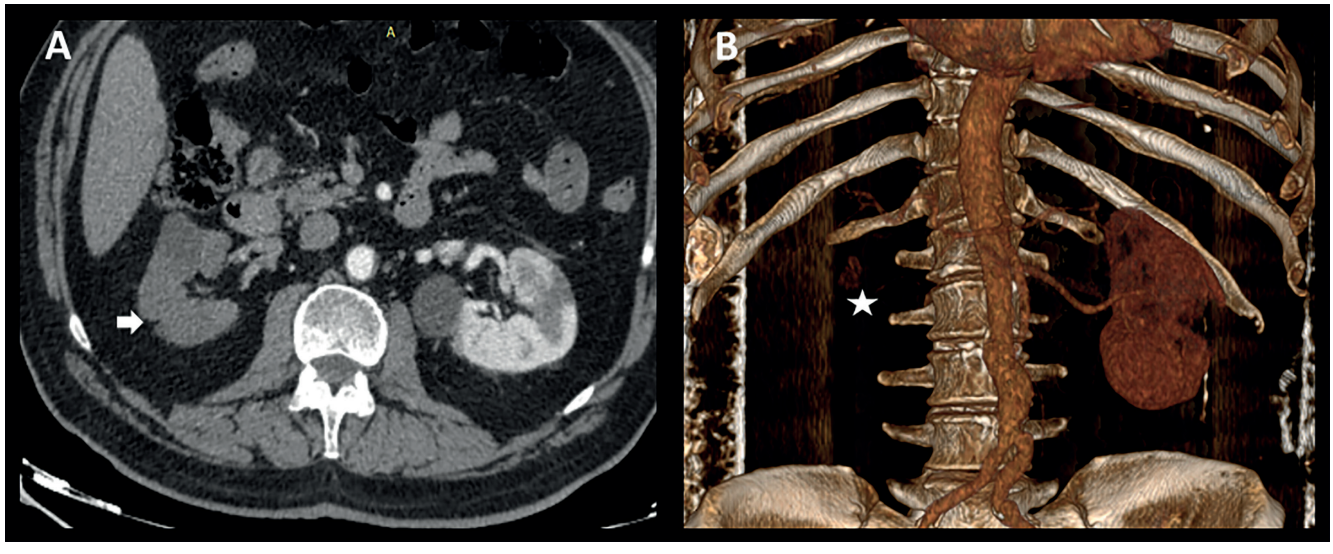

Figure 1. A. The abdominal angiographic computed tomography showing that no contrast engagement in the right kidney (arrow). **B.** 3D reconstruction of the abdominal angiographic computed tomography showing no perfusion in the right renal artery region (star).

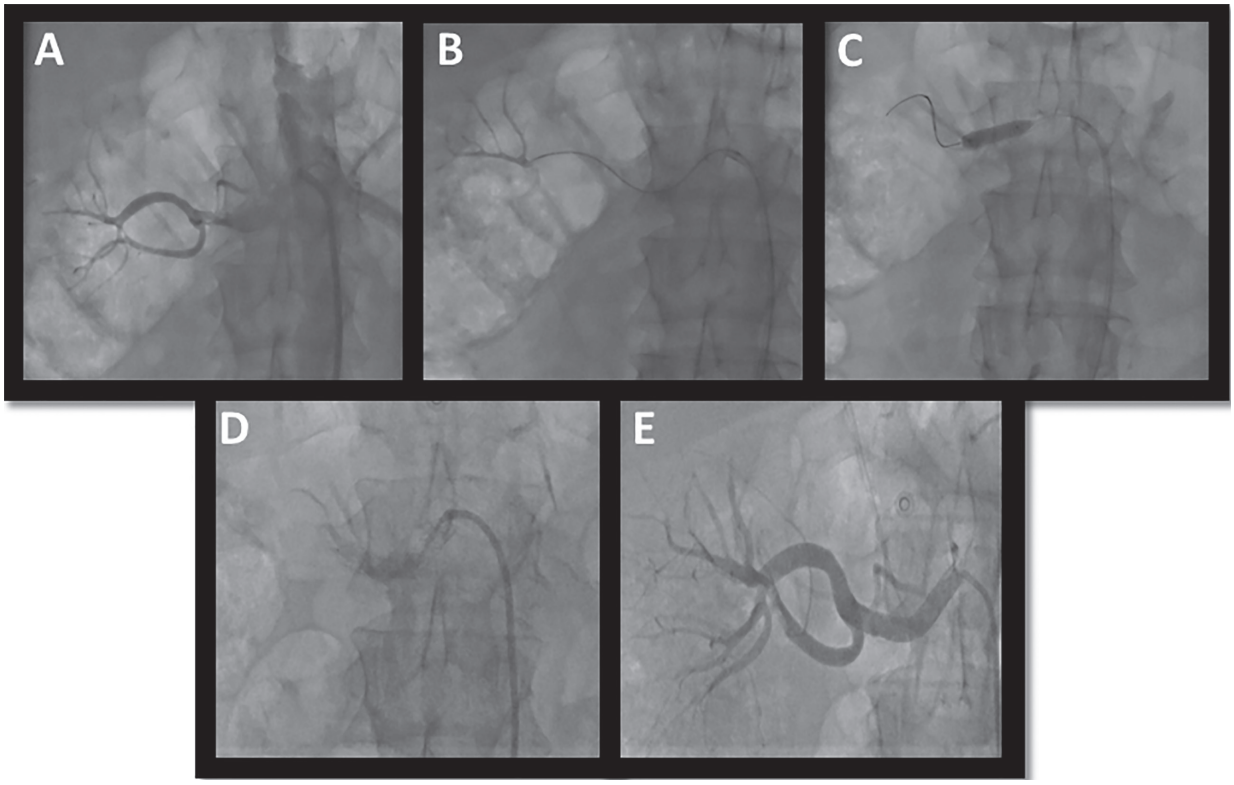

Figure 2. A. The right renal artery with dense thrombus filled. **B.** Evaluating distal run-off with the Corsair Pro microcatheter. **C.** Renal stent implanting. **D.** The Pigtail catheter in the mid renal artery. **E.** Control angiography of the right renal artery.

The infusion was continued for 24 hours. During tPA infusion, the patient experienced a slight improvement in the flank pain. When the tPA infusion was finished, an unfractionated heparin infusion was started. Control renal angiography was performed after 24 hours when the tPA infusion was stopped. Renal stents were open with good distal flow (Figure 2E). The patient was well and symptom-free after the intervention and did not need hemodialysis. His renal functions improved; his creatinine value and lactate dehydrogenase levels decreased progressively. The patient was discharged five days after the intervention with warfarin and clopidogrel treatment.

DISCUSSION

The renal artery thrombosis is a relatively rare clinical entity. Clinical findings are often nonspecific and can mimic many other pathological conditions. The delaying of the diagnosis may cause irreversible renal parenchymal damage that leads to end state renal disease and also death[4].

Domanovits et al. suggested that for all patients presenting with the triad; high risk of a thromboembolic event, persisting flank/abdominal/back pain, elevated serum levels of lactate dehydrogenase and/or hematuria within 24 hours after pain onset, CT should be performed to detect possible renal infarction or other abdominal lesions[5]. Our patient had diabetes mellitus, hypertension, and atrial fibrillation without anticoagulant treatment. We considered that renal artery thrombosis is most likely related to atrial fibrillation. Atrial fibrillation was found to be the most frequent etiologic factor for renal infarction due to thrombosis of the renal artery in case series and reports[1,3,6].

The treatment strategy for renal emboli is unclear. The strategy depends on several factors; the time between the onset of clinical symptoms and diagnosis and the underlying causes. Some case studies have demonstrated that medical management with anticoagulants or intravenous or intra arterial thrombolytics is feasible[4,5]. Response to thrombolytic therapy may be related to the duration from initial symptoms and signs to a definitive diagnosis[2]. Nephrectomy was suggested to the patient at the referred hospital. Because of our patient was complaining of persistent right flank pain and nausea with an increase in creatinine value and a decrease in diuresis, we thought that the renal ischemic process may benefit from invasive strategy and thrombolytic therapy.

During the procedure, catheter engagement was challenging and prolonged the procedure time. Evaluating the distal run-

off in a dense thrombus filled artery was important for the renal artery patency and the success of the thrombolytic procedure. We decided to apply catheter-directed intraarterial thrombolytic. After the failure of several attempts to insert the catheter because of a lack of support, we implanted a renal stent to better engage and support. As predictable, renal stent implantation wasn't enough for the flow patency in this thrombus dense condition alone. Subsequently, we decided to apply catheter-directed intraarterial thrombolytic. Because of the lack of enough support and catheter engagement, during a 5.0 x 20 mm balloon was inflated into the distal stent, the Pigtail catheter was inserted into the mid renal artery region on through the second grand slam guidewire. For providing effective and safe thrombolysis, we performed ultraslow thrombolytic therapy which is documented most commonly in the treatment of prosthetic valve thrombosis via the Pigtail catheter[7]. We applied a bolus 10 mg tPA before the infusion. Since an acceptable outcome in renal functions was achieved, the patient was discharged with clopidogrel and warfarin to prevent recurrent embolism due to atrial fibrillation.

CONCLUSION

Although the treatment strategy for the renal artery embolism is unclear and depends on the admission time and the underlying reason, we successfully applied catheter-directed intraarterial ultra-slow thrombolytic infusion to the patient that was suggested nephrectomy at the referred hospital. The procedure was challenging due to catheter engagement issues so that we also applied the renal stent. That kind of invasive treatment strategies can be applied at experienced centers. Before suggesting nephrectomy, it is important to consider invasive interventions and thrombolysis according to the clinical condition of the patient. The patient may benefit from percutaneous strategy and thrombolysis with better outcomes.

Informed Consent: Informed consent form was obtained from patient.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - SU, EA; Data Collection - SU, DÇ; Writing - SU; Critical Revision - ZŞ, EA; Final Approval - SU; Overall Responsibility - SU.

Conflict of Interest: The authors have no conflicts of interest to declare.

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Right Coronary Endarterectomy with Stent Removal Before Right Coronary Artery Bypass During Coronary Artery Bypass Grafting Surgery

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A 62-year-old male patient was admitted to the cardiology clinic with chest pain. Previously, there was a history of eight coronary stent interventions in four separate sessions, and after coronary angiography, multivessel disease was detected and referred to us for coronary artery bypass grafting (CABG) surgery. After the necessary preparations, 4 x CABG was applied with LIMA-LAD, Ao-D1, Ao-CxOM2, Ao-RCA body on December 28, 2020. Endarterectomy was applied to the patient's left anterior descending artery and right coronary artery vessels before bypass grafting. Right coronary artery was opened prior to crux and endarterectomy was performed. During the procedure, the 5 cm stent material was successfully removed together with the endarterectomy plaque by patting it proximally. The patient was discharged after a stable intensive care and service period.

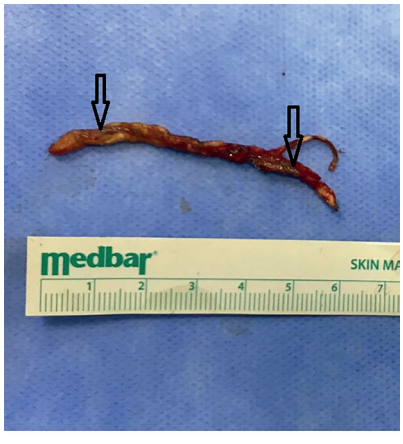

Figure 1. Image of the stent removed with the endarterectomy material during right coronary endarterectomy (the part between the arrows shows the stent).

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Mitral Annulus Caseous Calcification: Not A Conundrum with Cardiac Computerized Tomography

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A 58-year-old woman with atrial fibrillation was referred for mitral valve replacement due to mitral valve mass on echocardiography. Transesophageal and transthoracic echocardiography showed an echogenic, round mass attached to the basal portion of the posterior mitral valve, mild degeneration of both mitral leaflets and moderate mitral regurgitation. Cardiac computerized tomography (CT) was planned to further assess the mass and its relationship with the mitral apparatus. Cardiac CT showed densely calcified caseous thickening of the mitral annulus that was measured 32 x 13 mm and encircling the posterior mitral annulus which protruded towards the posterior leaflet without disruption of the mitral apparatus. The heart team assessed the patient with integrated findings of transesophageal echocardiography and cardiac CT and decided to manage conservatively.

Although mitral annulus calcification is frequent in older population, caseous calcification of the mitral annulus is rare and detected fewer than 0.07% of patients with echocardiography[1]. Its mass-like appearance and coarse calcifications may pose a diagnostic challenge in echocardiography which may result in initial misdiagnoses as thrombus, vegetation or tumoral lesions. Cardiac CT is a superior tool to assess the calcific nature of the mass and demonstrate its location and relationship with the mitral annulus. The correct diagnose is of importance as surgical management of caseous mitral calcification may result in mitral annular disruption during surgery.

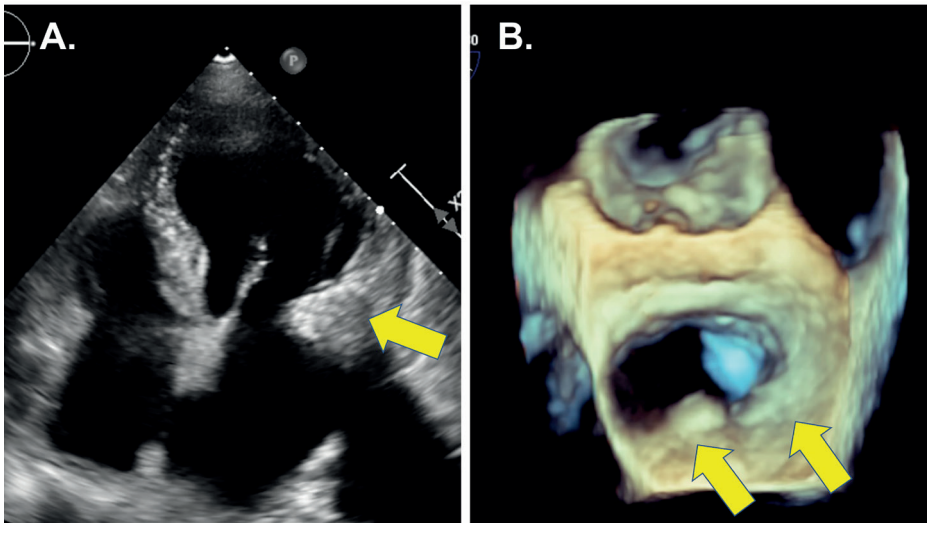

Figure 1. 4 chamber TTE **(A)** and 3D-TEE **(B)** images show a hyperechoic lesion with (arrow) acoustic shadowing protruding towards the posterior mitral valve.

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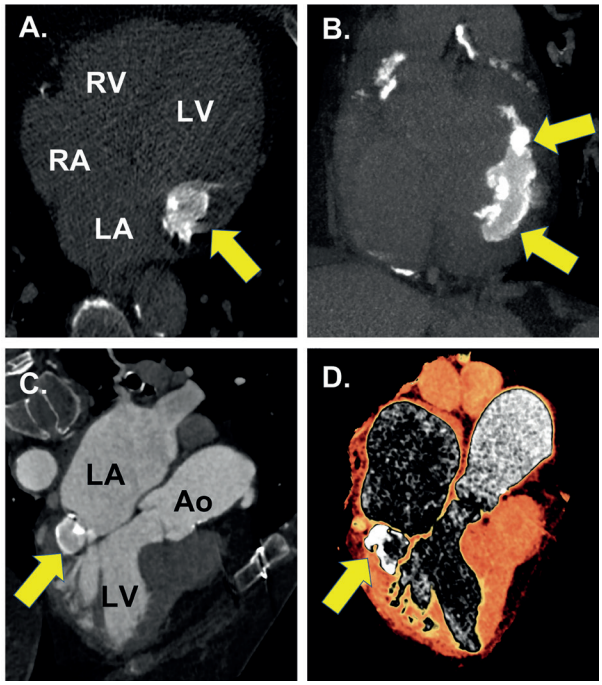

Figure 2. 4 chamber **(A)** and short axis **(B)** nonenhanced cardiac computerized tomography images show a densely calcified lesion (arrows) in the mitral annulus. 3 chamber image of contrast enhanced computerized tomography **(C)** and volume rendered reformatted **(D)** images demonstrate that the lesion protrudes towards posterior mitral valve.

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