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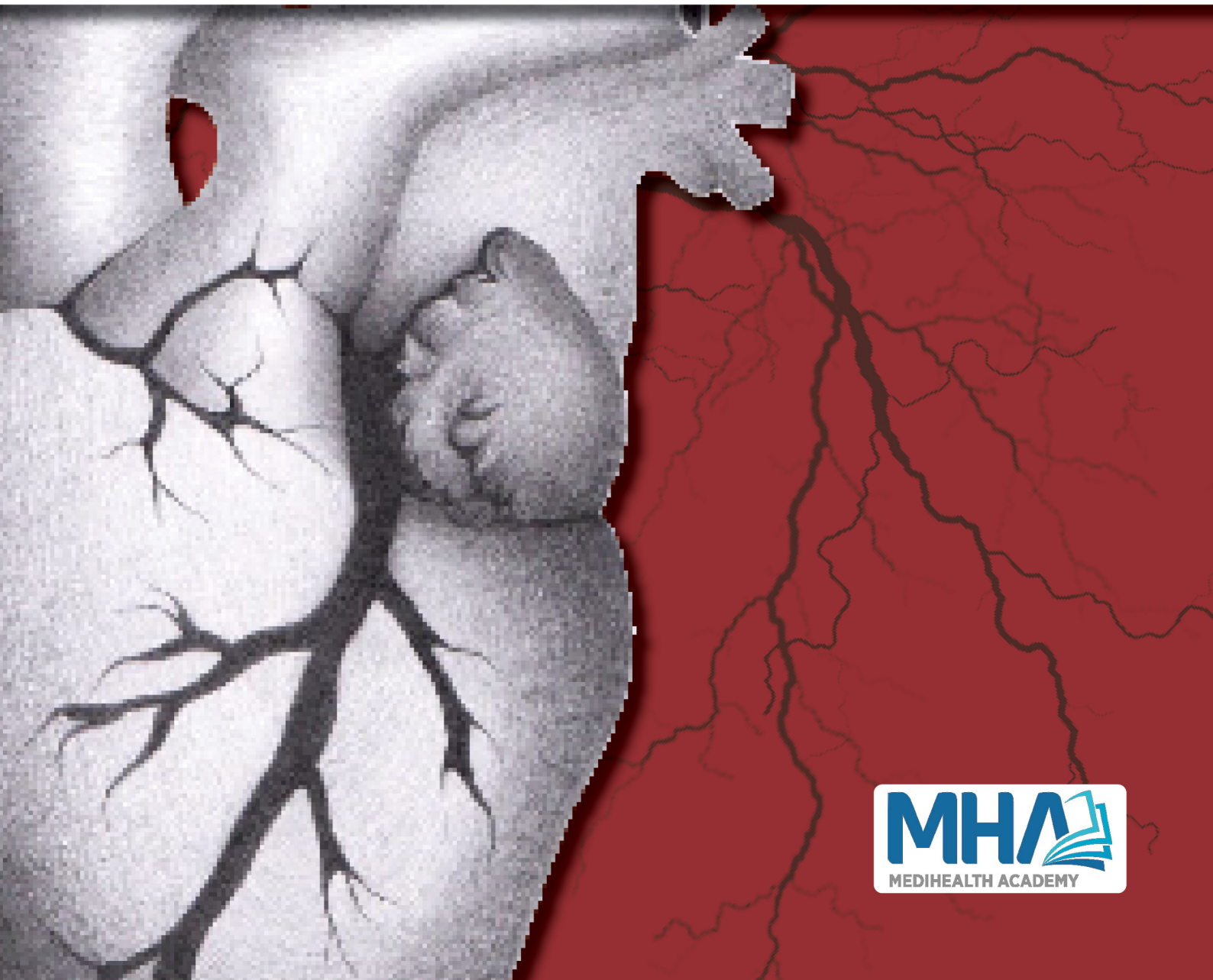

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ORIGINAL ARTICLES

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Original Article

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Balloon embolization of bronchial artery: a new technique in massive hemoptysis

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ABSTRACT

Aims: Massive hemoptysis, characterized by severe respiratory bleeding, requires immediate medical attention due to its high mortality rate. We described our experience with the parachute balloon embolization procedure for life-threatening massive hemoptysis in this article.

Methods: The study was planned for 14 patients who presented with massive hemoptysis, had a high surgical risk, and failed medical and bronchoscopic treatment. The bleeding focus was embolized by placing the balloon, which was cut in half and separated from its shaft, using the new parachute technique.

Results: Hemorrhage was effectively controlled in all individuals. One patient died during the in hospital follow-up. During the 6-month follow-up period, there were no instances of repeated bleeding detected in the 13 patients.

Conclusion: The use of balloon embolization using the parachute approach can be an effective and safe bail out treatment option for those with severe hemoptysis. Furthermore, this technique may facilitate the development of new treatment modalities and the creation of novel devices in the future.

Keywords: Massive hemoptysis, artery embolization, life threatening hemoptysis, bronchial artery

INTRODUCTION

Hemoptysis is defined as the expulsion of blood originating from under the vocal cords, that is, from the lower airways.[1,2] Different classifications have been made according to the amount of bleeding. The definition of large hemoptysis is a topic of ongoing discussion, with considerable hemoptysis often defined as any amount ranging from 100 to 1,000 ml ml/day.[3] Massive hemoptysis is a critical medical condition characterized by significant bleeding from the respiratory tract, which necessitates urgent intervention due to its substantial risk of fatality. If untreated, it has a high mortality and morbidity rate. The main cause of death in patients with massive hemoptysis is not bleeding, but asphyxia secondary to bleeding. In contrast to hemorrhage occurring in other circumstances, a limited quantity of blood has the potential to quickly flood the respiratory passages, so impeding the process of oxygenation and breathing.[4] This obstruction might result in hypoxia and subsequent circulatory failure. Approximately 15% of hemoptysis cases are classified as life-threatening hemoptysis and require immediate life-saving intervention.[5] Approaches to life-threatening hemoptysis include medical treatment, bronchoscopic approach, and bronchial artery embolization (BAE) and surgical resection treatments.[6] Since the 1970s, endovascular intervention therapy has preceded surgical treatment in experienced centers, as it has a lower mortality and morbidity rate compared to surgical treatment.[6,7] In our article, we presented our experience with a new balloon embolization method, which we call the parachute technique, in the treatment of life-threatening massive hemoptysis.

METHODS

Ethics

The study was conducted with the permission of Fırat University Non-interventional Researches Ethics Committee (Date: 31.12.2020, Descision No: 2020/17-36). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Population

The study was conducted on patients with massive hemoptysis who were admitted to our hospital between January 2018 and December 2020. Bronchial artery embolization was planned for patients who were unsuccessful in medical treatment and bronchoscopic treatment and who had a high surgical risk. 14 patients meeting these criteria were included in the study.

Diagnostic Tools

Emergency computed tomography (CT) angiography and bronchoscopy are used to identify bleeding foci in patients. CT angiography is a high-sensitivity imaging modality of choice to evaluate the lung parenchyma, the number and anatomy of bronchial arteries, and to determine the localization of bronchial artery bleeding (**Figure 1**). Additionally, the identification of bleeding foci was accomplished with the use of bronchoscopy, which served both diagnostic and potentially therapeutic purposes.

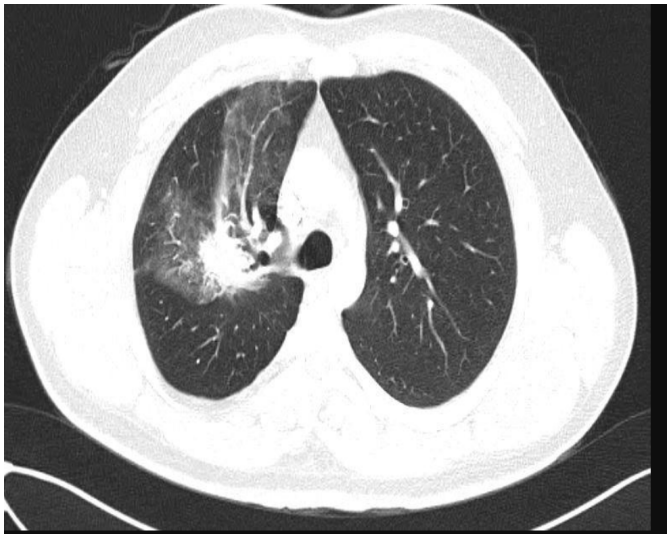

Figure 1. Computed tomography showing bleeding in the middle zone of the right lung

Pulmonary Intervention

BAE was performed in all cases by entering through the femoral artery. Diagnostic angiography of the aortic arch and descending thoracic aorta was performed to view the bronchial artery by advancing a 5-F multihole catheter (Pigtail Cook, Bloomington, Indiana) over a 0.035-inch hydrophilic guidewire (Terumo, Tokyo, Japan) into the thoracic aorta. Afterwards, the artery was engaged with 7F Amplatz Left or Amplatz right 2 catheters. The embolization process was planned with the method we call the parachute technique. Balloon diameters between 2.0 and 4.0 were selected depending on the target artery (Solaris, medtronic). Ballons were inflated to a pressure of 4 atm. Downloaded after 30 seconds. Then the balloon part was separated by cutting from the distal shaft part. The balloon was cut in half (**Figure 2**). The two formed parts (the main balloon shaft and the cut distal part of the balloon) were separately loaded on the floppy wire with the cut side of the balloon opposite to the flow direction (parachute effect). Using 0.014 wire, it was attempted to be moved to the lesion region (**Figure 3**). The cut shaft of the balloon was pushed with its half, and the material to be left was stabilized by keeping the balloon shaft fixed to the proximal bronchial artery. Because of the unidirectional artery flow, the balloon was expanded slightly and positioned in the lesion area as a result. And the wire was pulled slowly and retracted (**Figure 4**). The balloon shaft was then pulled back from the remaining piece. If satisfactory embolization was not achieved, the same process was repeated in the bleeding pulmonary artery branch. Arterial bleeding was stopped with controlled iatrogenic embolization.

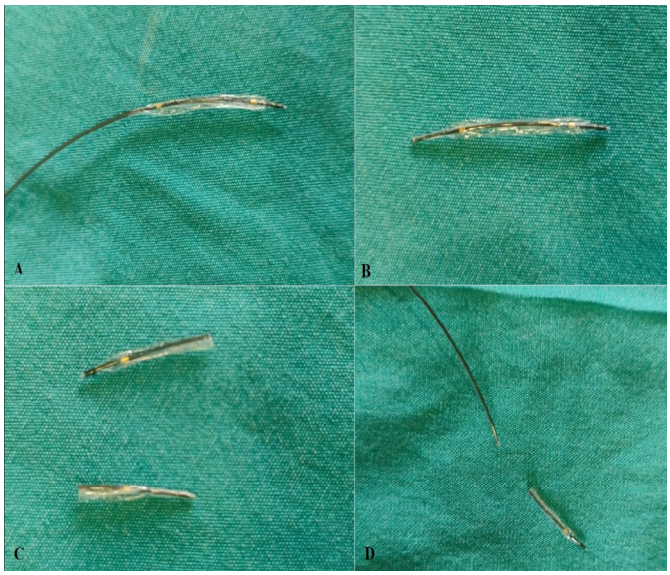

Figure 2. A. Ballons were inflated to a pressure of 4 atm. Downloaded after 30 seconds, **B.** Then the balloon part was separated by cutting from the distal shaft part, **C.** The balloon was cut in half, **D.** The main balloon shaft and the cut distal part of the balloon were prepared separately load on the floppy wire with the cut side of the balloon opposite to the flow direction (parachute effect)

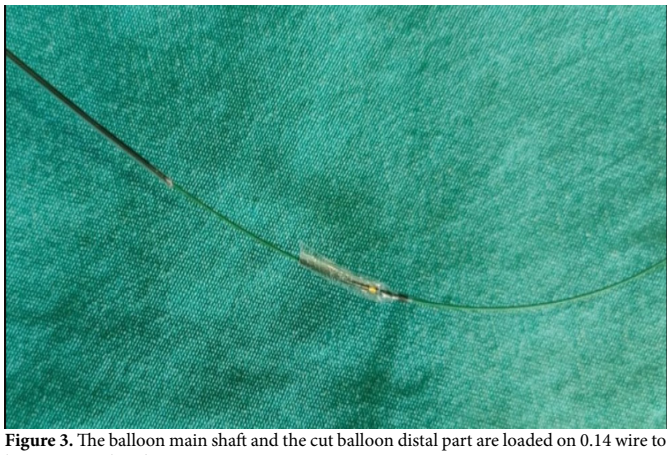

Figure 3. The balloon main shaft and the cut balloon distal part are loaded on 0.14 wire to be transported to the target artery

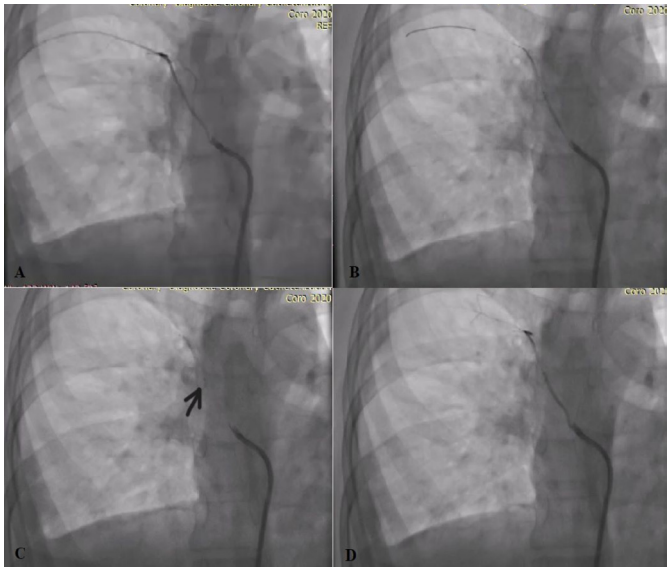

Figure 4. A. Bronchial artery was engaged with 7F amplatz left or amplatz right 2 catheters, **B.** The cut shaft of the balloon was pushed with its half, and the material to be left was stabilized by keeping the balloon shaft fixed to the proximal bronchial artery. Due to the unidirectional flow of the artery, the balloon was slightly expanded and placed in the location of the lesion, **C.** After the wire is retracted, the balloon is observed inside the artery (arrow), **D.** Control injection confirms that the vessel is occluded

RESULTS

The age range of the patients was between 26-79 years. 3 patients were female, 11 patients were male. 6 patients had lung cancer, 3 patients had tuberculosis, 1 patient had emphysema, 1 patient had hydatid cyst. The etiological characteristics of the patients are presented in the **Table**.

The objective of this study was to evaluate the immediate and prolonged outcomes of cases following selective bronchial system angiography and bronchial artery embolization. Significant observations related to hemoptysis on angiography include extravasation of contrast material, abnormal staining of lung tissue, tortuous course along the bronchial artery, an enlarged bronchial artery (more than 2 mm), and the existence of abnormal connections between bronchopulmonary arteries and veins. All patients exhibited a larger diameter of the bronchial artery. In all cases, with the exception of the increase in bronchial artery diameter, at least one other pathological sign was identified. The detected bleeding amounts, bleeding focus and embolized target vessel are presented in the **Table**.

Only one of 14 patients died 3 days after the intervention. A patient experienced severe bleeding as a result of the invasion of the left pulmonary artery. Consequently, the patient underwent surgery and underwent a left-sided pneumonectomy.

5 of our patients needed intensive care for 2-6 days (average 3.6 days).The number of hospitalization days, including the intensive care and service, of the patients, excluding the patient with Exitus, was between 2 and 10 days, and the patient was discharged with recovery in an average of 5.6 days. During the 6-month follow-up examination of the patients, there were no instances of complications or recurrence of bleeding.

DISCUSSION

Massive hemoptysis accounts for approximately 5% of all occurrences of hemoptysis and typically suggests the presence of a potentially serious respiratory or systemic illness. Mortality associated with major hemoptysis ranges from 6.5% to 38%.[8,9] The patient should be provided with advanced cardiac life support and stabilized as soon as possible. Medical treatment, bronchoscopic treatment, surgical treatments and angiographic embolization methods are the treatment options for patients. In our study, we demonstrated the effectiveness of an alternative pulmonary artery embolization method.

Table. Clinical information about patients who underwent intervention

Case	Age	Sex	Diagnosis	Hemoptysis (cc)	Focus of bleeding in bronchoscopy	Embolization location	Materiel (balloon)	Bronchial artery diameter (mm)	Duration of stay in the hospital
1	61	Male	Right middle lobe cavitary lesion	600	Right middle lobe	Right middle lobe feeding artery	3.0x12, 3.0x14	3	3 days intensive care, exitus
2	69	Male	Emphysema	450	Right upper lobe	Right main bronchial artery	3.0x24, 4.0x10	5	4 days service
3	64	Male	Right upper lobe squamous epithelium ca	200	Right upper lobe	Right middle lobe and upper lobe bronchial artery	2.5x15, 2.0x15	4	5 days service
4	57	Male	Left upper lobe	350	Left upper lobe	Left upper lobe bronchial artery	3.0x14	3	3 days service
5	52	Male	Right metastatic lung ca	550	Right upper lobe	Right main bronchial artery	4.0x10	4	10 days service
6	53	Male	Left hilar lung squamous epithelium ca	850	Left main bronchus	Left main bronchial artery	2.5x12, 2.75x15, 2.25x24	6	6 days intensive care, 4 days service
7	26	Female	Right middle lobe cavitary lesion	300	Right upper, middle and lower lobe	Right middle and lower lobe bronchial artery	2.5x24, 2.5x28	5	3 days intensive, 3 days service
8	65	Male	Left upper lobe squamous epithelium ca	400	Left upper lobe	Left main bronchial artery	3.0x18, 3.0x24	6	4 days intensive, 2 days service
9	64	Male	Left upper lobe squamous epithelium ca	350	Left main bronchus	Left main bronchial artery	3.0x24, 4.0x10	6.5	9 days service
10	60	Male	Bleeding from the left lower lobe	300	Left lower lobe	Left main bronchial artery	2.0x15, 2.0x10	4	3 days service
11	61	Male	Left upper lobe operated squamous epithelium ca	250	Left lower lobe	Left main bronchial artery	3.0x23, 3.0x14	6	2 days intensive care 2 days service
12	33	Male	Operated right upper lobe hydatid cyst	350	Right upper lobe	Right upper lobe bronchial artery	3.0x15, 4.0x10, 4.0x8	7	2 days service
13	79	Female	Previous tuberculosis, right destroyed lung, left emphysematous lung	300	Bilateral lung	Right and left main bronchial arteries	3.0x18, 3.0x18, 3.0x18	6.5	4 days service
14	73	Female	Right upper lobe	400	Right upper lobe	Right main bronchial artery	3.0x18	5	3 days service

Generally bronchoscopy is the preferred method in unstable patients. It can be applied at the bedside. When large blood clots cannot be removed effectively with bronchoscopy, it is highly effective to remove the frozen clot with a bronchoscope by embedding the cryoprobe into the clot. If there is no success in bronchoscopic and medical treatment, there are surgical and BAE treatment options. The chances of surgical treatment are low due to the low lung capacity of the patients and other accompanying health problems. Due to the low complication rate and high success rate in the treatment of BAE compared to surgical treatment, it has been a frequently used treatment method recently.[9] Hence, research on the BAE and alternative methodologies like ours hold significant worth.

The BAE indications include patients who are unable to undergo surgery, patients who refuse surgery but still require curative treatment, and patients who need temporary stabilization before surgical resection or medical treatment if other treatments have failed to control bleeding, thus enabling elective surgery. There are no absolute contraindications for bronchial artery embolization treatment, but coagulopathy, contrast allergy and renal failure are relative contraindications. We included in the study patients with massive bleeding findings and those who had failed other treatment options.

The pulmonary and bronchial arteries are the primary sources of blood supply to the lungs and their supporting structures.[10] The bronchial vessels typically arise from the aorta or intercostal arteries and enter the lung at the hilum. They then branch off at the mainstem bronchus to provide blood supply to the lower trachea, extrapulmonary airways, and supporting structures.[11] Angiographically, the bronchial arteries originate from the descending thoracic aorta between the upper T5 and lower T6 vertebral bodies in 70% of individuals.

In patients with hemoptysis, a little quantity of blood has the capacity to rapidly spill over into the respiratory system, so disrupting oxygenation and breathing, even if the bleeding is minimal. Therefore, there is no clear amount of bleeding in life-threatening massive hemoptysis.[12] However, associated mortality is rather high and has been shown to be mainly related to the rate of bleeding.[13] We observed that there was a relatively large amount of bleeding in the exitus case (600cc).

When compared to the mortality rates revealed by other studies in the literature, the BAE technique with the parachute method appears to be effective. In-hospital mortality occurred in only one patient. In addition, recurrent and persistent hemoptysis may occur after embolization and can be seen within 6-12 months in 10-20% of cases.[14] No recurrent bleeding occurred in BAE patients with the parachute method during their 6-month follow-up. This method is effective and safe in the short and long term. However, studies with higher case numbers and longer follow-up periods are needed on this subject.

The common embolizing agent utilized was polyvinyl alcohol, with a growing trend towards the adoption of glue in recent years.[15] We identified the site of bleeding by diagnostic techniques and thereafter carried out focused embolization. This led to an improvement in processing efficiency and a reduction in processing time.

Five of the patients required intensive care after the procedure. 8 patients whose hemodynamic stability was achieved were followed in the inpatient ward. Procedure times were not documented in the study data, but it was observed that it was partially effective in a shorter time than other treatment options. Therefore, long intensive care needs were not observed in patients who received effective intervention in a short time.

A potential complication of the parachute approach is the migration of the free balloon from the vascular region. However, migration is unlikely due to unidirectional blood flow in the distal vascular bed. We did not observe any such complications in our cases. An additional potential hazard could be the occurrence of an infection. Prophylactic antibiotics may be administered to minimize the likelihood of infection.

These cases were considered as an invasive solution when the supply chain was broken during the COVID-19 period and the coil material was not available. The difference of our balloon embolization is that by dividing the balloon into two, placing the open side of the balloon opposite to the flow, the balloon expands with the effect of the current and obtaining a larger embolized area with a amaller material.

Limitations

The lack of a control interval in our study is one of the limitations of the study, but the results obtained have shown that the technique is useful.

CONLUSION

In our study, we presented 14 patients who underwent BAE using a new method called the parachute technique. The bronchial artery was embolized successfully in all patients. Our technique did not involve the use of embolization material. Instead, arterial embolization was carried out using the parachute technique, which involved the placement of handmade modified balloons in the direction of blood flow. There were less complications because no embolization material was utilized. Also, the cost has been very cheap. In summary, balloon embolization with the parachute technique may be an effective and safe treatment option in patients with massive hemoptysis. And in this regard, it may pave the way for new treatment modalities and the creation of novel devices in the future.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted with the permission of Fırat University Non-interventional Researches Ethics Committee (Date: 31.12.2020, Descision No: 2020/17-36).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Weinberger SE, Lipson DA. Cough and hemoptysis. In: Fauci AS, Braunwald E, Kasper DL, et al., eds. Harrison's principles of internal medicine. 17th ed. New York, NY: McGraw-Hill; 2008:225-228.
2. Spiro SG, Albert RK, Jett JR. Clinical respiratory medicine: expert consult. 3rd ed. Philadelphia, Pa.: Mosby; 2008.
3. Davidson K, Shojaee S. Managing massive hemoptysis. *Chest*. 2020;157(1): 77-88. doi:10.1016/j.chest.2019.07.012
4. Sakr L, Dutau H. Massive hemoptysis: an update on the role of bronchoscopy in diagnosis and management. *Respiration.* 2010;80(1)38-58.
5. Deshwal H, Sinha A, Mehta AC. Life-threatening hemoptysis. *Semin Respir Crit Care Med*. 2021;42(1):145-159. doi:10.1055/s-0040-1714386
6. Prey B, Francis A, Williams J, et al. Evaluation and treatment of massive hemoptysis. *Surg Clin North Am*. 2022;102(3):465-481. doi:10.1016/j.suc. 2021.11.002
7. Remy J, Voisin C, Ribet M, et al. Treatment, by embolization, of severe or repeated hemoptysis associated with systemic hypervascularization. *La Nouvelle Presse Medicale*. 1973;2(31):2060.
8. Fartoukh M, Khoshnood B, Parrot A, et al. Early prediction of in-hospital mortality of patients with hemoptysis: an approach to defining severe hemoptysis. *Respiration; Int Rev Thorac Dis*. 2012;83(2):106-114. doi:10. 1159/000331501
9. Radchenko C, Alraiyes AH, Shojaee S. A systematic approach to the management of massive hemoptysis. *J Thorac Dis*. 2017;9(Suppl 10): S1069-S1086. doi:10.21037/jtd.2017.06.41
10. Walker CM, Rosado-de-Christenson ML, Martínez-Jiménez S, et al. Bronchial arteries: anatomy, function, hypertrophy, and anomalies. *Radiographics*. 2015;35(1):32-49. doi:10.1148/rg.351140089
11. Baile EM. The anatomy and physiology of the bronchial circulation. *J Aerosol Med*. 1996;9(1):1-6. doi:10.1089/jam.1996.9.1
12. Khalil A, Soussan M, Mangiapan G, Fartoukh M, Parrot A, Carette MF. Utility of high-resolution chest CT scan in the emergency management of haemoptysis in the intensive care unit: severity, localization and aetiology. *Br J Radiol*. 2007;80(949):21-25.
13. Corey R, Hla KM. Major and massive hemoptysis: reassessment of conservative management. Am J Med Sci. 1987;294(5):301-309.
14. Jin F, Li Q, Bai C, et al. Chinese expert recommendation for diagnosis and treatment of massive hemoptysis. *Respiration; Int Rev Thorac Dis*. 2020; 99(1):83-92. doi:10.1159/000502156
15. Panda A, Bhalla AS, Goyal A. Bronchial artery embolization in hemoptysis: a systematic review. *Diagn Interv Radiol*. 2017;23(4):307-317.doi:10.5152/ dir.2017.16454

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Original Article

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Chronotropic incompetence in coronary slow flow

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ABSTRACT

Aims: Previous studies have associated coronary slow flow (CSF) and chronotropic incompetence (CI) with increased mortality. There is no established treatment protocol for CSF. In this study, we aimed to answer questions such as "Is there CI in patients with CSF? If so, is there an increase in the frequency of hospital admissions due to cardiac complaints in these patients?"

Methods: The study included 29 patients with CSF detected according to thrombolysis in myocardial infarction (TIMI) frame count during angiography and 27 healthy volunteers with normal coronary artery as a healty group. The relationship between coronary slow flow and chronotropic incompetence between the patient and healthy healty groups and the differences between these and healty individuals were compared.

Results: The maximum heart rate reached during the treadmill exercise test was found to be statistically significantly lower in patients with coronary slow flow compared to the healty group (p=0.045). The presence of chronotropic incompetence in the patient group with coronary slow flow was found to be statistically significantly higher than the healty group (p=0.038). However, there was no significant difference between the chronotropic indexes (p=0.953). Duke treadmill scores (DTS) were found to be similar between the groups (p>0.05).

Conclusion: Patients with coronary slow flow were found to have statistically significant higher chronotropic incompetence in the treadmill exercise test. However, no significant difference was observed between the groups in the chronotropic index values, which are an indicator of chronotropic incompetence. These results suggest the presence of autonomic dysfunction in coronary slow flow phenomenon and that chronotropic incompetence may be caused by coronary slow flow phenomenon and should be investigated in etiology.

Keywords: Coronary slow flow, chronotropic incompetence, treadmill exercise test, chronotropic index

INTRODUCTION

The coronary arteries provide blood flow to the heart, along with the supply of nutrients and oxygen. This allows the heart to pump blood to itself and to the circulatory system in our body. Coronary slow flow was defined by Tambe et al.[1] as the delay in the passage of contrast material to the distal part of the epicardial coronary arteries angiographically.[1] It is known as cardiac syndrome Y. Patients with slow coronary flow may experience recurrent chest pain at rest or with exercise. Many patients with slow coronary flow undergo index diagnostic angiography after the onset of acute coronary syndrome and electrocardiographic changes. The incidence in patients with chest pain undergoing diagnostic catheterization is 1-7%.[1] In conclusion, recurrent angina in patients with slow coronary flow causes frequent hospital readmissions and poor quality of life. Mortality in patients with slow coronary flow is reportedly approximately <1%.[2] Slow coronary flow is more common in men, smokers, obese and young patients. It is known that both systolic and diastolic functions are impaired in patients with slow coronary flow according to the data obtained from echocardiographic imaging.[2] Slow coronary flow has been reported to be associated with life-threatening arrhythmias and sudden cardiac death, and it has been thought that this may be due to increased QTc dispersion.[3] In clinical practice, coronary flow assessment is performed by the semi-quantitative method of TIMI flow grading or quantitatively by the TIMI Frame counting (TFC) method.[4] TIMI frame count system and myocardial perfusion degree are angiographic markers of the effectiveness of coronary reperfusion at the epicardial artery and microcirculation levels.[5] Coronary slow flow is diagnosed by the absence of ≥40% angiographic stenosis, TIMI-2 flow in at least one epicardial coronary artery (≥3 beats required to opacify the vessel) or TFC >27 frames (in images obtained at 30 frames/sec).[6] Quantitatively, a TFC measurement corrected for all coronary arteries >27 frames are considered diagnostic of CSF. The LAD has been reported to be 1.7 times longer than the TIMI frame count (36.2±2.6 frames), RCA mean (20.4±3.0 frames), and CX artery counts (22.2±4.1 frames). A correction factor of 1.7 is used for the LAD.[4] The LAD is the most affected vessel. However, multivessel involvement represents more severe, widespread disease and may be a sign of poorer prognosis.[1] The exact etiology and pathogenesis of coronary slow flow are unclear. Furthermore, many questions remain as to whether this pathology is limited to the coronary arteries or is a manifestation of systemic vascular disease. Multiple causes

have been suggested, including endothelial dysfunction, small vessel disease, microvascular dysfunction, morphological and functional abnormalities of blood cells, metabolic disorders, increased inflammation, and latent atherosclerosis.[7,8] Various theories have been used to explain the pathogenesis of coronary slow flow, but there are still unanswered questions that will require longer series and new studies to resolve. Since the etiology of coronary slow flow has not been fully elucidated, there is no clear treatment. Treatments are applied for symptoms and risk factors such as hypertension and diabetes mellitus. Heart rate at any given moment reflects the balance between the sympathetic and parasympathetic autonomic nervous systems.

Resting heart rate (HR) in humans is usually much lower (60–80 beats/min) because of the dominant influence of the vagus nerve. Chronotropic incopotency is generally defined as the failure of the heart to increase its rate in proportion to increased activity or demand. It is common in patients with cardiovascular disease, causing exercise intolerance that impairs quality of life. It is an independent predictor of major adverse cardiovascular events and overall mortality.[9] However, the importance of chronotropic incopotency is underappreciated and is often overlooked in clinical practice, in part because of its vague definition, the possible dependence on aging, the confounding effects of medications, and the need for formal exercise testing for definitive diagnosis. The association between chronotropic incopotency and increased cardiac and all-cause mortality was first reported more than 30 years ago by Hinkle and colleagues.[10] Ellestad and colleagues confirmed an increased risk of cardiac events after long-term follow-up of patients with this phenomenon.[11]

Treadmill exercise testing indirectly detects myocardial ischemia, which is the physiological consequence of a mismatch between myocardial oxygen delivery (coronary blood flow) and myocardial oxygen demand.[12] In general, Treadmill exercise testing is evaluated by three main parameters: clinical symptoms and signs (chest pain, low exercise capacity); electrocardiography (ECG) abnormalities (ST segment abnormalities, arrhythmias); and hemodynamic response (exercise-induced hypotension).[13] Inability to exercise for >6 minutes on the Bruce protocol in the treadmill exercise test or inability to increase heart rate to >85% of age-expected heart rate are important indicators of increased risk of coronary events, with 5-year survival rates ranging from 50% to 72%. Heart rate changes, both during and after exercise, are strong predictors of sudden death in asymptomatic and selected clinical populations, including those with coronary artery disease or heart failure.

Chronotropic incopotency is most commonly diagnosed by failure of the heart rate to reach 85% of the age-expected heart rate. The chronotropic index is defined as an indicator of heart rate reserve. Azarbal et al.[14] showed that a low heart rate reserve percentage was a superior predictor compared with failure to reach 85% of the age-expected heart rate, as the latter method identified 2.2 times more individuals at increased risk of cardiac death.

In this study, we aimed to find answers to questions such as "Is there chronotropic incopotency in patients with slow coronary flow? If so, is there an increase in the frequency of hospital admissions with cardiac complaints in these patients?"

METHODS

Ethics

The study was conducted with the permission of the Ethics Committee of Kırıkkale University Faculty of Medicine (Date: 22.02.2023, Decision No: 2023/02).

Study Design and Patient Selection

The study was designed as a retrospective cross-sectional study. Individuals aged 18 years and older who were evaluated in the outpatient clinic between 2021-2023 with complaints such as chest pain and shortness of breath were invited to participate in the study. After the objectives of the study were explained and written consent was obtained from the patients, the basic characteristics and clinical data of the participants were recorded. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the Helsinki declaration and its later amendments or comparable ethical standards.

Patients who applied with anginal complaints such as chest pain and shortness of breath, who underwent 12-lead ECG, echocardiography and blood tests, and then underwent exercise testing and coronary angiography as advanced tests were included in our study. Patients aged 18 years and over were included in the study. Patients under the age of 18, with serious heart valve diseases such as aortic stenosis, severe mitral regurgitation or mechanical prosthetic heart valves, Patients with severe structural or congenital heart disease, Patients with previously diagnosed coronary artery disease (CAD) or a history of coronary bypass surgery by angiography, Patients with arrhythmia and permanent pacemakers, pulmonary hypertension, patients with chronic renal failure, severe liver dysfunction, primary pulmonary pathology, pregnant women and BMI>35kg/m^2 were excluded from the study. A total of 29 patients with TIMI frame counting detected according to TIMI frame count during angiography were included in this study. The healthy healty group consisted of 27 healthy individuals who applied to the cardiology clinic with similar complaints and who did not have any other disease that could be included in the exclusion criteria and who had normal coronary angiography

Cardiovascular Examination and Blood Tests

All patients and healthy individuals included in the study were first recorded for demographic characteristics and general systemic examinations were performed. Height, weight and body-mass index (BMI) were recorded. After physical examination, ECG, lipid panel, thyroid function tests, electrolytes, kidney function tests, liver function tests, biochemical tests including hormones and hemogram examination were performed. Echocardiography and treadmill exercise tests were performed for complaints of patients and healthy individuals. Coronary angiography was performed electively via femoral or radial access after written consent was obtained from patients for whom coronary angiography was decided as a result of physical examination and examinations.

Echocardiography

The echocardiography data of the patients and healthy individuals used in our study were obtained from the data storage of the GE (General Electric Company, Indianapolis,

Indiana USA) Vivid E9 device in the echocardiography laboratory and from the hospital information management system where patient data is stored.

Treadmill Exercise Test

It was performed in our laboratory with the GE CASE exercise testing system brand treadmill exercise device in accordance with the Bruce protocol and accompanied by an experienced nurse. The medications of patients using anti-ischemic drugs were stopped 48 hours before the test. The test was performed without the effect of any drug. Typical angina pectoris that limits effort, horizontal or downward-sloping ST depression of 1 mm and above, and insufficient increase or decrease in blood pressure contrary to expectations were taken as positivity criteria. Tests with suspicious chest pain, not reaching the expected target heart rate according to age, showing ST changes that did not meet the positivity criteria or having low diagnostic value due to baseline ECG changes were considered suspicious/possible positive. The patients' initial heart rates and maximum heart rates were measured. The expected heart rate according to age was calculated with the formula 220-age.[12]

The presence of chronotropic insufficiency in patients was accepted as not reaching 80% of the expected heart rate according to age. Heart rate reserve was calculated as the change in heart rate from the resting time to the peak exercise time during the exercise test. chronotropic index is obtained by dividing the change in HR from the resting time to the peak exercise time by the difference between the resting HR and the age-expected heart rate.[12] We also used this formula in our study.

KI=(HR peak-HR resting)/(Age-expected heart rate-HR resting)x100 Duke treadmill score (DTS) was calculated. Patients with a treadmill score ≥5 were classified as low risk, those between -10 and 4 as moderate risk, and those with a treadmill score below -10 as high risk. DTS was calculated using the following formula: DTS= Exercise duration (min)-(5xmaximum ST segment deviation)-(4xangina score)

Coronary Angiography

All cases underwent selective right and left coronary angiography using the GE optima CL323i device using the femoral or radial artery approaches. Coronary arteries were imaged in standard positions at least 5 using right and left oblique, cranial and caudal angles. TIMI frame counting method was used to determine the presence of coronary slow flow.[4] The frame where the contrast material entered the coronary artery was accepted as the first frame. The last frame was determined according to the literature according to the coronary artery. The distal bifurcation called whisker for LAD, the distal bifurcation of the longest responsible branch for CX, and the frame where the first side branch of the posterolateral artery (PL) emerged for RCA were determined as the last frame. An average of 6–8 ml of contrast material was injected for each exposure. Coronary arteries were imaged at a speed of 15 frames/sec. While making calculations, adjustments were made to a speed of 30 frames/sec. In addition, the corrected LAD TIMI frame count was obtained by dividing the LAD frame count by 1.7. A TIMI frame count of >27 without stenosis or obstruction in one or more coronary arteries was evaluated as the presence of coronary slow flow phenomenon.[15]

Statistical Analysis

The data obtained as a result of the research were analyzed in a computer environment using SPSS (Statistical Package for Social Sciences) 18.0 package program. In descriptive analyses, frequency data were shown as number (n) and percentage (%), and numerical data were shown using mean±standard deviation. Chi-square (X^2) test and Fisher's exact chi-square test were used to compare categorical data. The conformity of numerical data to normal distribution was examined using the Kolmogorov-Smirnov test. The distribution of normally distributed numerical data in two independent groups was evaluated with the independent samples T test, and the distribution of non-normally distributed numerical data was evaluated with the Mann Whitney U test. The level of statistical significance was accepted as $p<0.05$ for all tests.

RESULTS

This study included 29 patients who were evaluated with complaints of chest pain and shortness of breath in the cardiology outpatient clinic of Kırıkkale University Faculty of Medicine and who were diagnosed with slow coronary flow by laboratory tests, electrocardiography, echocardiography, treadmill exercise test and then coronary angiography, and 27 healthy volunteers who were diagnosed with normal coronary arteries. 75.9% (22 patients) of the patients with slow coronary flow were male and 24.1% (7 patients) were female. In the healty group, 51.9% were male (14 patients) and 48.1% (13 patients) were female. The mean age of the patient group with slow coronary flow was 52.17±9.13; the mean age of the healty group was 49.14±8.65.

The comparison of all individuals included in the study as patient and healty groups is shown in **Table 1**. Hypertension was present in 12 patients (41.4%) in the patient group with slow coronary flow, while it was present in 4 patients (14.8%) in the healty group. The mean BMI and hypertension rate were found to be statistically significantly higher than in the healty group (p values; p=0.015, p=0.039, respectively). While 2 of 29 patients (6.9%) with slow coronary flow presented with angina in the first 6 months, 3 of 27 patients (11.1) in the healty group presented. No significant difference was found between the groups in presentations due to angina in the first 6 months. In the patient group with detected coronary slow flow, left atrium (LA) diameter, left ventricular (LV) end-diastolic and end-systolic diameters, LV end-diastolic volume, LV systolic mass were found to be statistically significantly higher than the healty group (p values; p=0.041, p=0.034, p=0.014, p=0.022, respectively).

Among patients with slow coronary flow, 79.3% (n=23) were detected in the LAD, 51.7% (n=15) in the Cx, and 69.0% (n=20) in the RCA artery. In the patient group with slow coronary flow, RCA TIMI frame average was 39.37±22.36, CX TIMI frame average was 40.34±25.93, LAD TIMI frame average was 48.73±19.07. In the healty group, RCA TIMI frame average was 19.03±6.50, CX TIMI frame average was 20.29±4.98, LAD TIMI frame average was 20.92±5.09. In the patient group with CFA, RCA, CX, LAD measurements were found to be statistically significantly higher compared to the healty group (p values; p<0.001, p<0.001, p<0.001, respectively). No statistically significant correlation was found between chronotropic index and RCA, CX and LAD measurements in patients with slow coronary flow (p>0.05).

In the treadmill exercise test results, while the average METs was 9.35±2.83 in the group with coronary slow flow, it was 9.84±2.47 in the healty group. While the average heart rate before exercise in the group with coronary slow flow was

Table 1. Comparison of the groups in terms of age, gender, smoking, BMI, HT, and re-admission to the hospital within the first 6 months

	Coronary slow flow group (n=29)	Control healty group(n=27)	p value
Age, mean ±SD	52.17±9.13	49.14±8.65	0.209
Gender, n (%)			
Male	22 (75.9)	14 (51.9)	0.061
Female	7 (24.1)	13 (48.1)	
Smoking, n (%)			
No	17 (58.6)	21 (77.8)	0.158
Yes	12 (41.4)	6 (22.2)	
BMI, mean ±SD (kg/m²)	29.35±3.38	27.21±2.91	**0.015**
HT, n (%)			
No	17 (58.6)	23 (85.2)	**0.039**
Yes	12 (41.4)*	4 (14.8)	
Re-admission to the hospital within the first 6 months, n (%)			
No	27 (93.1)	24 (88.9)	0.664
Yes	2 (6.9)	3 (11.1)	
Ekhocardiography			
EF (Teich) %	60.57±4.02	61.62±6.41	0.469
LA-DIA cm	3.40±0.39	3.16±0.44	**0.041**
LVIDd cm	4.62±0.50	4.23±0.79	**0.034**
LVIDs cm	3.12±0.37	2.82±0.48	**0.014**
EDV ml	100.10±24.73	85.48±20.96	**0.022**

*: Group from which the difference originates, BMI: Body-mass index, SD: Standard deviation, HT: Hypertension, EF: Ejection fraction, EDV: External ventricular drainage

83.82±12.87, it was 86.11±11.33 in the healty group. While the average maximum heart rate in the group with coronary slow flow was 83.82±12.87, it was 86.11±11.33 in the healty group. Maximum heart rate was statistically significantly lower in patients with coronary slow flow compared to the healty group (p=0.045). In the patient group with coronary slow flow included in the study, the presence of chronotropic insufficiency was found to be statistically significantly higher than in the healty group (p=0.038) (**Table 2**). However, no significant difference was found between the groups in chronotropic incopotency values, which are accepted as an indicator of chronotropic insufficiency. No statistically significant difference was found between the chronotropic index, chronotropic incopatency and hypertension according to the presence of diastolic dysfunction (p>0.05).

DISCUSSION

Despite numerous studies on coronary slow flow, no consensus has been reached on diagnosis, treatment, and clinical significance of the phenomenon.[16] The relationship between coronary slow flow and chronotropic incopotency and increased mortality has been previously demonstrated. There is no definitive treatment protocol for the coronary slow flow phenomenon.

Beltrame et al.[17] also reported that slow coronary flow is most commonly seen in young men, smokers, and patients presenting with acute coronary syndrome. Similarly, Hawkins et al.[15] predicted male gender and obesity as independent risk factors for the presence of slow coronary flow in their study. In contrast, Yılmaz et al.[18] reported that no statistically significant difference was found between the groups in terms of age, gender, hypertension and smoking frequency, while they reported that the incidence of metabolic syndrome increased in patients with slow coronary flow. Similarly, in the study conducted by Doğan et al.[19] no significant difference was found between the patients with slow coronary flow and the healty group in terms of age, gender, presence of HT, smoking status and lipid levels. In our study, no difference was found between the groups in terms of age, gender and smoking. However, BMI and the presence of HT were found to be statistically significantly higher in the slow coronary flow group compared to the healty group. In our study, there was a numerical difference between gender and smoking, but we think that the lack of statistical difference may be due to the small number of patients. The results of these data may vary with increasing the number of patients included in the study.

In a study conducted by Sanghvi et al.[20] hypertension, dyslipidemia and smoking were identified as independent determinants of coronary slow flow, and the most common symptom was presentation with acute coronary syndrome. In addition, a relationship was identified between coronary slow flow and increased insulin resistance and glucose intolerance.[21] Binak et al.[22] did not find any difference between fasting plasma lipid and glucose levels in their study, but they stated that there was a relationship between glucose intolerance and coronary slow flow in their study. These studies indicate that there is

Table 2. Comparison of groups in terms of failure to reach 80% of age-expected heart rate, chronotropic index, Duke treadmill score

	Coronary slow flow group (n=29)	Control healty group (n=27)	p value
Terms of failure to reach 80% of age-expected heart rate			
No	19 (65.5)	24 (88.9)	**0.038**
Yes	10 (34.5)*	3 (11.1)	
Chronotropic index (CI), mean ±SD	0.67±0.23	0.67±0.15	0.953
CI			
Normal	12 (41.4)	6 (22.2)	0.125
Abnormal	17 (58.6)	21 (77.8)	
DUKE, n (%)			
Low risk	14 (48.3)	18 (66.7)	0.165
Medium risk	15 (51.7)	9 (33.3)	
Duke treadmill score (DTS), mean ±SD	3.76±4.98	4.73±3.77	0.417

*: Group from which the difference originates, SD: Standard deviation

a relationship between coronary slow flow and metabolic syndrome. In our study, we did not find any significant difference between lipid profiles and glucose values. We think that this difference may be due to the exclusion of diabetic and chronic disease patients from our study.

Beltrame et al.[17] reported that more than 80% of patients experienced recurrent chest pain; almost 20% of the affected patients required re-admission to the coronary care unit. In our study, we found that there was no difference in the presentation to our clinic due to recurrent chest pain between the groups during the first 6 months of follow-up. We attributed the lack of difference between the groups to the short follow-up period, the small sample size, and the possibility that the patients presented to different clinics.

While there are studies indicating that LV ejection fraction is normal in slow coronary flow, there are also studies detecting LV systolic and diastolic dysfunction in patients with slow coronary flow.[23,24] Sezgin et al.[25] also reported diastolic filling abnormalities in patients with coronary slow flow and demonstrated diastolic dysfunction. In our study, there was no significant difference in LV ejection fractions. We think that this may be due to the exclusion of patients with heart failure and moderate-severe valvular functional disorders from our study. Narimani et al. found significant differences between the groups in LVESD, LVEDD, EF, E waves, A waves, E/A ratio, DT and IVRT. They also reported that the lateral wall E and S waves were lower in these patients.[26] In our study, values such as LV end-diastolic and end-systolic diameters, LV end-diastolic volume, LV systolic mass were found to be statistically significantly higher in patients with slow coronary flow compared to the healty group. In the study conducted by Shui et al.[27] it was determined that the left atrial diameter was increased and the left atrial functions were impaired in patients with slow coronary flow. In our study, the left atrial diameter was found to be statistically significantly higher in patients with slow coronary flow compared to the healty group. However, due to the retrospective design of our study, we could not evaluate the LA functions of our patients in detail.

In our study, as in other studies, the artery with the most common slow coronary flow was the LAD. However, there are other studies in which the LAD was not most frequently involved.[28,29]

Elsherbiny et al.[30] in their study, found that patients with slow coronary flow had weaker peak exercise capacity than healties, and that there was a significant negative correlation with the mean TIMI frame count. They emphasized that there was deterioration in LV systolic and diastolic functions, which had a clinical effect on exercise capacity in patients with slow coronary flow, and that this situation was important for risk stratification and close follow-up of these patients.[30] In contrast, in the study conducted by Tekin et al.[31] no significant difference was observed between the slow coronary flow and healty groups in terms of maximum heart rates and METs at rest and during exercise. However, a decrease in heart rate recovery in the first minute was observed in patients with slow coronary flow. They suggested that decreased vagal activity may be responsible for slow coronary flow.[31] In the study by Aşkın et al.[32] which examined the relationship between heart rate recovery and coronary slow flow, no significant difference was observed between maximum HR at rest and during exercise and METs; however, HR recovery at the 1st, 2nd, 3rd and 5th minutes was found to be significantly lower in patients with coronary slow flow. In our study, there was no significant difference between resting heart rates and METs. However, maximum heart rates were significantly lower in the coronary slow flow group. In their study comparing stable CAD and healty groups, Chen et al.[33] found that heart rate recovery values and heart rate recovery change parameters were significantly lower in the stable CAD group compared to the healty group, and suggested that this suggested the presence of autonomic dysfunction in stable CAD patients. In particular, they found that delayed heart rate recovery and reduced heart rate variability were associated with stable CAD, while low heart rate recovery values were associated with severe coronary lesions in stable CAD patients. They suggested that the risk of stable CAD increased in patients with abnormal heart rate recovery and heart rate variability, and that abnormal heart rate recovery could be used to predict the severity of coronary lesions.[33] In our study, the number of patients with abnormal heart rate recovery in the first minute was higher in the coronary slow flow patient group, but no statistically significant difference was observed (p=0.052). These results suggest that the data may differ by increasing the number of patients in the study.

Youn et al.[34] investigated the relationship between coronary flow reserve and Duke treadmill score (DTS) in patients with microvascular angina, and examined 108 patients with chest pain and normal coronary angiography, and concluded that DTS is an index that reflects coronary flow reserve and helps clinicians determine the severity of ischemia in patients with microvascular angina. A statistically significant positive correlation was found between Duke treadmill score and coronary flow reserve in the study.[34] In our study, no significant difference was found between the duke treadmill scores of the patients included in the study. We thought that this could be due to the fact that our patients were not high-risk patients.

In the study conducted by Anjos et al.[35] which included patients with suspected coronary artery disease, the frequency of chronotropic incopotency was determined as 15.9%, and it was shown that the prevalence of symptoms and coronary risk factors was higher in the chronotropic incopotency group. In the study, patients with chronotropic incopotency exhibited lower heart rates at rest and during maximum exercise in the treadmill exercise test. They found that structural and ischemic abnormalities were more common in echocardiographic evaluations of patients with chronotropic incopotency. They also stated that chronotropic incopotency was associated with left ventricular dysfunction during intense exercise and was a marker of ischemia and severe coronary artery disease, and suggested that chronotropic incopotency was associated with critical right coronary artery lesions.[35] Similar to these results, in our study, a statistically significant difference was found in echocardiography findings and target heart rate values according to age in patients with slow coronary flow.

In a study comparing heart failure patients with preserved EF and healties, in which the mechanism of chronotropic insufficiency was tried to be explained, and in which exercise test and graded isoproterenol infusion were applied to measure cardiac beta receptor-mediated heart rate responses, it was stated that heart failure patients with preserved EF exhibited impaired cardiac beta receptor sensitivity compared to healties. The researchers stated that this could be due to increased plasma isoproterenol concentrations in HF patients with preserved EF and blunted heart rate response despite exercise, which could

be due to decreased sinus node beta receptor sensitivity.[36] In our study, no statistically significant difference was found between chronotropic index, chronotropic incopotency and HT presence according to the presence of diastolic dysfunction (p>0.05). We thought that this situation could be due to the small number of our patients, low mean age, and exclusion of diabetic patients and patients with BMI>35kg'm^2 from the study.

In our study, we conducted a study by calculating both the patients' failure to reach 80% of the expected heart rate according to age and the chronotropic index values. Chronotropic incopotency was observed statistically at a higher rate in the coronary slow flow group (p<0.05). The maximum heart rates of these patients were lower than in the healty group (p<0.05). However, we found that there was no significant difference between the groups in CI values, which are an indicator of HF and are thought to be superior in showing the presence of HF. Regardless of how HF is evaluated, an impaired chronotropic response is believed to partially reflect an underlying abnormality in autonomic nervous system function and has been associated with cardiovascular events.[37]

CONCLUSION

Although coronary blood flow is regulated by neurohumoral, endothelial, and metabolic factors, the pathophysiology of coronary slow flow has not been fully elucidated. It has been reported that there may be deterioration in LV systolic and diastolic functions in these patients and that coronary slow flow has an effect on exercise capacity. Since coronary slow flow causes frequently recurring anginal symptoms and neurohumoral factors are also thought to be effective in its etiopathogenesis, this study suggests that there may be chronotropic incopotency, which is frequently seen in the community and thought to be a result of autonomic dysfunction. Some data in our study may indicate the presence of autonomic dysfunction in coronary slow flow. However, new studies involving more patients are needed on this subject.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted with the permission of the Ethics Committee of Kırıkkale University Faculty of Medicine (Date: 22.02.2023, Decision No: 2023/02).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Zavala-Alarcon E, Cecena F, Little R, Bant A, Van Poppel S, Patel R. The no-flow phenomenon during diagnostic coronary angiography. *Cardiovasc Revasc Med*. 2005;6(3):126-132.
2. Barutcu I, Sezgin AT, Sezgin N, et al. Increased high sensitive CRP level and its significance in pathogenesis of slow coronary flow. *Angiology*. 2007; 58(4):401-407.
3. Atak R, Turhan H, Sezgin AT, et al. Effects of slow coronary artery flow on QT interval duration and dispersion. *Ann Noninvasive Electrocardiol*. 2003; 8(2):107-111.
4. Gibson CM, Cannon CP, Daley WL, et al. TIMI frame count: a quantitative method of assessing coronary artery flow. *Circulation*. 1996;93(5):879-888.
5. Group TS. *TIMI definitions for commonly used terms in clinical trials*. 2009.
6. Beltrame JF. Defining the coronary slow flow phenomenon. *Circ J*. 2012; 76(4):818-820.
7. Kalay N, Aytekin M, Kaya MG, et al. The relationship between inflammation and slow coronary flow: increased red cell distribution width and serum uric acid levels. *Turk Kardiyol Dern Ars*. 2011;39(6):463-468.
8. Kuyumcu MS, Kuyumcu A, Yayla Ç, et al. Nesfatin-1 levels in patients with slow coronary flow. *Kardiol Pol*. 2018;76(2):401-405.
9. Brubaker PH, Kitzman DW. Chronotropic incompetence: causes, consequences, and management. *Circulation*. 2011;123(9):1010-1020.
10. Hinkle LE Jr, Carver ST, Plakun A. Slow heart rates and increased risk of cardiac death in middle-aged men. *Arch Intern Med*. 1972;129(5):732-748.
11. Ellestad MH, Wan MK. Predictive implications of stress testing. Follow-up of 2700 subjects after maximum treadmill stress testing. *Circulation*. 1975; 51(2):363-369.
12. Chareonthaitawee P, Askew JW, Pellikka PA. *Exercise ECG testing: performing the test and interpreting the ECG results*. PA Pellikka (Ed.), TF Dardas(Ed.), Uptodate. https://www. uptodate.com/contents/exercise-ecg-testing-performing-the-testand-interpreting-the-ecgresults, 2020.
13. Jetté M, Sidney K, Blümchen G. Metabolic equivalents (METS) in exercise testing, exercise prescription, and evaluation of functional capacity. *Clin Cardiol*. 1990;13(8):555-565.
14. Azarbal B, Hayes SW, Lewin HC, Hachamovitch R, Cohen I, Berman DS. The incremental prognostic value of percentage of heart rate reserve achieved over myocardial perfusion single-photon emission computed tomography in the prediction of cardiac death and all-cause mortality: superiority over 85% of maximal age-predicted heart rate. *J Am Coll Cardiol*. 2004;44(2):423-430.
15. Hawkins BM, Stavrakis S, Rousan TA, Abu-Fadel M, Schechter E. Coronary slow flow--prevalence and clinical correlations. *Circ J*. 2012;76(4):936-942.
16. Yilmaz M, Dağli MN. Koroner yavaş akım. *Fırat Üniversitesi Sağlık Bilimleri Tip Dergisi*. 2016;30(3): p.147-152.
17. Beltrame JF, Limaye SB, Horowitz JD. The coronary slow flow phenomenon--a new coronary microvascular disorder. *Cardiology*. 2002;97(4):197-202.
18. Yilmaz H, Demir I, Uyar Z. Clinical and coronary angiographic characteristics of patients with coronary slow flow. *Acta Cardiol*. 2008;63(5): 579-584.
19. Dogan SM, Yildirim N, Gursurer M, Aydin M, Kalaycioglu E, Cam F. P-wave duration and dispersion in patients with coronary slow flow and its relationship with thrombolysis in myocardial infarction frame count. *J Electrocardiol*. 2008;41(1):55-59.
20. Sanghvi S, Mathur R, Baroopal A, Kumar A. Clinical, demographic, risk factor and angiographic profile of coronary slow flow phenomenon: a single centre experience. *Indian Heart J*. 2018;70 Suppl 3(Suppl 3):S290-S294.
21. Ozcan T, Gen R, Akbay E, et al. The correlation of thrombolysis in myocardial infarction frame count with insulin resistance in patients with slow coronary flow. *Coron Artery Dis*. 2008;19(8):591-595.
22. Binak E, Gunduz H, Sahin M, Kurtoglu N, Dindar I. The relation between impaired glucose tolerance and slow coronary flow. *Int J Cardiol*. 2006; 111(1):142-146.
23. Baykan M, Baykan EC, Turan S, et al. Assessment of left ventricular function and Tei index by tissue Doppler imaging in patients with slow coronary flow. *Echocardiography*. 2009;26(10):1167-1172.
24. Javadi DH, Sotudeh DS, Javadi DA, Rezaee DM, Hajikarimi DM. Echocardiographic evaluation of left and right ventricular function in patients with coronary slow flow syndrome: a comparative study. *Curr Probl Cardiol*. 2022;47(9):100925.
25. Sezgin AT, Topal E, Barutcu I, et al. Impaired left ventricle filling in slow coronary flow phenomenon: an echo-Doppler study. *Angiology*. 2005;56(4): 397-401.
26. Narimani S, Hosseinsabet A, Pourhosseini H. Effect of coronary slow flow on the longitudinal left ventricular function assessed by 2-dimensional speckle-tracking echocardiography. *J Ultrasound Med*. 2016;35(4):723-729.

27. Shui Z, Wang Y, Sun M, et al. The effect of coronary slow flow on left atrial structure and function. *Sci Rep*. 2021;11(1):7511.
28. Nurkalem Z, Gorgulu S, Uslu N, et al. Longitudinal left ventricular systolic function is impaired in patients with coronary slow flow. *Int J Cardiovasc Imaging*. 2009;25(1):25-32.
29. Seyyed Mohammadzad MH, Khademvatani K, Gardeshkhah S, Sedokani A. Echocardiographic and laboratory findings in coronary slow flow phenomenon: cross-sectional study and review. *BMC Cardiovasc Disord*. 2021;21(1):230.
30. Elsherbiny IA. Left ventricular function and exercise capacity in patients with slow coronary flow. *Echocardiography*. 2012;29(2):158-164.
31. Tekin G, Tekin A, Sezgin AT, et al., Association of slow coronary flow phenomenon with abnormal heart rate recovery. *Turk Kardiyol Dern Ars*. 2007;35(5):289-294
32. Askin L. Evaluation of heart rate recovery index in patients with coronary slow flow: preliminary results. *Eur Rev Med Pharmacol Sci*. 2021;25(24): 7941-7946.
33. Chen Y, Yu Y, Zou W, Zhang M, Wang Y, Gu Y. Association between cardiac autonomic nervous dysfunction and the severity of coronary lesions in patients with stable coronary artery disease. *J Int Med Res*. 2018;46(9):3729-3740.
34. Youn HJ, Park CS, Moon KW, et al. Relation between Duke treadmill score and coronary flow reserve using transesophageal Doppler echocardiography in patients with microvascular angina. *Int J Cardiol*. 2005;98(3):403-408.
35. Anjos-Andrade FD, Sousa AC, Barreto-Filho JA, et al. Chronotropic incompetence and coronary artery disease. *Acta Cardiol*. 2010;65(6):631-638.
36. Sarma S, Stoller D, Hendrix J, et al. Mechanisms of chronotropic ıncompetence in heart failure with preserved ejection fraction. *Circ Heart Fail*. 2020;13(3):e006331.
37. Lauer MS, Mehta R, Pashkow FJ, Okin PM, Lee K, Marwick TH. Association of chronotropic incompetence with echocardiographic ischemia and prognosis. *J Am Coll Cardiol*. 1998;32(5):1280-1286.

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Electrocardiographic indicators of atrial fibrillation in obstructive sleep apnea syndrome: a retrospective analysis of P-wave peak time

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ABSTRACT

Aims: Obstructive sleep apnea syndrome (OSAS) is a sleep-related breathing disorder characterized by hypopnea and apnea. Atrial fibrillation (AF) is an arrhythmia frequently encountered in cardiology practice, with concomitant heart disease and an increasing incidence with age. OSAS and AF are closely related as they have similar etiological risk factors and common pathophysiological processes such as inflammation, oxidative cellular damage, and autonomic nervous system dysregulation. P-wave peak time (PWPT) is the time from the beginning of the P-wave to its peak and is a recently defined electrocardiographic (ECG) parameter. Studies on the relationship between PWPT and cardiovascular events have been published recently. In this study, we aimed to evaluate the risk of AF in OSAS patients by determining a new ECG parameter, PWPT.

Methods: 52 OSAS patients and 41 healthy individuals as a control group were included in the study. The groups were compared in terms of demographic characteristics, laboratory findings, echocardiography and ECG findings. D2 and V1 leads were used for PWPT as recommended in the literature.

Results: When the patient group was compared with the control group, no difference was found in terms of demographic characteristics and laboratory findings. Compared with the control group, OSAS patients had significantly longer PWPT (PWPTV1 55.05msn±7.18 msn vs 48.91 msn±7.08 msn, p<.01, PWPTD2 54.13 msn±5.60 msn vs 46.20 msn±6.94 msn, p<.01).

Conclusion: We observed that PWPT was longer in OSAS patients than in controls, and our results suggest that OSAS patients are at risk of AF.

Keywords: Obstructive sleep apnea syndrome, atrial fibrillation, P-wave peak time

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a sleep-related breathing disorder characterized by hypopnea and apnea. These respiratory disorders cause increased respiratory effort, blood hypoxia, hypercapnia, repeated nocturnal awakenings, and intermittent hypoxia, which leads to increased sympathetic nervous activity.[1,2] The incidence of OSAS is 24% among men and 9% among women aged 30 to 60.[3,4] It is estimated that it affects approximately 1 billion people worldwide.[5] Polysomnography is the gold standard for diagnosis and uses the number of apneas and hypopneas per hour of sleep [apnea-hypopnea index (AHI)]. For OSAS diagnosis, AHI must be >5, and when AHI is ≥30, it is considered severe OSAS.[6]

The relationship between OSAS and cardiovascular disease (CVD) is well-documented, often associated with hypertension (HT), heart failure (HF), atrial fibrillation (AF), coronary artery disease (CAD), and stroke.[7,8] AF is a common arrhythmia, with its prevalence increasing alongside concomitant heart disease and advancing age.[9] AF is associated with increased mortality and morbidity (thromboembolic and cardiovascular events, decreased quality of life, decreased exercise capacity, and decompensated HF).[10] Although causality between OSAS and AF has not yet been established, epidemiological studies suggest that OSAS doubles the risk of AF.[6] Furthermore, AF recurrence after cardioversion is significantly higher in untreated OSAS patients than in well-treated OSAS patients.[11]

Electrocardiography (ECG) is the main diagnostic tool for the diagnosis and treatment of CVD, especially in ischemic and arrhythmic conditions. Studies have been conducted on the availability of standard ECG and P wave indices (due to AF mechanisms).

P-wave peak time (PWPT) is the time from the beginning of the P wave to its peak. It is considered a new index of atrial depolarization, and recent studies have shown a relationship between PWPT and CAD severity, left ventricular end-diastolic pressure, absence of coronary reflux, and left atrial volume index (LAVI).[12-14] This new parameter may be used as an indicator of the risk of developing AF.[15,16] In this article, we aim to determine the PWPT times in patients with OSAS and evaluate the risk of AF in patients with OSAS based on this index.

METHODS

The study was conducted with the permission of Kayseri City Hospital Clinical Researches Ethics Committee (Date: 12.12.2023, Decision No: 957). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The study included patients diagnosed via polysomnography in the sleep laboratory of the chest diseases department between 2020 and 2022 (AHI >5 and previously untreated). The study was planned retrospectively and all medical histories, physical examinations, laboratory findings, 12-lead ECG and transthoracic echocardiography records were obtained from archive files and/or computer records. The control group comprised age- and gender-matched patients without respiratory disease suspicion, based on medical history, physical examination, and echocardiography findings.

In addition, none of the patients included in the study had a history of paroxysmal AF. Patients with uninterpretable ECGs (left bundle branch block, presence of pacemaker, U waves and negative T waves on pre-stimulus ECGs), history of ischemic heart disease, non-sinus rhythm and/or arrhythmia (atrial or ventricular) and pacemaker history, segmental or global wall motion abnormalities, moderate to severe valvular heart disease, structural heart disease, endocrine neoplasms, parathyroid cancer, thyroid cancer or hyperparathyroidism, renal failure, hypertrophic cardiomyopathy, severe valvular disease, hypokalemia and hyperkalemia, hypomagnesemia and hypermagnesemia, creatinine clearance (CrCl) <60 ml/min, and patients with severe comorbidities were excluded from the study.

Sleep Test

Polysomnographic evaluation was performed in the sleep laboratory by continuous monitoring and analysis of ECG, electroencephalogram, electromyogram, pulse oximetry, electrooculogram, nasal airflow, snoring, leg movements, thoracic and abdominal movements, and body position. Polysomnographic records were evaluated by computer-assisted manual scoring according to the criteria of the American Academy of sleep medicine by physicians experienced in sleep disorders and polysomnography. OSAS was defined as the number of apneic and hypopneic events per hour during sleep.[17] Apnea was defined as the absence of airflow for at least 10 seconds. Hypopnea was defined as the reduction of airflow with 4% oxygen desaturation lasting at least 10 seconds with subsequent arousal.

Electrocardiogram Analysis

All standard 12-lead ECGs were performed in the supine position and at rest using an ECG device (Philips brand) standardized to 1 mV/cm and 25 mm/s paper speed. All ECGs were scanned and transferred to personal computers. ECGs were magnified 5-fold and measured using an electronic caliper (Cardio Calipers software version 3.3; Iconico.com, Philadelphia, PA, USA) for the necessary measurements. To reduce inaccurate measurements, ECG assessments were conducted by two cardiologists who were blinded to clinical information.

The PWPT in lead D2 (PWPTD2) was measured as the time from the onset of the P-wave to its peak in lead D2, and the PWPT in lead V1 (PWPTV1) was defined as the time between the onset of the P-wave and the lower limit of negative deflection in patients with biphasic or pure negative P-wave morphology (**Figure**).

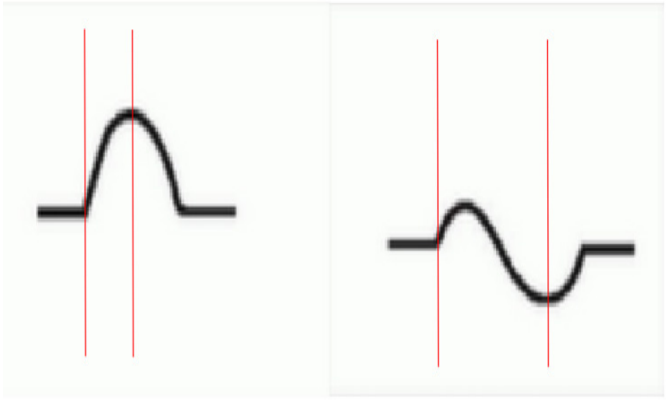

Figure. Measurement of P-wave peak time on electrocardiograms, **A.** Measurement of P-wave peak time in the lead D2 (positive wave), **B.** Measurement of P-wave peak time in the lead V1 (biphasic wave)
* Figure is used with permission from Yucel YILMAZ, MD.

Echocardiography

Patients and healthy volunteers underwent conventional echocardiographic examination with an M4S-RS (1.5-3.6 MHz) cardiac transducer and Vingmed System 5 (General Electronic Horten, Norway) echocardiograph. Left ventricular diastolic (LVIDd) and systolic (LVIDs) diameters, interventricular septum (IVSWT), and posterior wall (LVPWT) diastolic thicknesses were measured in the parasternal long axis with M-mode echocardiography according to the standards set by the American Echocardiography Association. The ejection fraction was calculated using the Teichholz formula.

Statistical Analysis

Statistical analyses were performed using the SPSS statistical software package for Windows version 21.0 (SPSS Inc., Chicago, IL, USA). The distributional characteristics of the data were determined using the Kolmogorov-Smirnov test. Independent samples t-test was used for parametric scale variables. Mann-Whitney U test was used for nonparametric scale variables. The $\chi 2$ (chi-square) test was used for the univariate analysis of categorical variables. Variables were expressed as mean±SD (standard deviation); categorical variables were expressed as percentages. A probability value of $p<0.05$ was considered to be significant, and two-tailed p values were used for all statistical analyses.

RESULTS

Baseline clinical and demographic characteristics of the study groups are presented in **Table 1**. There were no statistically

significant differences between the patient and control groups in terms of gender, age, smoking status, diabetes, and hypertension (p>0.05). In the patient group with OSAS, diastolic blood pressure was elevated and BMI was high (p<0.01).

Table 1. Baseline characteristics of the study populations

	OSAS (n=52)	Control (n=41)	p
Age (years)	52±9	51±4	NS
Gender (male/female)	35/17	27/16	NS
Systolic blood pressure (mmHg)	115±10.9	110±6	NS
Diastolic blood pressure (mmHg)	85±5.9	70±8	0,04
Stature (cm)	172±6	168±8	NS
Weight (kg)	89±17	70±7	<0,001
Body mass index (kg/m²)	30.24±5.9	24±2	<0,001

OSAS: Obstructive sleep apnea syndrome NS: Not statistically significant
Independent samples t-test was used for parametric scale variables. Variables were expressed as mean±SD (standard deviation); categorical variables were expressed as percentages.

The ECG parameters of the groups are shown in **Table 2**. Heart rate and QRS duration were similar between the groups (p<0.05). PWPTV1 and PWPTD2 were higher in OSAS patients compared to the control group (50.25±7 msec vs. 56.07±8.33 msec p<0.01 and 48.05±5.91 msec vs. 54.57±6.28 msec p<0.01, respectively).

Table 2. Echocardiography characteristics of the study population

Variables	OSAS (n=52)	Control (n=41)	p value
LVEDD (cm)	4.56±0.99	4.39±1	.367
LVESD (cm)	3.05±.86	3.41±1.01	.883
IVSD (cm)	0.9±.52	1.01±0.5	.625
PWD (cm)	0.92±0.29	1.01±0.6	.764
LVEF	62.1±3.7	63.9±3.8	.158

Data are expressed as mean±standard deviation for normally distributed data and percentage (%) for categorical variables. PHPT: Primary hyperparathyroidism, LVEDD: Left ventricular end diastole diameter, LVESD: Left ventricular end systole diameter, IVSD: Interventricular septal diameter, PWD: Posterior wall diameter, LVEF: Left ventricular ejection fraction

Table 3. Electrocardiographic characteristics of the study population

Variables	Control group (41)	OSAS (52)	p
Heart rate (beat/min)	79.3±7.6	81.7±9.7	.017
PR interval (ms)	141±14	145±16	0.891
PWPTV1 (ms)	48.91±7.08	55.05±7.18	**<.01**
PWPTD2 (ms)	46.20±6.94	54.13±5.60	**<.01**

PWPTD2: P-wave peak time obtained from D2 lead, PWPTV1: P-wave peak time obtained from V1 lead, Data are expressed as mean±standard deviation for normally distributed data and percentage (%) for categorical variables.

DISCUSSION

This is the first randomized study to show that PWPT prolongation detected by ECG analysis was higher in OSAS patients included in the patient group than in those included in the control group.

The pathophysiology of cardiovascular effects in OSAS can be explained as follows. Recurrent airway obstructions trigger hypoxemia, hypercapnia, intrathoracic pressure fluctuations, reoxygenation and sleep arousals.[8,18,19] All these recurrent attacks can activate various cardiovascular mechanisms such as vasoconstriction, tachycardia, acute blood pressure elevations and decrease in cardiac variability, which trigger sympathetic activation, and also increase in left ventricular wall stress, increase in afterload, acute diastolic dysfunction, left atrial stress, left atrial enlargement, hypercoagulability, oxidative stress and endothelial dysfunction can occur. Finally, all these mechanisms are associated with hypertension, systolic and diastolic dysfunction, coronary artery disease, sinus node dysfunction (sick sinus syndrome), atrioventricular block, AF, ventricular ectopy or even ventricular tachycardia and sudden cardiac death.[6]

AF is the most common arrhythmia in older ages and is associated with significant morbidity and mortality. Thus, primary prevention and identification of individuals at-risk have become more important. The atrial remodeling theory seems plausible to explain the predisposition to AF in patients with OSAS.[20-22] Sudden negative intrathoracic pressures may lead to repetitive atrial distension and gradual left atrial enlargement.[23] As a result of left atrial enlargement, there may be remodeling of the pulmonary vein ostia, a known site for initiating and propagating AF.[24]

Previous studies have shown that a P-wave terminal strength of >0.04 mm/s is an independent predictor of AF.[25] P-wave terminal strength is the algebraic product of the duration and depth of the negative terminal portion of the P-wave. Goda et al.[26] reported that PWTF has high sensitivity for estimating PAF in patients with acute ischaemic stroke. Although Baturova et al.[27] reported that PWTF may not be a good predictor of PAF in patients with acute ischaemic stroke, Öz et al.[16] and Çinar et al.[28] showed a significant relationship between PWPT and AF in patients with acute ischaemic stroke. Platonov et al.[29] showed that prolonged PWD is associated with a history of PAF. Yıldırım et al.[15] previously reported PWPT predicted paroxysmal AF in patients with a history of AF. In contrast, Burak et al.[14] found that only PWPT was associated with more extensive coronary atherosclerosis in patients with acute coronary syndrome. Yıldız et al.[12] showed that a prolonged PWPT was independently associated with an increased LAVI in hemodialysis patients. In our study, we found prolongation in PWPT in ECGs of patients with OSAS. When evaluated together with the literature, it can be assumed that prolongation of PWPT found in OSAS patients in this study will increase the risk of developing AF.

Limitations

The current study has some limitations. The study is a single-center, retrospective study with a limited number of patients. We do not know how long the patients had the disease before diagnosis. Although values such as PWPT are secondary markers of arrhythmia, we did not perform long-term clinical follow-up and rhythm Holter monitoring to detect the development of arrhythmia. Patients in our control group did not undergo sleep testing, which may have led to false results. OSAS patients were not grouped according to disease severity; further studies that include OSAS patients more proportionally to disease severity may yield different results. We also did not evaluate the relationship between AHI and atrial arrhythmia parameters.

CONCLUSION

In conclusion, the findings of this study suggest that PWPT, derived from ECG-a simple, easily measured, and cost-effective test-could serve as a predictive marker for AF risk in OSAS patients. More comprehensive and multicenter studies should be conducted to better analyze all possible predictors of AF and to make more robust recommendations for the future.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted with the permission of Kayseri City Hospital Clinical Researches Ethics Committee (Date: 12.12.2023, Decision No: 957).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Lévy P, Kohler M, McNicholas WT, et al. Obstructive sleep apnoea syndrome. *Nat Rev Dis Primers*. 2015;1(1):15015.
2. Lavie L. Oxidative stress in obstructive sleep apnea and intermittent hypoxia--revisited--the bad ugly and good: implications to the heart and brain. *Sleep Med Rev*. 2015;20:27-45.
3. Salzano G, Maglitto F, Bisogno A, et al. Obstructive sleep apnoea/hypopnoea syndrome: relationship with obesity and management in obese patients. *Acta Otorhinolaryngol Ital*. 2021;41(2):120-130.
4. Senaratna CV, Perret JL, Lodge CJ, et al. Prevalence of obstructive sleep apnea in the general population: a systematic review. *Sleep Med Rev.* 2017;34:70-81.
5. Benjafield AV, Ayas NT, Eastwood PR, et al. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. *Lancet Respir Med*. 2019;7(8):687-698.
6. Martí-Almor J, Jiménez-López J, Casteigt B, et al. Obstructive sleep apnea syndrome as a trigger of cardiac arrhythmias. *Curr Cardiol Rep*. 2021;23(3):20.
7. Marin JM, Agusti A, Villar I, et al. Association between treated and untreated obstructive sleep apnea and risk of hypertension. *JAMA*. 2012;307(20):2169-2176.
8. May AM, Van Wagoner DR, Mehra R. OSA and cardiac arrhythmogenesis: mechanistic insights. *Chest*. 2017;151(1):225-241.
9. Dilaveris PE, Gialafos EJ, Andrikopoulos GK, et al. Clinical and electrocardiographic predictors of recurrent atrial fibrillation. *Pacing Clin Electrophysiol*. 2000;23(3):352-358.
10. Chávez-González E, Donoiu I. Utility of P-wave dispersion in the prediction of atrial fibrillation. *Curr Health Sci J*. 2017;43(1):5-11.
11. Kanagala R, Murali NS, Friedman PA, et al. Obstructive sleep apnea and the recurrence of atrial fibrillation. *Circulation*. 2003;107(20):2589-2594.
12. Yıldız İ, Yildiz PÖ, Burak C, et al. P-wave peak time for predicting an increased left atrial volume index in hemodialysis patients. *Med Princ Pract*. 2020;29(3):262-269.
13. Çağdaş M, Karakoyun S, Yesin M, et al. The association between monocyte HDL-C ratio and SYNTAX score and SYNTAX score II in STEMI patients treated with primary PCI. *Acta Cardiol Sin*. 2018;34(1):23-30.
14. Burak C, Çağdaş M, Rencüzoğulları I, et al. Association of P wave peak time with left ventricular end-diastolic pressure in patients with hypertension. *J Clin Hypertens (Greenwich)*. 2019;21(5):608-615
15. Yıldırım E, Günay N, Bayam E, Keskin M, Ozturkeri B, Selcuk M. Relationship between paroxysmal atrial fibrillation and a novel electrocardiographic parameter P-wave peak time. *J Electrocardiol*. 2019;57:81-86.
16. Öz A, Cinar T, Kızılto Güler C, et al. Novel electrocardiography parameter for paroxysmal atrial fibrillation in acute ischaemic stroke patients: P-wave peak time. *Postgrad Med J*. 2020;96(1140):584-588.
17. Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American academy of sleep medicine clinical practice guideline. *J Clin Sleep Med*. 2017;13(3):479-504.
18. Latina JM, Estes NAM, Garlitski AC. The relationship between obstructive sleep apnea and atrial fibrillation: a complex interplay. *Pulm Med*. 2013;2013(1):621736.
19. Patel N, Donahue C, Shenoy A, Patel A, El-Sherif N. Obstructive sleep apnea and arrhythmia: a systemic review. *Int J Cardiol*. 2017;228:967-970.
20. Dimitri H, Ng M, Brooks AG, et al. Atrial remodeling in obstructive sleep apnea: implications for atrial fibrillation. *Heart Rhythm*. 2012;9(3):321-327.
21. Arzt M, Young T, Finn L, Skatrud JB, Bradley TD. Association of sleep-disordered breathing and the occurrence of stroke. *Am J Respir Crit Care Med*. 2005;172(11):1447-1451.
22. Lau DH, Mackenzie L, Kelly DJ, et al. Hypertension and atrial fibrillation: evidence of progressive atrial remodeling with electrostructural correlate in a conscious chronically instrumented ovine model. *Heart Rhythm*. 2010;7(9):1282-1290.
23. Otto ME, Belohlavek M, Romero-Corral A, et al. Comparison of cardiac structural and functional changes in obese otherwise healthy adults with versus without obstructive sleep apnea. *Am J Cardiol*. 2007;99(9):1298-1302.
24. Haïssaguerre M, Jaïs P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med*. 1998;339(10):659-666.
25. Platonov PG. P-wave morphology: underlying mechanisms and clinical implications. *Ann Noninvasive Electrocardiol*. 2012;17(3):161-169.
26. Goda T, Sugiyama Y, Ohara N, et al. P-wave terminal force in lead v1 predicts paroxysmal atrial fibrillation in acute ischemic stroke. *J Stroke Cerebrovasc Dis*. 2017;26(9):19121915.
27. Baturova MA, Sheldon SH, Carlson J, et al. Electrocardiographic and echocardiographic predictors of paroxysmal atrial fibrillation detected after ischemic stroke. *BMC Cardiovasc Disord*. 2016;16(1):209.
28. Çinar T, Hayiroğlu Mİ, Selçuk M, et al. Evaluation of electrocardiographic P-wave parameters in predicting long-term atrial fibrillation in patients with acute ischemic stroke. *Arq Neuropsiquiatr*. 2022;80(9):877-884.
29. Platonov PG. Atrial conduction and atrial fibrillation: what can we learn from surface ECG? *Cardiol J*. 2008;15(5):402-407.

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The impact of systemic immune inflammation index and neutrophil/lymphocyte ratio on mortality in patients undergoing surgery for infective endocarditis

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ABSTRACT

Aims: Infective endocarditis (IE) is a severe cardiac pathology associated with high morbidity and mortality. Early identification of disease severity and mortality risk using simple, rapid, and cost-effective tests can significantly improve clinical outcomes. This study aims to provide clinicians with valuable information on the prognostic importance of immune inflammation index (SIII) and neutrophil/lymphocyte ratio (NLR) in the management of IE patients and to guide potentially more effective perioperative interventions.

Methods: This study retrospectively investigates the relationship between the SIII, NLR, and mortality in patients who underwent surgical treatment for IE between March 2020 and November 2023. A total of 100 patients over the age of 18 were included in the study. Data were collected on various clinical parameters, and statistical analyses were performed using SPSS 26.0.

Results: The mean age of the patients included in the study was 53.85 years (age range: 21-83). Seventy percent of the patients were male %. It was found that 70% of the patients had native-type endocarditis. Furthermore, 59% of the patients exhibited growth in their blood cultures. The systemic immune-inflammation index (SII) values also showed a statistically significant difference (p=0.041), with higher SII values observed in patients who experienced mortality compared to those without. Furthermore, NLR values exhibited a statistically significant difference (p<0.001), with patients who experienced mortality having higher NLR values compared to their non-mortality counterparts. A statistically significant relationship was identified between the patients' in-hospital mortality status and the need for postoperative hemodialysis (HD) (p<0.001).

Conclusion: The risk of developing mortality increases as patients' NLO values increase (OR: 1.357, p=0.005). However, the SII values of the patients did not have a statistically significant effect on mortality (p=0.536). The developed multivariate model correctly classifies 79% of the cases. In the multivariate logistic regression analysis, age, postoperative HD requirement and N/L ratio were found to be effective in predicting mortality.

Keywords: Infective endocarditis, systemic immune inflammation index, neutrophil/lymphocyte ratio, mortality, prognostic markers

INTRODUCTION

Infective endocarditis (IE) is a complex and life-threatening infection that affects the endocardial surface of the heart, particularly the heart valves. Despite advancements in antimicrobial therapy and surgical techniques, IE continues to pose significant challenges in clinical practice due to its high morbidity and mortality rates. The pathogenesis of IE involves the colonization of heart valves by microorganisms, leading to the formation of vegetations composed of platelets, fibrin, microorganisms, and inflammatory cells. These vegetations can cause severe complications, including valvular destruction, heart failure, systemic embolization, and persistent bacteremia.[1]

The clinical presentation of IE is highly variable, ranging from subacute symptoms to acute septicemia. Patients may present with fever, heart murmurs, petechiae, and signs of embolic events, making the diagnosis challenging.[2] The modified Duke criteria, incorporating clinical, microbiological, and echocardiographic findings, are the cornerstone for diagnosing IE. However, assessing the severity and prognosis of the disease remains intricate, necessitating reliable biomarkers that can guide clinical decision-making. Inflammation is a key component in the pathophysiology of IE, and inflammatory markers have been extensively studied for their prognostic

potential. Among these markers, the systemic immune inflammation index (SIII) and the neutrophil/lymphocyte ratio (NLR) have emerged as promising indicators. The SIII, calculated using platelet, neutrophil, and LYMs, provides a comprehensive measure of the body's inflammatory state. Similarly, the NLR, derived from the ratio of neutrophils to lymphocytes, reflects the balance between the body's innate inflammatory response and adaptive immune regulation.[3] The SIII is defined as (PltxNEU)/LYM. This index captures the interplay between thrombocytes, which are involved in clot formation and immune response, and leukocytes, which mediate inflammation and immune defense. High SIII values have been associated with poor outcomes in various cardiovascular diseases, suggesting its potential utility as a prognostic marker in IE. Elevated SIII indicates a heightened inflammatory state, which may correlate with disease severity and adverse clinical outcomes.[4] Similarly, the NLR is a straightforward and cost-effective marker that indicates the ratio of neutrophils, key players in the acute inflammatory response, to lymphocytes, crucial components of the adaptive immune system. An elevated NLR has been linked to worse outcomes in conditions such as acute coronary syndrome, heart failure, and stroke. Given the significant role of inflammation in the pathogenesis of IE, it is plausible that the NLR could serve as a valuable prognostic tool. Despite the recognized potential of SIII and NLR, there is a dearth of research specifically evaluating their prognostic significance in IE patients undergoing surgical treatment.[5] Early identification of patients at high risk of poor outcomes using these readily available markers could facilitate timely and targeted therapeutic interventions, ultimately improving patient outcomes.[6] This study aims to investigate the relationship between SIII, NLR, and mortality in patients who underwent surgical treatment for IE at our clinic between March 2020 and November 2023. By retrospectively analyzing a cohort of 100 patients, we seek to determine whether these indices can serve as reliable markers for predicting mortality and disease severity during the perioperative period. Understanding these relationships could provide clinicians with valuable insights into patient stratification and management, potentially guiding more effective perioperative care.[7] IE remains a formidable challenge in cardiology, with high stakes for patient outcomes. The integration of simple, easily measurable inflammatory indices such as SIII and NLR into clinical practice holds promise for enhancing patient management. By elucidating the prognostic value of these markers, our study endeavors to contribute to the growing body of knowledge in this area. Ultimately, our goal is to improve clinical outcomes for patients with IE by providing clinicians with robust, accessible tools for early risk assessment and intervention.[8]

METHODS

Ethics

The study was planned and approval of the of Başakşehir Çam and Sakura City Hospital Ethics Committee was obtained (Date: 18.01.2024, Decision No: E-96317027-514.10-234538482) and the study was conducted in accordance with the Declaration of Helsinki Ethical Principles and Good Clinical Practices. All data were anonymized to maintain patient confidentiality.

Study Design and Setting

This retrospective clinical study was conducted at Başakşehir Çam and Sakura City Hospital. The research focused on patients who underwent surgical treatment for IE between March 2020 and November 2023. The study aimed to evaluate the relationship between the SIII, NLR, and mortality in this patient population.

Patient Selection

A total of 100 patients over the age of 18, who received surgical treatment for IE during the specified period, were included in the study. Both male and female patients were considered, ensuring a comprehensive analysis across genders. The inclusion criteria required patients to have complete medical records with necessary laboratory and clinical data. Patients who had incomplete data or who died preoperatively were excluded from the study.

Data Collection

Data were retrospectively collected from patient medical records and included demographic information, clinical history, laboratory results, and surgical details. The parameters assessed were:

- **Demographic and Clinical Variables**: Age, gender, operation date, CPB time (Cardiopulmonary Bypass time), cross-clamp time, preoperative emboli status, preoperative stroke status, history of cardiac surgery, diabetes mellitus, hypertension, smoking status, chronic obstructive pulmonary disease (COPD), hyperlipidemia, chronic kidney disease (CKD).
- **Laboratory Parameters**: Hemoglobin (Hb), hematocrit (Hct), white blood cell count (Wbc), platelet count (Plt), neutrophil count (NEU), lymphocyte count (LYM), international normalized ratio (INR), activated partial thromboplastin time (APTT), C-reactive protein (CRP), creatinine, glomerular filtration rate (GFR), sodium (Na), potassium (K), alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, glucose levels, blood culture results, and causative microorganisms.
- **Surgical and Postoperative Data**: Type of surgery, presence of prosthetic valve endocarditis, culture-negative and culture-positive status, mortality, extubation times, intensive care unit (ICU) stay duration, hospital stay duration, presence of vegetations on aortic and mitral valves, multiple valve involvement, left ventricular ejection fraction (EF), postoperative day 1 albumin and lymphocyte levels.

Statistical Analysis

The data were evaluated using IBM SPSS 26 software (IBM Corp. Released 2019). The assumption of normality was examined using the Kolmogorov-Smirnov and Shapiro-Wilk tests. For the comparison of normally distributed data based on in-hospital mortality status, an independent two-sample t-test was employed, while the Mann-Whitney U test was used for the comparison of non-normally distributed data. The comparison of categorical data based on in-hospital mortality status was conducted using the Pearson chi-square test and Yates correction. Factors affecting in-hospital mortality were analyzed using logistic regression analysis. The significance level was set at $p<0.05$.

Index Calculations

The SIII was calculated using the formula: SIII=(PltxNEU)/LYM. The NLR was calculated as the ratio of neutrophils to lymphocytes. These indices were computed using the laboratory data collected from the patients medical records.

Study Duration

The study was planned to be completed within three months following ethical approval, including data collection, entry, and statistical analysis. By analyzing the relationship between SIII, NLR, and mortality in patients undergoing surgery for IE, this study aims to provide clinicians with valuable prognostic tools that are simple, cost-effective, and easily accessible, potentially improving patient management and outcomes in this high risk population.

RESULTS

The mean age of the patients included in the study was 53.85 years (age range: 21-83). Seventy percent of the patients were male. It was observed that 41% of the patients were smokers. Upon examining the chronic diseases present among the patients, it was found that 75% had hypertension. Additionally, 39% of the patients had a history of cardiac surgery. Preoperative embolism was observed in 20% of the patients, while preoperative stroke was noted in 26%. It was found that 70% of the patients had native-type endocarditis. Furthermore, 59% of the patients exhibited growth in their blood cultures. The mean EF of the patients was 52.96% (EF range: 25-65) (Table 1).

A statistically significant difference in age was observed among patients based on their mortality status (p<0.001). The mean age of patients who did not experience mortality was 49.67 years, whereas the mean age of patients who experienced mortality was significantly higher at 61.97 years. Furthermore, no statistically significant relationship was found between patients' mortality status and other demographic and clinical characteristics (p>0.05).

A statistically significant difference was identified in Hb levels among patients based on their in-hospital mortality status (p=0.007), with patients who experienced mortality exhibiting lower Hb levels compared to those who did not. Similarly, Hct values demonstrated a statistically significant difference (p=0.005), indicating that patients who experienced mortality had lower Hct levels than their counterparts. LYM also revealed a statistically significant difference (p=0.001), with lower LYM values observed in patients who experienced mortality compared to those who did not. Plt exhibited a statistically significant difference (p=0.033), with patients who experienced mortality showing lower Plt values than those without mortality. INR values displayed a statistically significant difference (p=0.049), with patients who experienced mortality having higher INR values compared to their non-mortality counterparts. CRP levels showed a statistically significant difference (p=0.028), with higher CRP values found in patients who experienced mortality compared to those who did not. Glucose levels also demonstrated a statistically significant difference (p<0.001), with patients who experienced mortality exhibiting elevated glucose levels compared to their

Table 1. Examination of demographic and patient characteristics according to in-hospital mortality status

	In hospital mortality		Total (n=100)	SS	p
	Negative (n=66)	Positive (n=34)			
Age	49.67±15.05	61.97±11.07	53.85±14.96	-4.639	**<0.001**[t]
Gender					
Women	16 (24.2)	14 (41.2)	30 (30)	2.311	0.128[y]
Men	50 (75.8)	20 (58.8)	70 (70)		
Smoke					
Negative	37 (56.1)	22 (64.7)	59 (59)	0.382	0.537[y]
Positive	29 (43.9)	12 (35.3)	41 (41)		
Chronic diseases*					
Hypertension	37 (72.5)	23 (79.3)	60 (75)	8.475	0.132[x]
Diabetes mellitus	19 (37.3)	19 (65.5)	38 (47.5)		
Hyperlipidemia	16 (31.4)	12 (41.4)	28 (35)		
Chronic kidney disease	15 (29.4)	12 (41.4)	27 (33.8)		
COPD	14 (27.5)	7 (24.1)	21 (26.3)		
History of cardiac surgery					
Negative	41 (62.1)	20 (58.8)	61 (61)	0.011	0.917[y]
Positive	25 (37.9)	14 (41.2)	39 (39)		
Preoperative embolism					
Negative	54 (81.8)	26 (76.5)	80 (80)	0.136	0.712[y]
Positive	12 (18.2)	8 (23.5)	20 (20)		
Preoperative stroke					
Negative	51 (77.3)	23 (67.6)	74 (74)	0.638	0.424[y]
Positive	15 (22.7)	11 (32.4)	26 (26)		
Type of endocarditis					
Native	44 (66.7)	26 (76.5)	70 (70)	0.613	0.434[y]
Prosthetic	22 (33.3)	8 (23.5)	30 (30)		
Colonization in blood culture					
Negative	27 (40.9)	14 (41.2)	41 (41)	0.000	1.000[y]
Positive	39 (59.1)	20 (58.8)	59 (59)		
EF (%)	55 (25 - 65)	57.5 (30 - 65)	55 (25 - 65)	-0.557	0.578[m]

t: Independent two sample t test, m: Mann Whitney U test, y: Yates correction, x: Pearson Chi-Square test, multiple response mean±standart deviation, median (minimum-maximum), n (%), SS: Statistical significance, COPD: Chronic obtructive pulmonary disease, EF: Ejection fraction

non-mortality counterparts. Creatinine levels revealed a statistically significant difference (p=0.023), with patients who experienced mortality having higher creatinine values than those without mortality. GFR values exhibited a statistically significant difference (p=0.003), with patients who experienced mortality showing lower GFR values compared to their non-mortality counterparts. Albumin levels demonstrated a statistically significant difference (p<0.001), with patients who experienced mortality having lower albumin values than those who did not. The systemic immune-inflammation index (SII) values also showed a statistically significant difference (p=0.041), with higher SII values observed in patients who experienced mortality compared to those without. Furthermore, NLR values exhibited a statistically significant difference (p<0.001), with patients who experienced mortality having higher NLR values compared to their non-mortality counterparts. However, no statistically significant relationship was found between patients' in-hospital mortality status and other preoperative laboratory tests (p>0.05) (**Table 2**).

A statistically significant difference was found in the durations of cardiopulmonary bypass (CPB) among patients based on their in-hospital mortality status (p=0.046), with patients who experienced mortality having longer CPB durations. There is a statistically significant difference in the lengths of stay in the ICU according to the patients' in-hospital mortality status (p=0.001). The length of stay in the ICU for patients who experienced mortality was found to be higher compared to those who did not. A statistically significant relationship was identified between the patients' in-hospital mortality status and the need for postoperative hemodialysis (HD) (p<0.001). The proportion of patients requiring postoperative HD among those who did not experience mortality was 12.1%, whereas this proportion was significantly higher at 55.9% among patients who experienced mortality. No statistically significant relationship was found between the patients' in-hospital mortality status and other intraoperative and postoperative variables (p>0.05) (**Table 3**).

Table 2. Examination of preoperative laboratory tests according to in-hospital mortality status

	In hospital mortality		Total (n=100)	SS	p
	Negative (n=66)	Positive (n=34)			
Hb	9.94±1.61	9.01±1.58	9.63±1.65	2.776	**0.007[t]**
Hct	30.7±4.69	27.83±4.78	29.73±4.89	2.882	**0.005[t]**
Wbc	8.57 (0.74-30.74)	10.18 (2.9-48.07)	9.44 (0.74-48.07)	-1.313	0.189[m]
Neu	5.87 (0.28-26.96)	7.71 (1.85-39.1)	6.58 (0.28-39.1)	-1.717	0.086[m]
Lym	1.5 (0.29-3.77)	1.08 (0.25-5.7)	1.32 (0.25-5.7)	-3.286	**0.001[m]**
Plt	226 (38-478)	186 (26-568)	223.5 (26-568)	-2.136	**0.033[m]**
INR	1.13 (0.9-6.9)	1.3 (0.9-3.14)	1.18 (0.9-6.9)	-1.971	**0.049[m]**
APTT	35.75±9.37	38.16±8.31	36.57±9.05	-1.261	0.210[t]
CRP	44.15 (1-343.7)	87.8 (2.6-311.5)	47.89 (1-343.7)	-2.198	**0.028[m]**
Glukoz	112.5 (68-299)	145.5 (78-306)	115.5 (68-306)	-3.577	**<0.001[m]**
Kreatinin	1 (0.43-9.69)	1.55 (0.45-4.83)	1.11 (0.43-9.69)	-2.278	**0.023[m]**
GFR	85.5 (6-137)	47 (8-125)	65.5 (6-137)	-2.991	**0.003[m]**
Na	136 (129-163)	137.5 (123-156)	136 (123-163)	-1.153	0.249[m]
K	4.2±0.49	4.05±0.69	4.14±0.57	1.119	0.268[t]
ALT	20.5 (3-303)	13 (3-176)	16.5 (3-303)	-1.664	0.096[m]
AST	22 (7-188)	25 (9-99)	24 (7-188)	-0.630	0.529[m]
Albumin	32.77±6.03	26.79±6.24	30.74±6.71	4.641	**<0.001[t]**
SII	1053.02 (34.32-3887.92)	1424.45 (158.57-5582.59)	1074.55 (34.32-5582.59)	-2.045	**0.041[m]**
NLO	4.23 (0.9-16.07)	8.95 (1.39-28.66)	5.33 (0.9-28.66)	-3.915	**<0.001[m]**

t: Independent two sample T test, m: Mann-Whitney U test, mean±standart deviation, median (minimum-maximum), Hb: Hemoglobin, Hct: Hematocrit, Wbc: White blood cell count, Neu: Neutrophil count, Lym: Lymphocyte count, Plt: Platelet count, INR: International normalized ratio, APTT: Activated partial thromboplastin time, CRP: C-reactive protein, GFR: Glomerular filtration rate, Na: Sodium, K: Potassium, ALT: Alanine aminotransferase, AST: Aspartate aminotransferas, SII: Systemic Immune-Inflammation Index, NLO: Newborn life outcomes, SS: Statistical significance

Table 3. Comparison of intraoperative and postoperative variables based on in-hospital mortality status

	In hospital mortality		Total (n=100)	SS	p
	Negative (n=66)	Positive (n=34)			
Type of operation					
Elective	44 (66.7)	20 (58.8)	64 (64)	0.307	0.579[y]
Emergency	22 (33.3)	14 (41.2)	36 (36)		
Type of valve					
Mechanical	51 (77.3)	23 (67.6)	74 (74)	0.638	0.424[y]
Bioprosthesis	15 (22.7)	11 (32.4)	26 (26)		
CPB time	156.5 (58-403)	201 (39-460)	168 (39-460)	-1.998	**0.046[m]**
X clamp time	119.5 (0-329)	118.5 (0-337)	119 (0-337)	-0.258	0.796[m]
ICU time	3 (1-27)	11 (1-49)	4 (1-49)	-3.479	**0.001[m]**
Need for postoperative hemodialysis					
Negative	58 (87.9)	15 (44.1)	73 (73)	19.8	**<0.001[y]**
Positive	8 (12.1)	19 (55.9)	27 (27)		

m: Mann Whitney U Test, y: Yates Correction, median (minimum-maximum), n (%), CPB: Cardiopulmonary bypass, ICU: Intensive care unit, SS: Statistical significance

The effects of age, postoperative HD requirement, surgical intervention index (SII), and newborn life outcomes (NLO) values on patients' in-hospital mortality status were investigated using univariate and multivariate logistic regression models (**Table 4**). The univariate analysis revealed that the effects of age, postoperative HD requirement, SII, and NLO variables on in-hospital mortality were statistically significant ($p<0.05$). The risk of developing mortality increases as patients' ages increase (OR: 1.071, $p<0.001$). Patients requiring postoperative HD have a higher risk of developing mortality compared to those who do not require postoperative HD (OR: 9.183, $p<0.001$). The risk of developing mortality increases as patients' SII values increase (OR: 1.001, $p=0.005$). Additionally, the risk of developing mortality increases as patients' NLO values increase (OR: 1.219, $p<0.001$).

The multivariate analysis indicated that the combined effects of age, postoperative HD requirement, and NLO variables on in-hospital mortality were statistically significant ($p<0.05$). The risk of developing mortality increases as patients' ages increase (OR: 1.089, $p=0.001$). Patients requiring postoperative HD have a higher risk of developing mortality compared to those who do not require postoperative HD (OR: 7.531, $p=0.002$). The risk of developing mortality increases as patients' NLO values increase (OR: 1.357, $p=0.005$). However, the SII values of the patients did not have a statistically significant effect on mortality ($p=0.536$). The developed multivariate model correctly classifies 79% of the cases.

DISCUSSION

IE is a serious and often fatal condition that continues to challenge clinicians with its complex presentation and high risk of complications. Our study focused on evaluating the prognostic value of the SIII and NLR in patients undergoing surgical treatment for IE. The results showed that higher SIII and NLR values were significantly associated with increased mortality, suggesting their potential benefit as prognostic markers. However, in multivariate logistic regression analysis, NLR was found to be more effective in predicting mortality. In addition, according to the multivariate logistic regression analysis, age and the need for postoperative HD were also found to be effective in predicting mortality.

Our findings align with several studies that have highlighted the significance of inflammatory markers in predicting outcomes in IE. For instance, a study by Chen Y et al.[9] found that an elevated NLR was a strong independent predictor of mortality in patients with IE. The researchers observed that patients with higher NLR values had worse outcomes, which is consistent with our findings where the mortality group had significantly higher NLR values.

Research by Agus HZ et al.[10] demonstrated that systemic inflammation plays a critical role in the progression and prognosis of IE. They showed that markers of systemic inflammation, including the SIII, were significantly elevated in patients with adverse outcomes. This supports our observation that higher SIII values are associated with increased mortality, indicating severe systemic inflammation.

The differences in laboratory parameters between survivors and non-survivors in our study further highlight the impact of inflammation and immune response on patient outcomes. For example, we found that patients who did not survive had lower Hb and Hct levels, higher Wbcs, and elevated CRP levels. These findings are in line with those of Ali Hassan et al.[11] who reported that anemia and elevated inflammatory markers were significant predictors of poor prognosis in IE.

Our study also found that renal function and the need for postoperative HD were associated with mortality in the mortality group, as indicated by higher creatinine levels and lower GFR. This finding was echoed by Chaudry, Mavish S et al.[12] who identified renal dysfunction as a common complication that significantly increases the risk of mortality in IE. The interaction between renal failure and systemic inflammation is likely to exacerbate the severity of IE, leading to worse outcomes.

Extended hospital stays observed in non-survivors in our study reflect the increased complexity and severity of their clinical course. This is consistent with findings from the International Collaboration on Endocarditis-Prospective Cohort Study Durante-Mangoni E et al.[13] which reported that patients with severe IE complications often require prolonged hospitalization. These prolonged hospital stays underscore the need for early identification and aggressive management of high risk patients.

Several studies have explored the prognostic value of other biomarkers in IE. For example, Bekir K et al.[14] investigated the role of procalcitonin as a predictor of mortality in IE and found that higher procalcitonin levels were associated with increased risk of death. While our study focused on SIII and NLR, incorporating a broader range of biomarkers could enhance the predictive accuracy and provide a more comprehensive assessment of patient risk.

In comparing our findings with those of other studies, it is evident that while some parameters like SIII and NLR consistently emerge as significant prognostic markers, the specific thresholds and their predictive accuracy can vary. For example, a study by Meshaal, M.S[15] suggested slightly different cutoff values for NLR in predicting mortality, which could be due to differences in patient populations and clinical settings. This variability underscores the need for further research to

Table 4. Examination of the effects of age, postoperative hemodialysis (HD) requirement, surgical intervention index (SII), and newborn life outcomes (NLO) variables on in-hospital mortality status

	Univariate		Multivariate	
	OR (%95 CI)	p	OR (%95 CI)	p
Age	1.071 (1.032 - 1.112)	**<0.001**	1.089 (1.034 - 1.146)	**0.001**
Need for hemodialysis	9.183 (3.37 - 25.021)	**<0.001**	7.531 (2.137 - 26.535)	**0.002**
SII	1.001 (1 - 1.001)	**0.005**	1 (0.999 - 1.001)	0.536
NLO	1.219 (1.096 - 1.356)	**<0.001**	1.357 (1.098 - 1.677)	**0.005**

OR: Odds ratio, Accuracy=0.790, SII: Systemic Immune-inflammation Index, NLO: Newborn life outcomes

standardize these markers and validate their prognostic utility across diverse cohorts.

The relationship between systemic inflammation and other clinical parameters such as renal function, anemia, and extended hospital stays highlights the multifaceted nature of IE and its complications. Studies like that of Regunath H et al.[16] have emphasized the importance of a multidisciplinary approach in managing IE, integrating cardiology, infectious disease, nephrology, and critical care expertise to optimize patient outcomes.

Our study adds to the growing body of evidence supporting the use of inflammatory markers such as SIII and NLR in predicting mortality in IE patients. These markers offer a simple, cost-effective means of stratifying risk and guiding clinical decision-making. Future research should focus on refining these indices, exploring their integration into clinical practice, and examining their interplay with other prognostic factors to enhance patient outcomes in IE. By continuing to investigate and validate these biomarkers, we can improve our ability to identify high-risk patients early and implement targeted interventions to reduce mortality and improve the quality of care for those affected by this serious condition.

CONCLUSION

Our study highlights the significant prognostic value of SIII and NLR in predicting mortality in patients undergoing IE surgery. Although SIII was found to be significantly higher in the mortality group, it did not play a role in predicting mortality. NLR, on the other hand, was found to be significantly higher in both mortality group and significantly higher in predicting mortality. Therefore, according to the multivariate logistic regression analysis, age, postoperative HD requirement and NLR were found to be effective in predicting mortality.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was planned and approval of the of Başakşehir Çam and Sakura City Hospital Ethics Committee was obtained (Date: 18.01.2024, Decision No: E-96317027-514.10-234538482).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Turak O, Özcan F, Işleyen A, et al. Usefulness of neutrophil-to-lymphocyte ratio to predict in-hospital outcomes in infective endocarditis. *Can J Cardiol*. 2013;29(12):1672-1678.
2. Yuan M, Ren F, Gao D. The Value of SII in Predicting the Mortality of Patients with Heart Failure. *Dis Markers*. 2022;2022:3455372. doi:10.1155/2022/3455372
3. Yang YL, Wu CH, Hsu PF, et al. Systemic immune-inflammation index (SII) predicted clinical outcome in patients with coronary artery disease. *Eur J Clin Invest*. 2020;50(5):e13230. doi:10.1111/eci.13230
4. Saylik F, Akbulut T. Systemic ımmune-ınflammation ındex predicts major cardiovascular adverse events in patients with st-segment elevated myocardial ınfarction. *Arq Bras Cardiol*. 2022;119(1):14-22. doi:10.36660/abc.20210412
5. Öcal L, Keskin M, Cerşit S, et al. Systemic immune-inflammation index predicts in-hospital and long-term outcomes in patients with ST-segment elevation myocardial infarction. *Coron Artery Dis*. 2022;33(4):251-260. doi:10.1097/MCA.0000000000001117
6. Tascini C, Aimo A, Arzilli C, et al. Procalcitonin, white blood cell count and C-reactive protein as predictors of S. aureus infection and mortality in infective endocarditis. *Int J Cardiol*. 2020;301:190-194. doi:10.1016/j.ijcard.2019.08.013
7. Nunes MCP, Guimarães-Júnior MH, Murta Pinto PHO, et al. Outcomes of infective endocarditis in the current era: Early predictors of a poor prognosis. *Int J Infect Dis*. 2018;68:102-107. doi:10.1016/j.ijid.2018.01.016
8. Meshaal MS, Nagi A, Eldamaty A, Elnaggar W, Gaber M, Rizk H. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as independent predictors of outcome in infective endocarditis (IE). *Egypt Heart J*. 2019;71(1):13.
9. Chen Y, Ye LJ, Wu Y, et al. Neutrophil-Lymphocyte Ratio in Predicting Infective Endocarditis: A Case-Control Retrospective Study. *Mediators Inflamm*. 2020;2020:8586418.
10. Agus HZ, Kahraman S, Arslan C, et al. Systemic immune-inflammation index predicts mortality in infective endocarditis. *J Saudi Heart Assoc*. 2020;32(1):58-64. doi: 10.37616/2212-5043.1010
11. Hassan A, Radwan M, ELSaidy MA, Mai A, ELmonem S, Alkassas AF. "Diagnostic use of serum ferritin as a predictor of hospital outcome at admission in patients with infective endocarditis". *Cardiol Angiol: An Int J*. 2023;12(3):96-104. doi:10.9734/ca/2023/v12i3330
12. Chaudry MS, Carlson N, Gislason GH, et al. Risk of infective endocarditis in patients with end stage renal disease. *Clin J Am Soc Nephrol*. 2017;12(11):1814-1822.
13. Durante-Mangoni E, Bradley S, Selton-Suty C, et al. Current features of infective endocarditis in elderly patients: results of the International Collaboration on endocarditis prospective cohort study. *Arch Intern Med*. 2008;168(19):2095-2103. doi:10.1001/archinte.168.19.2095
14. Kocazeybek B, Küçükoğlu S, Oner YA. Procalcitonin and C-reactive protein in infective endocarditis: correlation with etiology and prognosis. *Chemotherapy*. 2003;49(1-2):76-84. doi:10.1159/000069777
15. Meshaal MS, Nagi A, Eldamaty A, Elnaggar W, Gaber M, Rizk H. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as independent predictors of outcome in infective endocarditis (IE). *Egypt Heart J*. 2019;71(1):13.
16. Regunath H, Vasudevan A, Vyas K, et al. A Quality ımprovement ınitiative: developing a multi-disciplinary team for infective endocarditis. *Mo Med*. 2019;116(4):291-296.

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Investigation of the relationship between nutrition and coronary slow flow-coronary ectasia in patients with acute coronary syndrome

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ABSTRACT

Aims: It is known that malnutrition is associated with various diseases and poor prognosis, but the relationship of this condition with slow coronary flow and coronary ectasia (CE) is not clearly known. In our study, we tried to examine the relationship between malnutrition and slow flow-CE in acute coronary syndrome (ACS) patients.

Methods: We examined the relationship between Controlled Nutritional Status (CONUT) score, Nutritional Risk Index (NRI) score and Prognostic Nutrition Index (PNI) score in patients who underwent coronary angiography due to ACS and were found to have CE-slow flow.

Results: According to the Conut score, malnutrition was not found out in 57% of the patients, but mild malnutrition was found out in 30%, moderate malnutrition in 10% and severe malnutrition in 1 patient; according to the PNI score, malnutrition was not found out in 61% of the patients, but moderate malnutrition was found outin 19%, severe malnutrition was found out in 18% and coronary slow flow (CSF)-ectasia wasfound out in 44% of these patients (p=0.003, p=0.002).

Conclusion: Malnutrition is associated with slow flow and CE in patients with ACS. Nutritional assessment and corrective measures are vital for this patient group. Clinical studies are required toevaluate these patients prospectively.

Keywords: CONUT score, NRI score, PNI score, malnutrition

INTRODUCTION

Mortality in patients with acute coronary syndrome (ACS) is still high despite all the advances in treatment.[1] Coronary ectasia (CE) and slow flow were found out during coronary angiography in ACS patients.[2] Coronary microvascular disease was found out in some patients in histopathological studies[3], but the exact pathophysiology is still not understood. Identification of high-risk patients in coronary artery disease is significant in terms of management of patient risk factors. Malnutrition has been found to be associated with poor prognosis of cancer, kidney disease, heart failure and ACS.[4] It is essential that nutrition is a modifiable factor compared to other risk factors.[5] Malnutrition is one of the important issues that is not sufficiently highlighted in risk management in ACS patients.

In this study, we aimed to evaluate malnutrition in patients with and without slow flow phenomenon in ACS patients and to examine the relationship between ectasia and slow flow phenomenon.

METHODS

This study was approved by Mardin Artuklu University Faculty of Medicine Non-interventional Clinical Researches Ethics Committee Date:05.11.2024, Decision No: 2024/11-1). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients who were admitted to our hospital due to ACS in 2023 were retrospectively scanned through the hospital information system. 107 patients diagnosed with myocardial infarction in accordance with the '2023 ESC Guidelines for the management of ACSs' were included in the study. Coronary slow flow phenomenon (CSFP) is defined as a condition in which opaque material reaches the distal coronary vessels late during angiography, despite the absence of significant epicardial coronary artery stenosis. This phenomenon can be seen in normal or near-normal coronary arteries, indicating a dysfunction in the microvascular circulation.[6] In addition, CE refers to the abnormal dilatation of the coronary artery, defined as an arterial segment dilated by at least 1.5 times

the diameter of the adjacent normal segment, demonstrated by coronary angiography.[7] This condition can lead to various complications, including myocardial ischemia, due to altered hemodynamics and the potential for thrombosis in the dilated segment.[7]

CSFP and CE are important clinical conditions that can cause structural changes in microvascular function and coronary circulation and lead to coronary ischemia. Cardiogenic shock, serious active and chronic infection, active bleeding, autoimmune diseases, pregnancy, aortic dissection, acute pulmonary edema, hypertrophic cardiomyopathy, endocarditis, percarditis, major surgery, and oncology patients undergoing active treatment were excluded from the study (**Figure 1**).

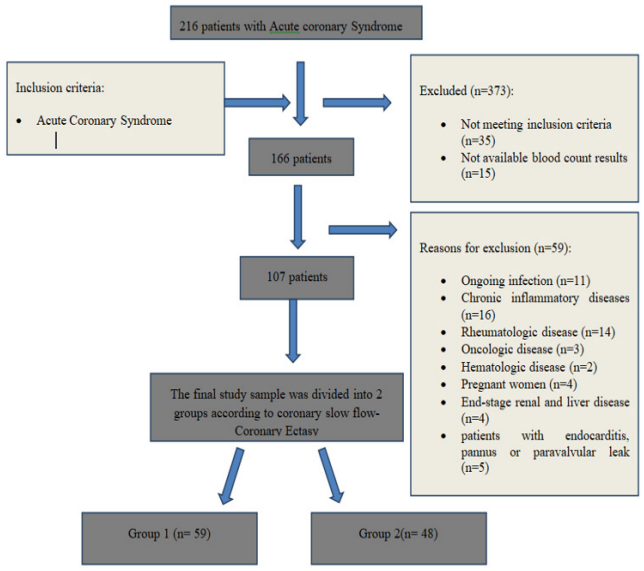

Figure 1. Flow chart of the study population

Adequate Nutrition Screening Tools

Body-mass index (BMI), defined as body mass (in kilograms) divided by the square of body height (in meters), was calculated for all patients. According to BMI, patients were classified as underweight (<18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), and overweight (>25.0). The Controlled Nutritional Status score (CONUT) was developed by Ulibarri et al.[8] and was used as a screening tool for the nutritional status of hospitalized patients in 2005. It is calculated using serum albumin, cholesterol, and total lymphocyte count. A score from 0 to 1 is considered normal; scores from 2 to 4, 5 to 8, and 9 to 12 reflect mild, moderate, and severe malnutrition, respectively. The Nutritional Risk Index (NRI) is a nutritional assessment score that has become popular in recent years due to its simplicity and strong prognostic value in various medical and surgical patient populations. Buzby et al.[9] initially defined NRI using the formula 1.519 serum albumin (g/l)+41.7 (current body weight [kg]/normal body weight [kg]). According to previous studies[10] and using the Lorenz formulas, normal body weight was replaced by ideal body weight; that is, height (cm)-100–([height (cm)-150]/4) for men and height (cm) -100–([height (cm)-150]/2.5) for women.[11] In accordance with previous studies[11], we defined weight as: current body weight/ ideal body weight=1 (when current body weight exceeds ideal body weight). Patients were classified into 4 nutritional risk categories based on their baseline NRI values as defined in previous studies: severe nutritional risk (NRI <83.5), moderate nutritional risk (83.5 < NRI <97.5), mild nutritional risk (97.5 < NRI <100), and no nutritional risk (>100 NRI). The Prognostic Nutrition Index score (PNI) was calculated using the formula 10* serum albumin (g/dl)+0.005 *total lymphocyte count (mm^3).[12] A score of >38 is considered normal; scores between 35 and 38 and <35 reflect moderate and severe malnutrition, respectively. There is no category for mild malnutrition for PNI.

Statistical Analysis

Data were analyzed using SPSS version 25.0 for Windows (IBM Corp., Armonk, NY, USA). Subjective methods and objective methods, Lilliefors and Shapiro-Wilk tests, were used to assess the normal distribution of continuous variables. Continuous variables were expressed as mean±standard deviation (SD) or median (interquartile range), and categorical variables were expressed as percentages. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. Comparisons between multiple groups were made using one-way analysis of variance (ANOVA) test or Kruskal Wallis test, and Fisher's exact test was applied for categorical variables when appropriate. $p<0.05$ was considered statistically significant.

RESULTS

Our study included 48 (45%) patients with ectasia-slow coronary flow group detected and 59 (55%) patients without ectasia-slow coronary flow who underwent angiography in 2023. Of the patients with ectasia-slow coronary flow detected, 8 (16.7%) had ST elevation myocardial infarction (STEMI), 18 (37.5%) had NSTEMI (Non ST elevation myocardial infarction), 22 (45.9%) had USAP (Unstable angina pectoris). In the undetected group, 11 (18.6%) had STEMI, 32 (54.2%) had NSTEMI, and 16 (27.1%) had USAP, respectively (p=0.046) (**Table 1**). The prevalence of DM (diabetes mellitus) was lower in patients with ectatic-slow coronary flow compared to patients without it ((7(14.6%) vs. 21(35.6%) p=0.014)). 74 (69%) of the patients were male and 33 (31%) were female (p=0.111) all were white. The mean age was 59.9(±10.5) in the group with ectasia-slow coronary group and 61.2(±11.3) in the group without it (p=0.546). Left ventricular ejection fraction was 52.4 (25-60) in the group with ectasia - slow coronary flow group and 55.6(40-65) in the group without it (p=0.056). While BMI was calculated below 25 in 46 patients, BMI was calculated above 25 in 59 patients. More data on the basic characteristics of the study population are given in **Table 1**.

Malnutrition was observed in 40% of the patients with CONUT score, in all patients with NRI score, and in 37% with PNI (**Table 2**). According to CONUT score, malnutrition was observed in 30% (n=33) of the patients. Moderate-severe malnutrition was found out in 10% (n=12) of the patients with Conut score, in all patients with NRI score, and in 37% (n=41) of the patients with PNI score (**Table 2**).

In malnutrition prevalence there was no relationship between CONUT score, NRI score, PNI score and patients with BMI below or above 25 (p=0.081,p=0.159,p=0.375) (**Table 3, Figure 2**). No statistically significant difference was found out between genders in terms of malnutrition prevalence (CONUT score, NRI score and PNI score) (p=0.540, p=0.558, p=0.078) (**Table 4, Figure 3**). Additionally, no statistically significant difference was observed between the laboratory

Table 1. Baseline characteristics of study population

		Non-coronary slow flow-ectasy (n=59)	Coronary slow flow-ectasy (n=48)	p value
Gender (female/male), n (%)		22 (37%)/37 (62%)	11 (22%)/37 (77%)	0.111
Age, (years)		61.2 (±11.3)	59.9 (±10.5)	0.546
Height (centimeter)		163.96 (±6.6)	164.1 (±6.4)	0.649
Weight (kilogram)		68.98 (±13.2)	68.09 (±12.1)	0.720
Body-mass index (kg/m²)		23.34 (±5.8)	24.4 (±2.1)	0.286
Heart rate (minute)		73.06 (±12.5)	81.6 (±24.7)	0.122
EF, % (IQR)		52.4 (25-60)	55.6 (40-65)	0.056
HT, n (%)		33 (55.9%)	25 (52.1%)	0.695
DM, n (%)		21 (35.6%)	7 (14.6%)	**0.014**
HPL, n (%)		24 (40.7%)	17 (35.4)	0.581
Smoking, n(%)		18 (30.5%)	16 (33.3%)	0.758
COPD, n(%)		3(5.1%)	3(6.3%)	0.759
Previous PCI, n%		18 (30.5%)	11 (22.9%)	0.380
Previous CABGO, n%		2 (3.4%)	1 (2.1%)	0.680
Hospitalization day, IQR		2,95 (1-8)	2.52 (1-16)	0.217
Myocardial infarction types	STEMI, n(%)	11 (18.6%)	8 (16.7%)	**0,046**
	NSTEMI, n(%)	32 (54.2%)	18 (37.5%)	
	SAP, n(%)	15 (25.4%)	18 (37.5%)	
	USAP, n(%)	1 (1.7%)	1 (2.1%)	
	Type 2 MI, n(%)	0 (0%)	3 (6.3%)	

EF :Ejection fraction, IQR: Interquartile range, HT :Hypertension, DM: Diabetes mellitus, HPL :Hyperlipidemia,COPD: Chronic obstrictive pulmonary disease, PCI: Percutaneous coronary intervention, CABGO :Coronary artery bypass graft operation, STEMI: ST elevation myocardial infarction, NSTEMI: Non-ST elevation myocardial infarction , SAP: Stabil angina pectoris, USAP: Unstabil angina pectoris, MI :Myocardial infarction

Table 2. Prevalance of malnutrition according to three different scoring system

Nutritional indeces	Absent	Mild	Moderate	Severe
CONUT score	0-1	2-4	5-8	9-12
Albumin, g/dl (score)	>3.49 (77)	3-3.49 (29)	2.5-3 (1)	<2.5(0)
Total cholesterol mg/dl	>179 (90)	140-179 (17)	100-139 (0)	<100(0)
Lymphocyte count, (10^3/mm^3)	>1.59 (99)	1.2-1.59 (8)	0.8-1.19 (0)	<0.8(0)
Study population, n (non-coronary slow flow-ectasy/ coronary slow flow-ectasy), (%)	62 (44+18) (57%)	33 (10+23) (30%)	11 (4+7) (10%)	1(1+0) (<1%)
NRI, points	>99	97-5-99.99	83.5-97.49	<83.5
Formula 1.489* serum albumin (g/dl)+41.7 (weight in kilograms/ideal weight)				
Study population, n (non-coronary slow flow-ectasy/ coronary slow flow-ectasy), (%)	(0%) (0)	(0%) (0)	(2+0) (<1%)	(57+48) (>99%)
PNI score, points	>38	-	35-38	<35
Formula 10*serum albumi (g/dl)+0,005* total lymphocyte count (mm^3)				
Study population, n (non-coronary slow flow-ectasy/ coronary slow flow-ectasy), (%)	(43+23) (61%)	-	(11+10) (19%)	(5+15) (18%)

NRI: Nutritional Risk Index, CONUT: Controlled Nutritional Status Score, PNI: Prognostic Nutrition Index

Table 3. BMI and nutritional indeces

Nutritional indeces	**Absent**	**Mild**	**Moderate**	**Severe**	**p value**
CONUT score, n, (BMI<24.9; BMI>25)	22/39	16/18	8/3	0/1	0.081
NRI, points, n, (BMI<24.9; BMI>25)	0/0	0/0	0/2	46/59	0.159
PNI score, points, n, (BMI<24.9; BMI>25)	27/39	-	8/13	11/9	0.375

NRI: Nutritional risk index, CONUT: Controlled nutritional status score, PNI: Prognostic nutrition index, BMI: Body-mass index

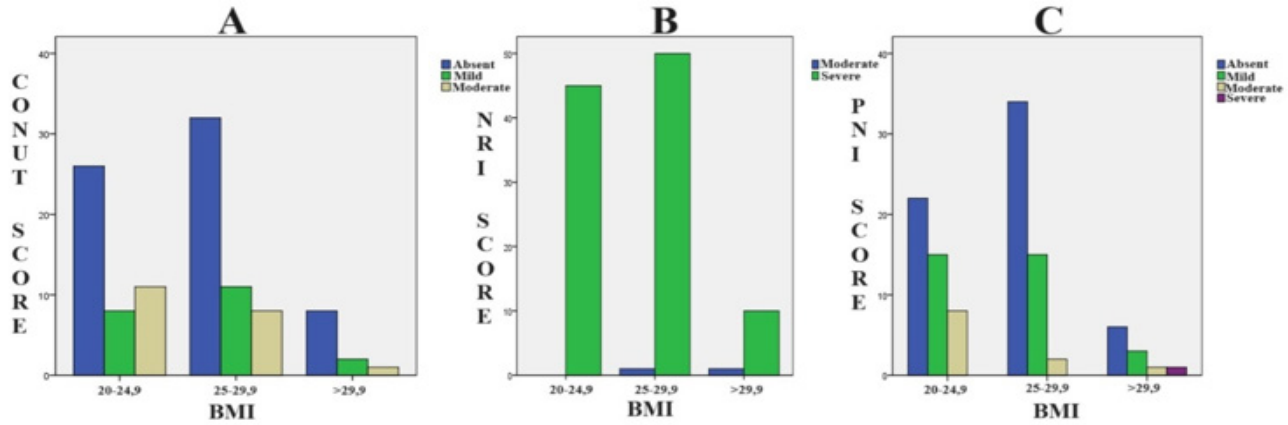

Figure 2. Malnutrition and body-mass index

Table 4. Body-mass index and gender

Nutritional indeces	Absent	Mild	Moderate	Severe	p value
CONUT score, n, (female/male)	19/43	11/22	3/8	1/0	0.540
NRI, points, n, (female/male)	0/0	0/0	1/1	33/72	0.558
PNI score, points, n, (female/male)	18/48	-	6/15	10/10	0.078

NRI: Nutritional risk index, CONUT: Controlled nutritional status score, PNI: Prognostic nutrition index

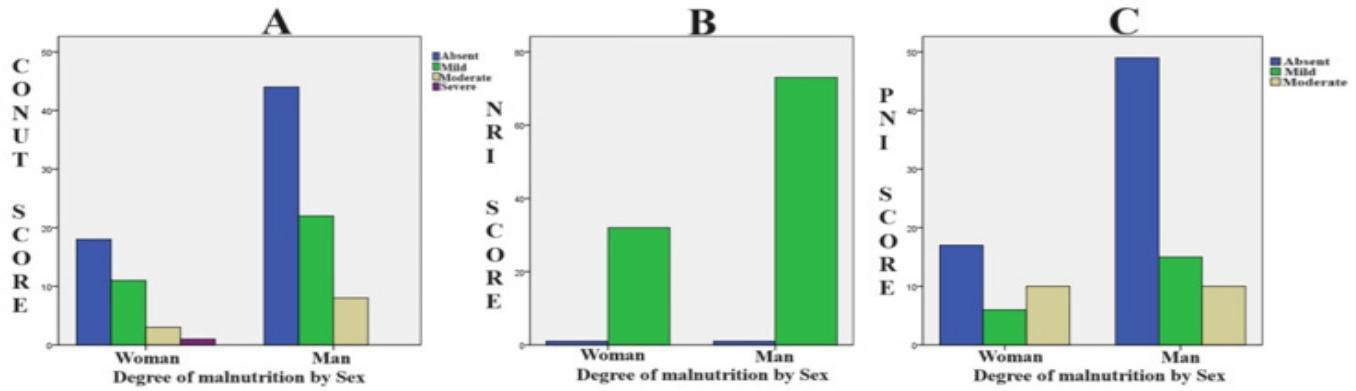

Figure 3. Malnutrition by gender

Tabel 5. Labaratory parameters

	Non-coronary slow flow-ectasy (n=59)	Coronary slow flow-ectasy	p value
WBC (x10³/uL)	9.3 (±3.0)	9.9 (±2.6)	0.285
Urea, (mg/dl)	36.7 (±15.6)	36.2 (±18.0)	0.891
Creatinine, (mg/dl)	0.9 (±0.2)	0.86 (±0.2)	0.242
CRP (mg/dL)	1.2 (±1.6)	1.7 (±3.2)	0.353
Total cholesterol (mg/dl)	187.3 (±55.5)	187.9 (±51.5)	0.957
HDL cholesterol (mg/dl)	42 (±11.5)	39.3 (±9.7)	0.203
LDL cholesterol (mg/dl)	106.4 (±41.1)	115.7 (±44.6)	0.277
Triglyceride (mg/dl) (IQR)	186.4 (49-1010)	162.2 (36-397)	0.307
Hgb (g/L)	13.8 (±1.6)	14.5 (±1.4)	0.034
Albumin (g/L)	4.0 (±0.4)	3.9 (±0.5)	0.163
Monocyte (10³/mm³)	0.6 (±0.2)	0.6 (±0.2)	0.749
Neutrophil (10³/mm³)	6.1 (±2.8)	6.6 (±2.6)	0.377
Lymphocyte (10³/mm³)	2.3 (±0.9)	1.7 (±0.6)	**0.000**
Platelet (10³/mm³)	248.1 (±71.7)	255.1 (±76.9)	0.632

WBC: White blood cell, CRP : C-reactive proteine , HDL : High-density lipoprotein, LDL: Low-density lipoproteine, Hgb :Hemoglobin, IQR: Interquartile range

parameters of the non-CSF-ecstasy group and the CSF-ecstasy group (except for lymphocyte count, p=0.000) (**Table 5**).

DISCUSSION

Malnutrition is common in patients with ACS. To our knowledge, this is the first study in literature to examine the relationship between malnutrition and CE slow flow phenomenon (CSF). Malnutrition is important because it is a modifiable risk factor in this patient group.[13] In our study, it was determined that 42% of patients (n=45) were malnourished according to the CONUT score, 99% of patients (n=107) according to the NRI score, and 37% of patients (n=46) according to the PNI score in ACS patients (**Table 2**). Severe malnutrition was observed in <1% of patients according to the CONUT score, 99% of patients according to the NRI score, and 18% according to the PNI score (**Table 2**). In patients with slow flow-CE, according to the CONUT score (n=18), malnutrition was not found out in 16% (n=23), mild malnutrition was found out in 21% (n=7), moderate malnutrition was found out in 6%, severe malnutrition was found out in 44% of patients according to the NRI score (n=48), and severe malnutrition was found out in 14% of patients according to the PNI score (n=15). In this study, p=0.000 for CONUT, p=0.2 for NRI, and p=0.003 for PNI were observed among the scores in determining malnutrition. There are few studies examining the relationship between malnutrition in ACS patients, for example, Tonet et al.[14] indicated that 44% of ACS patients had a risk of malnutrition. In addition, there is no study examining the relationship between CSF and malnutrition. For us, clinical cardiologists, malnutrition is often not recognized and treated. The use of these risk scores will contribute to the identification of malnourished patients in clinical practice.

The second point to be noted is that malnutrition can also be observed in overweight and obese people (**Table 3, Figure 2**). Sze et al.[13] reported that half of the patients with heart failure were malnourished according to the CONUT score. Screening for malnutrition should be performed in ACS patients regardless of weight.

The third important issue is the relationship between ACS and malnutrition. Yoo et al.[15] showed that malnutrition was associated with hospital mortality and complications in Korean patients with myocardial infarction using a geriatric nutritional risk table. Tonet et al.[14] demonstrated

that malnutrition assessed with the short-mini nutrition form was an independent and strong risk factor for all-cause mortality in elderly patients with ACS. However, Basta et al.[16] showed that CONUT score and PNI were not associated with follow-up mortality in STEMI patients undergoing primary PCI after an adjusted multivariate analysis. This study differs from other studies in that it had a high malnutrition rate (>80%) and a small sample size (n=945). In a retrospective study including patients with CAD, CONUT score was found to be associated with all-cause mortality.[17]

Another issue is the association of malnutrition with poor prognosis in ACS patients and that this may be an indicator of inflammation.[18] Increased cytokine production in chronic inflammatory diseases is associated with muscle catabolism, suppression of appetite and decreased albumin levels.[19] ACS occurs as a result of rupture of atherosclerotic plaques that form as a result of chronic inflammatory response in arterial walls.[19] At the same time, chronic inflammatory diseases are associated with low albumin levels.[19] Considering that malnutrition is also associated with inflammation, it can be considered that this is also associated with increased atherosclerotic burden. This term is called malnutrition inflammation-atherosclerosis syndrome.[20]

In our study, the parameter that best shows malnutrition was the PNI score, while the parameter that worst shows it was the NRI score. (p=0.002, p=0.159) (**Table 6, Figure 4**). While the CONUT score includes serum albumin, total cholesterol and total lymphocyte count, the PNI includes only albumin and lymphocyte count.[8] In our study, serum albumin, total cholesterol and lymphocyte count in patients are given in **Table 5**.

It is noteworthy that in studies conducted on the CONUT score, the prognostic value of total cholesterol was found to be inversely related to mortality.[21] No statistically significant difference was observed in our study (p=0.661). According to epidemiologists, these paradoxes can be given as an example of index event bias, where a risk factor determined at the first onset of the disease becomes inversely related after the event occurs.[22] When evaluated with risk factors for mortality, the effect of hyperlipidemia may be hidden.[23] Among other possible mechanisms for the underlying disease, the inverse relationship with total cholesterol reduces cholesterol levels and increases the risk of death. Dietary preferences, drug and alcohol use, smoking, and lifestyle choices may affect total cholesterol. There are many research articles considering low cholesterol to be a biomarker for simultaneous cachexia, malnutrition, cancer, and chronic diseases.[24,25]

Unlike the NRI, CONUT and PIN scores, it includes anthropometric measurements such as weight and height.[12] In our study, no relationship was observed between BMI and malnutrition (**Table 3, Figure 2**). In addition, unlike the NRI, PNI and CONUT scores, it does not include lymphocyte count. Malnutrition is also known to be the most common secondary cause of immunological disorders.

The reason for the decrease in the number of lymphocytes in ACS patients is not clear.[23] Failure to recognize or predict malnutrition may lead to nutritional immunity deficiency and susceptibility to infection, which may be associated with increased mortality.[26] All these demonstrate the importance of implementing adequate nutrition in daily practice. There are many screening tools for malnutrition, but there is no consensus on which one to use in ACS patients. However, the CONUT score, which can be used without a calculator, stands out in

Table 6. Nutritional indeces

Nutritional indeces	Non-coronary slow flow-ectasy (n=59)	Coronary slow flow-ectasy (n=48)	p value
CONUT score, points	0.36 (±0.68)	0.77 (±0.69)	**0.003**
Albumin, g/dl (score), points	0.24 (±0.9)	1.04 (±1.0)	**0.000**
Total cholesterol mg/dl, points	0.71 (±0.8)	0.65 (±0.69)	0.661
Lymphocyte count, (10^3/mm^3), points	0.37 (±0.7)	0.83 (±0.63)	**0.001**
NRI, points	2.97 (±0.18)	3.0 (±0.0)	0.159
PNI score, points	0.63 (±1.0)	1.35 (±1.36)	0.002

NRI: Nutritional risk index, CONUT: Controlled nutritional status score, PNI: Prognostic nutrition index

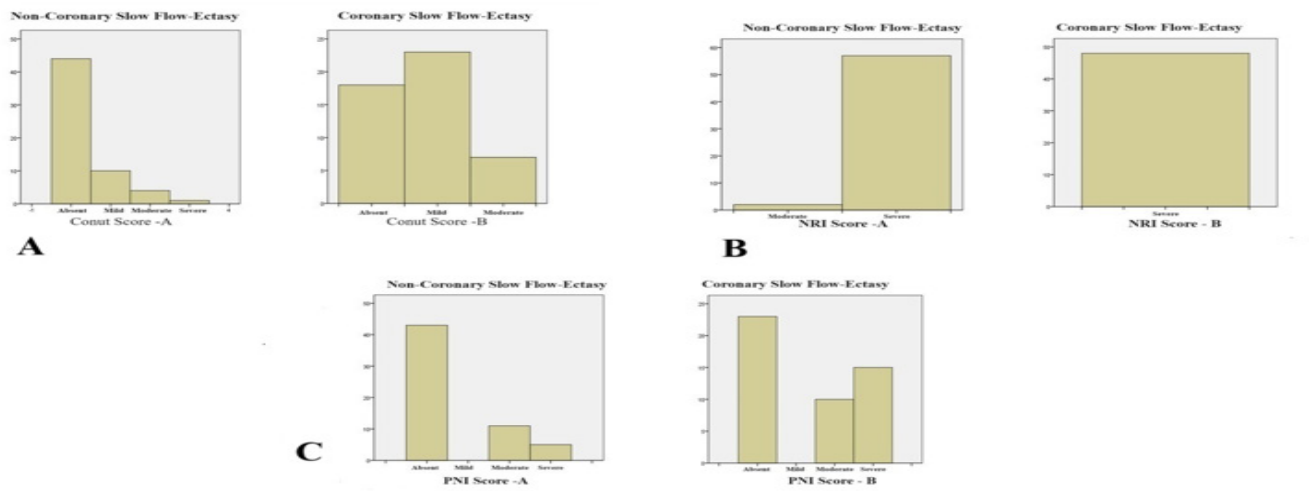

Figure 4. Box graphy coronary ectasy slow flow and non-coronary ectasy slow flow group

practice. In the future, developments in risk models may help clinicians evaluate the patient's metabolic status, mortality, risk of recurrence, and complications. Various multidisciplinary approaches have been developed to prevent malnutrition, including nutritional supplements or enrichment, counseling, and educational interventions.[27] Significant regression in atherosclerosis has been observed with dietary and lifestyle changes.[5] A multidisciplinary approach is necessary in the nutritional care process, involving all professions: medical doctors, nurses, cleaning staff, and representatives. In a randomized trial of inpatient medical treatment patients at nutritional risk, the use of individualized nutritional support in the hospital improved important clinical outcomes, including mortality.[28] However, nutritional interventions should be continued after discharge. How is malnutrition prevented and treated? Various strategies have been developed, including oral nutritional supplements, diet, food/fluid supplementation or fortification, and specific public health measures.[27] The ketogenic diet (KD) protects against the risk of malnutrition and cardiovascular complications such as diabetes and obesity, provides homeostasis of metabolites and regulation of glucose, sugar, and insulin levels.[29] In contrast, a high-sugar diet mediates insulin resistance, decreased fatty acid oxidation, and dyslipidemia[30], and is associated with an increased risk of sarcopenia and major cardiovascular events among participants with and without preexisting cardiovascular disease.[30] Public health measures such as providing education/information on healthy eating, applying nutritional labels to processed foods, and research on vegetable oils should be implemented by relevant institutions. The promotion of growing plants with high antioxidant activity and high protein content encourages patients to take protein.[30] Although dietary supplements can treat malnutrition, they should be considered as part of the treatment. Elderly people, especially those with cardiovascular comorbidities, are at high risk for inappropriate and excessive medication use.[31] Excessive medication use interferes with the liver's cytochrome P450 enzyme system, affecting absorption.[31] Cardiovascular comorbidities and malnutrition can lower serum albumin levels, and renal function may decline with aging, increasing toxicity, altering drug pharmacodynamics, and ultimately leading to prolonged length of stay, higher hospital costs, and higher mortality in elderly patients.[32]

CSF and coronary artery ectasia (CAE) may exacerbate ischemic conditions due to altered hemodynamics and flow dynamics. Studies have shown that patients with CAE often have structural changes in the coronary arteries and CSF. For example, the Hagen-Poiseuille equation shows that increased arterial diameter, as seen in ectatic vessels, leads to higher resistance and therefore slower blood flow.[33] This is especially evident in ectatic arteries, which may contribute to myocardial ischemia.[34] In addition, studies have shown a positive correlation between the size of CE and the TIMI frame count, indicating that larger ectatic segments are associated with slow flow.[34] This additive relationship is important in the management of patients at risk for adverse cardiovascular events.

Larger, well-conducted and well-designed furtherstudies are needed to estimate the impact on malnutrition and cardiovascular events.

Limitations

In addition to the previously highlighted strengths of the study, there are some limitations to our study. Our study was designed as a single-center retrospective, cross-sectional study. The relatively small sample size suggests that larger scale studies are required for this patient population. We did not compare nutritional screening tools with more complex and comprehensive nutritional assessments for prognostic value, since inadequacy in etiology is a complex issue, especially in elderly individuals. Our study was conducted with white people and did not include data relevant to education, marital status, and socioeconomicvariables. Nutritional status assessed with simple screening tools such as CONUT score, NRI, or PNI is uncertain because of the lack of comparison with comprehensive nutritional assessments such as subjective Gloal assessment and mini nutritional assessment. Blood parameter assessments were performed with blood samples taken from the patients at the time of admission, serial measurements were not performed. We did not examine nutritional status changes over time and their relationship with cardiovascular outcomes with inflammatory biomarkers.

CONCLUSION

Effective assessment of malnutritionis considered asan important step in the management of risk factors in ACS patients at risk for cardiovascular events. Its correction may help improve the prognosis in ACS patients.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was approved by Mardin Artuklu University Faculty of Medicine Non-interventional Clinical Researches Ethics Committee (Date:05.11.2024, Decision No: 2024/11-1).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Szummer K, Jernberg T, Wallentin L. From early pharmacology to recent pharmacology interventions in acute coronary syndromes: JACC state-of-the-art review. *J Am Coll Cardiol*. 2019;74(12):1618-1636.
2. Tambe AA, Demany MA, Zimmerman HA, Mascarenhas E. Angina pectoris and slow flow velocity of dye in coronary arteries-a new angiographic finding. *Am Heart J*. 1972;84(1):66 71.
3. Mangieri E, Macchiarelli G, Ciavolella M, et al. Slow coronary flow: clinical and histopathological features in patients with otherwise normal epicardial coronary arteries. *Cathet Cardiovasc Diagn*. 1996;37(4):375-381. doi:10.1002/(SICI)1097-0304(199604)37:4<375::AID-CCD7>3.0.CO;2-8

4. Zhang Q, Qian L, Liu T, et al. Prevalence and prognostic value of malnutrition among elderly cancer patients using three scoring systems. *Front Nutr*. 2021;8:738550. doi: 10.3389/fnut.2021.738550
5. Freeman AM, Morris PB, Barnard N, et al. Trending cardiovascular nutrition controversies. *J Am Coll Cardiol.* 2017;69(9):1172-1187.
6. Zhang HX, Ye N, Peng F, Pan LJ, Shi YJ, Gong H. Abnormality in coronary slow flow phenomenon detected by nailfold microcirculation microanalysis. *Chin Med J (Engl)*. 2021;134(11):1370-1372.
7. Lamtai, M., Fihri, Y., Faid, S., Nabil, L., Britel, D., Faliouni, H., … & Benyass, A. (2024). Coronary artery ectasia: case reports and literature review. *Cureus*. 2024;16(6):e62011.
8. Ignacio de Ulibarri J, Gonzalez-Madrono A, de Villar NG, et al. CONUT: a tool for controlling nutritional status. First validation in a hospital population. *Nutr Hosp*. 2005;20(1):38-45.
9. Buzby GP, Williford WO, Peterson OL, et al. A randomized clinical trial of total parenteral nutrition in malnourished surgical patients: the rationale and impact of previous clinical trials and pilot study on protocol design. *Am J Clin Nutr*. 1988;47(2 Suppl):357-365.
10. Bouillanne O, Morineau G, Dupont C, et al. Geriatric nutritional risk index: a new index for evaluating at-risk elderly medical patients. *Am J Clin Nutr*. 2005;82(4):777-783.
11. Minamisawa M, Seidelmann SB, Claggett B, et al. Impact of malnutrition using geriatric nutritional risk index in heart failure with preserved ejection fraction. *J Am Coll Cardiol HF*. 2019;7(8):664-675.
12. Buzby GP, Mullen JL, Matthews DC, Hobbs CL, Rosato EF. Prognostic nutritional index in gastrointestinal surgery. *Am J Surg*. 1980;139(1):160-167. doi: 10.1016/0002-9610(80)90246-9
13. Sze S, Pellicori P, Kazmi S, et al. Prevalence and prognostic significance of malnutrition using 3 scoring systems among outpatients with heart failure: a comparison with body-mass index. *JACC Heart Fail*. 2018;6(6):476-486. doi:10.1016/j.jchf.2018.02.018
14. Tonet E, Campo G, Maietti E, et al. Nutritional status and all-cause mortality in older adults with acute coronary syndrome. *Clin Nutr.* 2019; 38(6):2956-2957.
15. Yoo SH, Kook HY, Hong YJ, Kim JH, Ahn Y, Jeong MH. Influence of undernutrition at admission on clinical outcomes in patients with acute myocardial infarction. *J Cardiol*. 2017;69(3):555-560.
16. Basta G, Chatzianagnostou K, Paradossi U, et al. The prognostic impact of objective nutritional indices in elderly patients with ST-elevation myocardial infarction undergoing primary coronary intervention. *Int J Cardiol*. 2016;221:987-992.
17. Liu J, Huang Z, Huang H, et al. Malnutrition in patients with coronary artery disease: prevalence and mortality in a 46,485 Chinese cohort study. *Nutr Metab Cardiovasc Dis*. 2022;32(5):1186-1194. doi:10.1016/j.numecd. 2021.12.023
18. Kalantar-Zadeh K, Anker SD, Horwich TB, Fonarow GC. Nutritional and anti-inflammatory interventions in chronic heart failure. *Am J Cardiol.* 2008;101(11A):89E-103E.
19. Lehrke M, Millington SC, Lefterova M, et al. CXCL16 is a marker of inflammation, atherosclerosis, and acute coronary syndromes in humans. *J Am Coll Cardiol*. 2007;49(4):442-449.
20. Sueta D, Hokimoto S, Sakamoto K, et al. Validation of the high mortality rate of malnutritioninflammation-atherosclerosis syndrome: community-based observational study. *Int J Cardiol.* 2017;230:97-102.
21. Yousufuddin M, Takahashi PY, Major B, et al. Association between hyperlipidemia and mortality after incident acute myocardial infarction or acute decompensated heart failure: a propensity score matched cohort study and a meta-analysis. *BMJ Open*. 2019;9(12):e028638.
22. Dahabreh IJ, Kent DM. Index event bias as an explanation for the paradoxes of recurrence risk research. *JAMA*. 2011;305(8):822-823.
23. Belabed L, Charrueau C, Besson V, et al. Impairment of lymphocyte function in headinjured rats: effects of standard and immuneenhancing diets for enteral nutrition. *Clin Nutr*. 2006;25(5):832-841.
24. Rauchhaus M, Clark AL, Doehner W, et al. The relationship between cholesterol and survival in patients with chronic heart failure. *J Am Coll Cardiol*. 2003;42(11):1933-1940.
25. Ridker PM, Rifai N, Rose L, Buring JE, Cook NR. Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events. *N Engl J Med.* 2002;347(20):1557-1565.
26. Nakagomi A, Seino Y, Noma S, et al. Relationships between the serum cholesterol levels, production of monocyte proinflammatory cytokines and long-term prognosis in patients with chronic heart failure. *Intern Med*. 2014;53(21):2415-2424.
27. Bandayrel K, Wong S. Systematic literature review of randomized control trials assessing the effectiveness of nutrition interventions in community-dwelling older adults. *J Nutr Educ Behav*. 2011;43(4):251-262.
28. Schuetz P, Fehr R, Baechli V, et al. Individualised nutritional support in medical inpatients at nutritional risk: a randomised clinical trial. *Lancet*. 2019;393(10188):2312-2321.
29. Kumar S, Behl T, Sachdeva M, et al. Implicating the effect of ketogenic diet as a preventive measure to obesity and diabetes mellitus. *Life Sci*. 2021;264: 118661. doi:10.1016/j.lfs.2020.118661
30. Jenkins DJA, Dehghan M, Mente A, et al. Glycemic index, glycemic load, and cardiovascular disease and mortality. *N Engl J Med*. 2021;385(4):379-380. doi:10.1056/NEJMoa2007123
31. Krustev T, Milushewa P, Tachkov K, Mitov K, Petrova G. Evaluation of potentially inappropriate medication in older patients with cardiovascular diseasesSTOPP/START-based study. *Front Public Health*. 2022;10:1023171. doi:10.3389/ fpubh.2022.1023171
32. Vesa CM, Bungau SG. Novel molecules in diabetes mellitus, dyslipidemia and cardiovascular disease. *Int J Mol Sci*. 2023;24(4):4029. doi:10.3390/ ijms2404402
33. Manu N, Tripathy N, Divya N. (2020). A rare case of "coronary slow-flow phenomena" in an aviator: an approach to aeromedical disposition – a case report. *Indian J Aerospace Med*. 2020;64(1):46-49.
34. Tony H, Meng K, Wu B, Zeng Q. Among ectasia patients with coexisting coronary artery disease, tımı frame count correlates with ectasia size and markis type ıv ıs the commonest. *Cardiol Res Pract*. 2015;2015:282170. doi:10.1155/2015/282170

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The impact of body mass index on intraoperative and postoperative blood transfusion amounts in coronary artery bypass surgery

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ABSTRACT

Aims: The relationship between obesity, bleeding volume, and transfusion requirements during and after coronary artery bypass surgery remains unclear. This study aimed to investigate the impact of body-mass index (BMI) on the amount of intraoperative and postoperative blood transfusions in patients undergoing coronary artery bypass grafting (CABG).

Methods: This retrospective study included 288 patients who underwent isolated cardiopulmonary bypass for CABG between 2011 and 2017. Patients were stratified into five BMI categories: underweight (<18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25.0-29.9 kg/m^2), and obese (30.0 kg /m2 ≤ BMI <35.0 kg/m2), and morbid obese (BMI ≥35.0 kg/m^2). Demographic data, pump times, cross-clamp times, and the amounts of intraoperative and postoperative blood transfusions were retrospectively collected.

Results: Among the patients, obese and morbidly obese individuals comprised 38.2% of the cohort, while underweight patients accounted for only 1.0%. The number of bypassed vessels and mean cross-clamp times did not significantly differ between the BMI groups. The mean amount of blood transfused during surgery ranged from 1.66 to 3.43 units, with the highest amounts observed in the morbidly obese group. However, no significant differences were found in the amount of blood transfused postoperatively between the BMI groups.

Conclusion: Patients at the extremes of the BMI spectrum, specifically morbidly obese individuals, required higher amounts of blood transfusions intraoperatively compared to other groups. In contrast, postoperative transfusion amounts were comparable across all BMI categories. These findings underscore the importance of tailoring perioperative management strategies based on BMI levels to optimize patient outcomes.

Keywords: Blood transfusion, coronary artery bypass grafting, body mass index, obesity, intraoperative bleeding

INTRODUCTION

Obesity, a global public health challenge, is a major risk factor for cardiovascular diseases and is associated with adverse cardiovascular events in patients undergoing coronary artery bypass grafting (CABG).[1-3] Concurrently, obesity may also act as a protective factor in cardiac surgery.[4,5] Some studies have highlighted that underweight patients experience an increased risk of mortality and complications following CABG.[6-8] It has been reported that obesity, compared to a normal body-mass index (BMI), does not significantly elevate the risk of perioperative mortality or adverse outcomes in CABG patients.[9,10] Hence, the concept of the "obesity paradox" in cardiac surgery continues to be an increasingly intriguing subject of interest.[11,12]

Obese patients undergoing cardiac surgery often face a heightened risk of complications due to associated conditions, including a prothrombotic state and impaired microvascular function.[12] These situations can also lead to an increased use of blood products, which contributes to the occurrence of adverse events during the intraoperative and postoperative periods.[13,14] Conversely, some evidence suggests that perioperative bleeding and the need for blood transfusions may be reduced in obese patients undergoing CABG.[15,16] This reduction is hypothesized to result from the production of plasminogen activator inhibitor-1 (PAI-1) by adipocytes, which modulates the coagulation process.[17] Considering these findings, which are consistent with the obesity paradox, there is a need for further research on the impact of BMI on the use of blood products in patients undergoing CABG.

This study aimed to investigate the impact of BMI on the amount of intraoperative and postoperative blood transfusions in patients undergoing CABG.

METHODS

This retrospective study was conducted on patients who underwent CABG at the Cardiovascular Surgery Department of Çanakkale Onsekiz Mart University's Faculty of Medicine, between 2011 and 2016. The study was approved by the Çanakkale Onsekiz Mart University Ethics Committee (Date: 11.01.2018, Decision No: 02/1). The study was carried out in accordance with relevant ethical guidelines, including the principles outlined in the Declaration of Helsinki (2013 Brazil revision).

A total of 288 patients who underwent CABG were included in the study. Patients under the age of 18, those with a previous history of CABG, those with anemia, chronic liver disease, peripheral vascular disease, chronic kidney failure, those with history of bleeding, patients received antiaggregant within 5 days before the operation were excluded from the study.

The demographic and clinical data of the patients was retrospectively collected from patient files or the hospital's electronic information system. Patients were divided into five groups according to their BMI: underweight (<18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2), and obese (30 kg /m^2 ≤ BMI <35 kg/m^2), and morbid obese (BMI ≥35 kg/m^2).[18]

Statistical Analysis

All data were analyzed using IBM SPSS Statistics for Windows 20.0 (IBM Corp., Armonk, NY, USA). Numerical variables with a normal distribution, as determined by Kolmogorov-Smirnov tests, are presented as mean ± standard deviation, while non-normally distributed variables are expressed as median (min–max). Intergroup comparisons were performed using the Kruskal-Wallis H test, followed by Dunn's post hoc test for pairwise comparisons. Categorical variables are reported as frequencies and percentages, with comparisons between groups conducted using the Chi-square test or Fisher's exact test, as appropriate. A P-value of <0.05 (*) was considered statistically significant for all analyses.

RESULTS

The study population consisted of a total of 288 patients, including 208 male (72.2%) and 80 female (27.8%). The mean age of the patients was 62.9±9.6 years (range=37-87 years) and the mean BMI was 27.9±4.3 kg/m^2 (range=17.0–43.4 kg/m^2). When patients were classified according to their BMI levels, 1.0% were categorized as underweight (n=3), 27.4% as normal weight (n=79), 33.3% as overweight (n=96), 32.6% as obese (n=93), and 5.6% as morbid obese (n=16). In the entire population, the mean clamp time was 81.6±27.1 minutes (range=11-197 minutes), the median number of bypassed vessels was 2.9±0.8 (range=1-8 vessels), the median count of blood units used during surgery was 2 (range=0–13 units), and the median count of blood units used after surgery was 2.5 (range=0–13 units) (**Table 1**).

The demographic and clinical characteristics of the groups classified according to BMI levels are presented in **Table 2**. The underweight group was excluded from the statistical analyses due to the limited sample size. Accordingly, the mean age was lower in the morbid obese group compared to other groups (Normal weight: 65.1±9.5 vs. Overweight: 63.3±9.8 vs. Obese: 62.2±9.7 vs. Morbid obese: 57.0±8.5, p=0.013), while the ratio of female was higher (Normal weight: 19.0% vs. Overweight: 22.9% vs. Obese: 36.2% vs. Morbid obese: 57.2%, p = 0.005). The mean clamp time and the median number of bypassed vessels were found to be similar across the groups (p>0.05). The median perioperative number of blood units was higher in the morbid obese group compared to other groups (Normal weight: 2 vs. Overweight: 1.5 vs. Obese: 2 vs. Morbid obese: 3, p=0.012), while the median postoperative number of blood units did not show a significant difference among the groups (Normal weight: 2.5 vs. Overweight: 2 vs. Obese: 2.5 vs. Morbid obese: 3, p=0.116) (**Table 2**).

Table 1. Demographic and clinical characteristics of patients

Variables	All population n=288
Age, years	62.9±9.6
Gender, n (%)	
Female	208 (72.2)
Male	80 (27.8)
BMI, kg/m^2	27.9±4.3
Underweight	3 (1.0)
Normal weight	79 (27.4)
Overweight	96 (33.3)
Morbid obese	16 (5.6)
Clamp time, minute	81.6±27.1
Number of bypassed vessels	2.9±0.8
Count of blood units	
Perioperative	2.0 (0-13)
Postoperative	2.5 (0-13)

Numerical variables were shown as mean±standard deviation or median (min-max). Categorical variables were shown as numbers (%). BMI: Body-mass index

DISCUSSION

To the best of our knowledge, this study is among the few that evaluate perioperative and postoperative blood product utilization across different BMI categories, including morbidly obese individuals. The study's findings indicated that, although cross-clamp times and the number of bypassed vessels were similar across BMI groups, the number of perioperative blood units required was higher in the morbidly obese group. However, postoperative blood unit usage did not significantly differ between the groups.

Our study demonstrated an increased requirement for intraoperative blood transfusion in the morbidly obese group compared to other groups. This finding aligns with previous findings from Engelman et al.[19] who demonstrated that a low BMI (<20 kg/m^2) is associated with higher complication rates, including bleeding, in cardiac surgeries. The elevated intraoperative transfusion requirement observed in the morbidly obese group is consistent with studies suggesting that increased blood loss in obese patients is linked to prolonged operative times and greater surgical complexity.[20,21] Interestingly, postoperative transfusion needs did not differ significantly across BMI groups, suggesting that the perioperative hemodynamic instability seen in obese patients is more critical during surgery than in the recovery phase.

Our findings are consistent with several large cohort studies. For instance, Birkmeyer et al.[22] reported an increased need for re-exploration due to bleeding in obese patients undergoing CABG. Similarly, Potapov et al.[23] found that underweight patients had higher complication rates, including re-exploration for bleeding. In our cohort, although the underweight group

Table 2. Demographic and clinical characteristics of patients according to BMI classification

Variables	Underweight n=3	Normal weight n=79	Overweight n=96	Obese n=94	Morbid obese n=16	p-value
Age, years	62.7±8.1	65.1±9.5	63.3±9.8	62.2±9.7	**57.0±8.5**	0.013*
Gender, n (%)						
Male	3 (100)	64 (81.0)	74 (77.1)	60 (63.8)	7 (43.8)	0.005*
Female	0	15 (19.0)	22 (22.9)	34 (36.2)	9 (57.2)	
Height, cm	175.0±2.6	166.8±7.6	165.5±8.2	163.2±8.4	162.6±8.5	0.075
Weight, kg	55.3±1.2	**64.7±7.3**	**74.0±7.7**	**83.7±9.3**	**99.4±12.7**	<0.001*
Clamp time, minutes	88.7±26.8	77.6±26.1	79.2±27.2	84.6±30.4	77.1±27.2	0.550
Number of bypassed vessel	2 (2 - 3)	2.5 (1 - 4)	3 (1 - 6)	3 (1 - 8)	2.5 (1 - 4)	0.315
Number of blood unit						
Perioperative	2.5 (2 - 3)	2.0 (0 - 6)	1.5 (0 - 10)	2.0 (0 - 13)	**3.0 (0 - 9)**	0.012*
Postoperative	6 (3 - 10)	2.5 (0 - 12)	2.0 (0 - 15)	2.5 (0 - 28)	3.0 (0 - 12)	0.116

Numerical variables were shown as mean±standard deviation or median (min-max). Categorical variables were shown as numbers (%). The underweight group was excluded from the statistical analyses due to the limited sample size. BMI: Body-mass index

was excluded from statistical analysis due to small sample size, the observed trend of increased blood transfusion in low-BMI patients is notable and echoes concerns raised in prior research. Contrary to expectations, we did not observe a significant difference in postoperative blood transfusion requirements across BMI groups. This result contrasts with some studies that have linked obesity to prolonged mechanical ventilation and greater postoperative morbidity.[3,24-26] Our findings suggest that while BMI influences intraoperative blood management, it may not significantly affect postoperative transfusion requirements, potentially due to standardized postoperative care and hemodynamic management protocols.

The increased intraoperative blood transfusion in the morbidly obese group may be attributed to several factors. Obese patients often present with greater surgical challenges due to increased adipose tissue, which can complicate both dissection and homeostasis. Furthermore, the larger body surface area in these patients necessitates greater perfusion, which may increase blood loss during surgery. The observed trend towards increased intraoperative blood transfusion needs in underweight patients aligns with previous studies suggesting heightened perioperative risks in this population. Engelman et al.[19] similarly identified that low BMI was an independent predictor of increased mortality and complications, including bleeding, in cardiac surgery. For underweight patients, the higher transfusion requirements may be linked to frailty, malnutrition, and low baseline hemoglobin levels, all of which can predispose them to hemodynamic instability and increased bleeding. However, due to the small sample size, further research with larger cohorts is needed to confirm these findings.

From a clinical perspective, these findings underscore the importance of preoperative risk stratification and blood management protocols tailored to patients' BMI. Intraoperative strategies to minimize blood loss, such as optimizing coagulation status and utilizing blood-sparing techniques, should be prioritized, particularly in patients at both extremes of the BMI spectrum. The absence of significant differences in postoperative transfusion rates suggests that existing protocols for managing postoperative anemia and bleeding are effective across BMI categories. However, the higher intraoperative transfusion needs in morbidly obese and underweight patients call for heightened vigilance during surgery, with potential adjustments in blood management strategies for these groups.

Limitations

This study has several important limitations. First, the retrospective design and single-center nature of the study may limit the generalizability of the findings. Second, the BMI groups were not matched in terms of sample size, age, or gender, which could introduce potential confounding factors that were not fully accounted for. As noted in the findings section, the underweight BMI group was excluded from statistical analyses due to its small sample size. Our data indicate a trend toward an increased need for intraoperative blood transfusion in this group; however, the sample size was insufficient to draw statistically significant conclusions. Future studies with larger sample sizes are needed to better evaluate this relationship. Additionally, further investigation into the mechanisms underlying the increased intraoperative blood loss in obese patients may aid in the development of targeted interventions to reduce transfusion requirements.

CONCLUSION

Our study underscores a significant association between BMI and intraoperative blood transfusion requirements in patients undergoing CABG surgery. Patients at the extremes of the BMI spectrum, specifically morbidly obese individuals, required higher amounts of blood transfusions intraoperatively compared to other groups. In contrast, postoperative transfusion amounts were comparable across all BMI categories. These findings underscore the importance of tailoring perioperative management strategies based on BMI levels to optimize patient outcomes.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was approved by the Çanakkale Onsekiz Mart University Ethics Committee (Date: 11.01.2018, Decision No: 02/1).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Powell-Wiley TM, Poirier P, Burke LE, et al. Obesity and cardiovascular disease: a scientific statement from the American Heart Association. *Circulation*. 2021;143(21):e984-e1010. doi:10.1161/CIR.0000000000000973
2. Bagheri J. Effects of body mass index on the early surgical outcomes after coronary artery bypass grafting. *Turkish J Thorac Cardiovasc Surg*. 2014; 22(2):253-259
3. Perrotta S, Nilsson F, Brandrup-Wognsen G, Jeppsson A. Body mass index and outcome after coronary artery bypass surgery. *J Cardiovasc Surg (Torino)*. 2007;48(2):239-45.
4. Forgie K, Bozso SJ, Hong Y, et al. The effects of body mass index on outcomes for patients undergoing surgical aortic valve replacement. *BMC Cardiovasc Disord*. 2020;20(1):255. doi:10.1186/s12872-020-01528-8
5. Le-Bert G, Santana O, Pineda AM, Zamora C, Lamas GA, Lamelas J. The obesity paradox in elderly obese patients undergoing coronary artery bypass surgery. *Interact Cardiovasc Thorac Surg*. 2011;13(2):124-127. doi: 10.1510/icvts.2010.256677
6. Karthik S, Grayson AD, McCarron EE, Pullan DM, Desmond MJ. Reexploration for bleeding after coronary artery bypass surgery: risk factors, outcomes, and the effect of time delay. *Ann Thorac Surg*. 2004;78(2):527-534. doi:10.1016/j.athoracsur.2004.02.088
7. Engel AM, McDonough S, Smith JM. Does an obese body mass index affect hospital outcomes after coronary artery bypass graft surgery? *Ann Thorac Surg*. 2009;88(6):1793-800. doi:10.1016/j.athoracsur.2009.07.077
8. Allama A, Ibrahim I, Abdallah A, et al. Effect of body mass index on early clinical outcomes after cardiac surgery. *Asian Cardiovasc Thorac Ann*. 2014; 22(6):667-673. doi:10.1177/0218492313504092
9. Shirzad M, Karimi A, Armadi SH, et al. Effects of body-mass index on early outcome of coronary artery bypass surgery. *Minerva Chir*. 2009;64(1):17-23.
10. Reeves BC, Ascione R, Chamberlain MH, Angelini GD. Effect of body mass index on early outcomes in patients undergoing coronary artery bypass surgery. *J Am Coll Cardiol*. 2003;42(4):668-676. doi:10.1016/s0735-1097(03)00777-0
11. Gruberg L, Weissman NJ, Waksman R, et al. The impact of obesity on the short-term and long-term outcomes after percutaneous coronary intervention: the obesity paradox? *J Am Coll Cardiol*. 2002;39(4):578-584. doi:10.1016/s0735-1097(01)01802-2
12. Boly CA, Venhuizen M, Dekker NAM, Vonk ABA, Boer C, van den Brom CE. Comparison of microcirculatory perfusion in obese and non-obese patients undergoing cardiac surgery with cardiopulmonary bypass. *J Clin Med*. 2021;10(3):469 doi:10.3390/jcm10030469
13. Gurbuz O, Kumtepe G, Ozkan H, Karal IH, Ercan A, Ener S. Red blood cell distribution width predicts long term cardiovascular event after on-pump beating coronary artery bypass grafting. *J Cardiothorac Surg*. 2016;11(1):48. doi:10.1186/s13019-016-0465-4
14. Eranki A, Wilson-Smith A, Ali U, Merry C. Preoperative patient factors associated with blood product use in cardiac surgery, a retrospective cohort study. *J Cardiothorac Surg*. 2022;17(1):23. doi:10.1186/s13019-022-01770-5
15. Nolan HR, Ramaiah C. Effect of body mass index on postoperative transfusions and 24-hour chest-tube output. *Int J Angiol*. 2011;20(2):81-86. doi:10.1055/s-0031-1279676
16. Kartal H, Demirdas E, Sicim H, et al. The effect of body-mass index on postoperative bleeding and blood transfusion in patients with coronary bypass surgery. *Heart*. 2020;6:8.
17. Mertens I, Van Gaal LF. Obesity, haemostasis and the fibrinolytic system. *Obes Rev*. 2002;3(2):85-101. doi:10.1046/j.1467-789x.2002.00056.x
18. WHO. The International classification of adult underweight, overweight and obesity according to BMI. Geneva, Switzerland: World Health Organization, 2017. Available from: https://www.who.int/data/gho/data/themes/topics/topic-details/GHO/body-mass-index?introPage=intro_3.html.
19. Engelman DT, Adams DH, Byrne JG, et al. Impact of body mass index and albumin on morbidity and mortality after cardiac surgery. *J Thorac Cardiovasc Surg*. 1999;118(5):866-873.
20. Yap CH, Mohajeri M, Yii M. Obesity and early complications after cardiac surgery. *Med J Aust*. 2007;186(7):350-354. doi:10.5694/j.1326-5377.2007.tb00935.x
21. Jarvinen O, Julkunen J, Tarkka MR. Impact of obesity on outcome and changes in quality of life after coronary artery bypass grafting. *World J Surg*. 2007;31(2):318-325. doi:10.1007/s00268-006-0183-5
22. Birkmeyer NJ, Charlesworth DC, Hernandez F, et al. Obesity and risk of adverse outcomes associated with coronary artery bypass surgery. *Circulation*. 1998;97(17):1689-1694.
23. Potapov EV, Loebe M, Anker S, et al. Impact of body mass index on outcome in patients after coronary artery bypass grafting with and without valve surgery. *European Heart J*. 2003;24(21):1933-1941.
24. Keeling WB, Kilgo PD, Puskas JD, et al. Off-pump coronary artery bypass grafting attenuates morbidity and mortality for patients with low and high body mass index. *J Thorac Cardiovasc Surg*. 2013;146(6):1442-1448.
25. Reeves BC, Ascione R, Chamberlain MH, Angelini GD. Effect of body-mass index on early outcomes in patients undergoing coronary artery bypass surgery. *J Am College Cardiol*. 2003;42(4):668-676.
26. Sung S-H, Wu T-C, Huang C-H, Lin S-J, Chen J-W. Prognostic impact of body mass index in patients undergoing coronary artery bypass surgery. *Heart*. 2011;97(8):648-654.