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Original Article

MEDICINE PALLIATIVE CARE

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The relationship between triglyceride/high-density lipoprotein cholesterol ratio and the functional significance of coronary lesions

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ABSTRACT

Aims: Have shown that triglycerides (TG) are an independent risk factor for cardiovascular disease (CVD). Dyslipidemia characterized by low high-density lipoprotein cholesterol (HDL-C) has been shown to be associated with symptoms of coronary artery disease (CAD). In studies, the TG/HDL-C ratio has been found to be strongly associated with parameters indicative of the severity of coronary disease. In this study, we aimed to investigate whether the TG/HDL-C ratio is associated with the functional significance of moderate coronary artery lesions.

Methods: A total of 102 consecutive patients, 72 male and 30 female, who underwent measurement of fractional flow reserve (FFR) due to moderate coronary stenosis (quantitative coronary analysis 40-70%) on angiography were included in the study. An FFR value ≤0.80 was accepted for hemodynamic significance.

Results: Among the 102 patients included in the study, it was determined that 52 (50.9%) had significant functional stenosis. Left ventricular ejection fraction of Group II was lower than Group I (60 (55-62.5) vs. 55(50-60), p=0.006). The male patient ratio was higher in Group II, but the difference between the two groups was not significant (68% and 77%, respectively, p=0.072). Univariate and multivariate logistic regression analysis showed that TG/HDL-C (OR=1.278, 95% CI=1.078-1.514, p=0.005) was an independent determinant of significant functional stenosis. ROC analysis revealed that the TG/HDL-C value was 3.89 and provided 64% specificity and 61.5% sensitivity in predicting hemodynamically significant coronary artery stenosis.

Conclusion: Elevated TG/HDL-C values are associated with the functional significance of angiographically moderate coronary artery stenosis.

Keywords: Coronary artery disease, triglyceride, fractional flow reserve, HDL-C

INTRODUCTION

Qualitative assessment of coronary artery stenosis with coronary angiography (CA) may not always be reliable. Measurement of fractional flow reserve (FFR) with a coronary pressure wire is a reliable method used for the functional assessment of coronary artery lesions, particularly when stenosis ranges between 40% and 70%, to measure the hemodynamic significance of coronary artery lesions and objectively quantify the severity of ischemia caused by coronary stenosis.[1-3] Fractional flow reserve is employed to directly assess the pressure decrease across epicardial coronary narrowings. It is acknowledged as the gold standard for identifying myocardial ischemia and is endorsed for use by the ESC 2018 myocardial revascularization guidelines. FFR-guided percutaneous coronary intervention (PCI) has demonstrated superiority over angiographic-guided PCI.[4] FFR-guided PCI results in better short-term and long-term outcomes than does angiographyguided PCI or medical therapy alone.[3] Studies have shown that an increase in plasma triglyceride (TG) levels is associated with an increased risk of coronary artery disease (CAD) even after adjustment for high-density lipoprotein cholesterol (HDL-C) levels.[5] Studies indicate that TGs are an independent risk factor for cardiovascular disease (CVD). High serum TGs are associated with the presence of atherogenic lipoproteins and are linked to important CVD risk factors such as metabolic syndrome. Patients with high TG levels have been reported to experience a greater increase in plaque volume.[6] Gianturco and colleagues illustrated that elevated triglyceride levels amplify macrophage phagocytosis and foster the transformation of macrophages into foam cells.[7] It has been shown that TGs increase the risk independently of these risk factors.[8] HDL-C is a class of lipoproteins responsible for reverse cholesterol transport. Low HDL-C has been shown to be associated with signs of CAD.[9] HDL-C reduction is common in CAD and is used as an indicator in assessing CVD risk. Evidence has emerged indicating that HDL-C is directly involved in the

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inflammatory process of atherosclerosis and that its predictive value can be enhanced by integrating it with inflammatory parameters.[10] Studies have reported that due to the limitations of FFR in identifying unstable plaques and its susceptibility to other factors, the close association between TG/HDL-C and coronary artery disease suggests that TG/HDL-C may play a significant role in identifying high-risk patients.[11]

The aim of this study is to examine the relationship between the TG/HDL-C ratio, which combines two accessible laboratory parameters with prognostic and predictive efficacy, and the functional significance of intermediate coronary artery stenosis assessed by FFR measurement.

METHODS

The study protocol was approved by the Bursa City Hospital Clinical Researches Ethics Committee (Date: 20.12.2023, Decision No: 2023-21/15) and conducted according to the principles of the Helsinki Declaration. Due to the retrospective design of the study, written informed consent could not be obtained from the patients.

This retrospective study was conducted with a total of 102 consecutive patients diagnosed with single intermediate coronary stenosis (quantitatively defined as 40-70%) between January 2020 and December 2023, who were evaluated with FFR measurement, including 30 women and 72 men. Patients who underwent coronary angiography for stable angina pectoris indication were included in this study. Patients with acute coronary syndrome; moderate or severe valvular heart disease; significant arrhythmia; hemodynamic instability; second lesion in the index coronary artery; another coronary artery with ≥40% lumen narrowing (determined by coronary angiography); history of previous surgical or PCI; acute or chronic inflammatory or infectious diseases; conditions such as anemia, chronic kidney failure, malignancy, and alcohol use were excluded from the study. Hospital records and charts were reviewed to determine patients' demographic, clinical, and angiographic data. Patients presented to the hospital electively, and blood parameters were calculated from blood samples obtained from the antecubital region after an 8-hour fasting period. Measurements included lipid profile, serum creatinine, and complete blood count. Baseline TG/HDL-C values of patients were determined by dividing triglyceride levels by HDL cholesterol levels. The institutional local ethics committee approved the study protocol.

FFR measurements for intermediate lesions in the coronary artery (40-70% stenosis rate) were performed at the discretion of cardiologists. After intracoronary administration of a bolus of 5000 units of heparin following calibration, the lesion was examined using a guide catheter without coronary artery side holes. After calibration, a 0.014-inch pressure monitoring guide wire (Abbott, PressureWire X) was placed distal to the stenosis. Before FFR measurements, a 200 µg bolus of nitroglycerin was administered intracoronarily. The distal intracoronary pressure of patients was recorded by gradually increasing doses of intracoronary adenosine until hyperemia was induced. FFR was determined as the ratio between the mean distal intracoronary pressure at the peak of hyperemia and the mean aortic pressure.

An FFR value of ≤0.80 was defined as functionally significant. Patients with an FFR value >0.80 constituted Group I, and patients with an FFR value ≤0.80 constituted Group II.

Statistical Analysis

The necessary statistical analyses were performed using SPSS software version 20.0 for Windows (SPSS Inc., Chicago, IL, USA), and the distribution shapes of variables were analyzed using the Kolmogorov-Smirnov test. While categorical determinants were given as percentages and numbers, continuous variables were presented as mean±standard deviation or median with interquartile range, depending on the distribution model of the variables. The Mann-Whitney U-test was preferred to calculate differences between non-parametric continuous variables, and categorical variables were compared using the Pearson chi-square test. Possible confounding factors for the severity of coronary artery lesions were determined using univariate and multiple logistic regression analysis. The multiple regression model was used to test variables with p values <0.10 in univariate regression analysis. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal TG/HDL-C cutoff value to predict hemodynamically significant coronary artery stenosis. The level of statistical significance was set at<0.05.

RESULTS

The initial characteristics of patients are shown in. Significant functional stenosis was detected in 52 (50.9%) of the 102 patients included in the study. The left ventricular ejection fraction (EF) of Group II was lower than that of Group I (60 (55-62.5) vs. 55 (50-60), p=0.006). Although the proportion of male patients was higher in Group II, the difference between the two groups was not statistically significant (68% vs. 77%, p=0.072). There was no statistically significant difference between the two groups in terms of coronary risk factors, hyperlipidemia, hypertension, and diabetes mellitus. There was no statistically significant difference detected between the two groups in terms of coronary arteries undergoing FFR. The laboratory parameters of the two groups are reported in. Triglyceride levels were higher in Group II (129 (101-195) vs. 178 (122-269) mg/dl, p=0.010). The total cholesterol level was also higher in Group II, but the difference was not statistically significant. White blood cell (WBC) count (7.8 (6.5-9.2) vs. 9.5 (7.6-11.1) x103/µL, p=0.003), neutrophil count [4.6 (3.4-6.1) vs. 5.7 (4.2-7.3)x103/µL, p<0.026], and TG/HDL-C (3.74±2.13 vs. 6.14±4.37, p=0.003) were higher in Group II. Other laboratory data did not show significant differences between the two groups (Table 1). Univariate and multiple logistic regression analysis showed that TG/HDL-C (OR=1.278, 95% CI=1.078-1.514, p=0.005) was an independent determinant of significant functional stenosis (Table 2). ROC analysis revealed that a TG/HDL-C value of 3.89 had 64% specificity and 61.5% sensitivity in predicting hemodynamically significant coronary artery stenosis (Figure).

Table 1. Baseline characteristics and laboratory parameters of the study groups

	Total study population (n=102)		
Variables	Insignificant FFR (Group 1) (n= 50)	Significant FFR (Group 2) (n=52)	p value
Baseline characteristics			
Age, years	59.4±9.5	56.1±7.3	0.058
Male gender, n (%)	32 (64)	40 (76.9)	0.152
Diabetes mellitus, n (%)	16 (32)	20 (38.5)	0.495
Hypertension, n (%)	31 (62)	31 (59.6)	0.805
Dyslipidemia, n (%)	16 (32)	21 (40.4)	0.379
Current smokers, n (%)	21 (42)	28 (53.8)	0.231
Left ventricle EF, %	60 (55-62.5)	55 (50-60)	**0.006**
After adenosin FFR	0.86±0.03	0.74±0.03	**<0.001**
Body-mass index, kg/m^2	28.2(25.7-29.9)	28.4(26.4-29.9)	0.458
Laboratory parameters			
Glucose, mg/dl	105 (93-148)	110 (96-154)	0.364
Urea, mg/dl	14.1 (12.5-17)	13.7 (11-16.8)	0.286
Serum Creatinine, mg/dl	0.87 (0.74-1.00)	0.85 (0.75-0.99)	0.658
Total cholesterol, mg/dl	177.2±35	184.6±49.7	0.388
HDL cholesterol, mg/dl	42 (37-51)	38 (32-44)	**0.013**
LDL cholesterol, mg/dl	100.2±29.6	104.6±43.1	0.547
Triglycerides, mg/dl	129 (101-195)	178 (122-269)	**0.010**
WBC count, x10^3/µL	7.8 (6.5-9.2)	9.5 (7.6-11.1)	**0.003**
Neutrophil count, x10^3/µL	4.6 (3.4-6.1)	5.7 (4.2-7.3)	**<0.026**
Lymphocyte count, x10^3/µL	2.1 (1.6-2.6)	2.4 (1.9-2.9)	0.162
Hemoglobin, g/dl	13.8±1.8	13.7±2.1	0.639
RDW, fL	13.1 (12.4-14)	13.3 (12.5-14.1)	0.393
MPV, fL	10.4 (10-11.1)	10.1 (9.8-10.7)	0.026
Platelet count, x10^3/µL	244 (207-289)	268 (233-313)	0.072
TG/HDL-C	3.74±2.13	6.14±4.37	0.003
Coronary Arteries			
LAD	23	21	0.424
CX	14	15	0.568
RCA	13	16	0.385

All values are expressed as mean±standard deviation, median (25th and 75th interquartile range), and number (%). Abbreviations; CX: Circumflex, EF: Ejection fraction, FFR: Fractional flow reserve, HDL: High-density lipoprotein, LAD: Left anterior descending, LDL: Low-density lipoprotein, MPV: Mean platelet volume, RCA: Right coronary artery, RDW: Red cell distribution width, TG/HDL-C: Triglyceride/high-density lipoprotein cholesterol ratio, WBC: White blood cell. p values in bold signify statistically significant differences

Table 2. Univariate and multivariate logistic regression analysis showing the independent predictors for hemodynamically significant coronary artery stenosis

Variables	**Univariate analysis**		**Multivariate analysis**	
	OR (95% CI)	**p value**	**OR (95% CI)**	**p value**
Age	0.956 (0.911-1.002)	0.062	0.956 (0.906-1.008)	0.094
Neutrophil	1.235 (1.022-1.492)	0.029	0.995 (0.576-1.719)	0.986
TG/HDL-C	1.269 (1.090-1.477)	0.002	1.278 (1.078-1.514)	0.005
WBC	1.242 (1.053-1.465)	0.010	1.187 (0.739-1.906)	0.478

Abbreviations; CI: Confidence interval, TG/HDL-C: Triglyceride/high-density lipoprotein cholesterol ratio, OR: Odds ratio, WBC: White blood cell

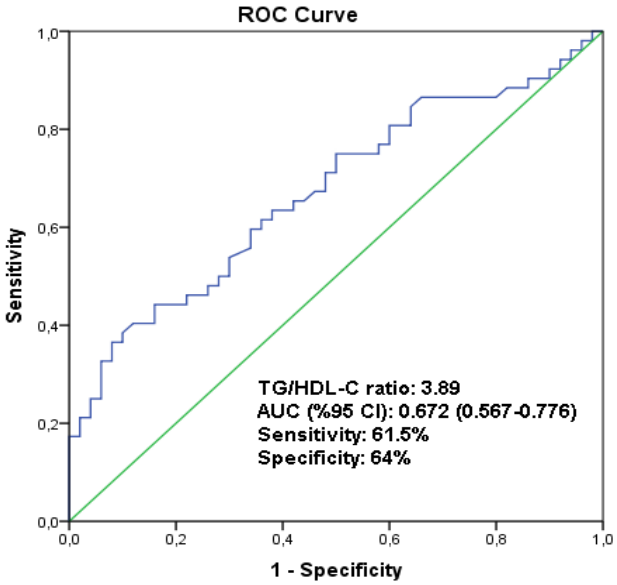

Figure. ROC curve analysis

DISCUSSION

In this study, we demonstrated that TG/HDL-C levels were significantly higher in patients with functionally significant coronary artery stenosis assessed by FFR measurement. We also found that TG/HDL-C was an independent determinant of hemodynamically significant coronary artery stenosis.

Qualitative assessment of stenosis seen with coronary angiography may not always be possible, and visible anatomical stenosis may not necessarily result in hemodynamic disturbance in the myocardial tissue.[12] Therefore, FFR measurement is a well-established method for the functional assessment of lesion severity. FFR measures the pressure drop across the stenosis by measuring pressure distal and proximal to the stenosis after achieving maximal hyperemia. This technique is linearly correlated with maximum myocardial blood flow provided by the respective coronary artery. Hemodynamically significant coronary artery stenosis reduces distal coronary artery pressure, thus reducing the ratio of distal coronary artery pressure to proximal coronary artery pressure and impairing myocardial tissue perfusion.[13] Pressure-derived FFR is an effective procedure for determining the hemodynamic significance of coronary artery stenosis and is superior to angiography when used to guide revascularization strategies.[14] In a study, patients with moderate coronary artery stenosis demonstrated similar outcomes regarding mortality, myocardial infarction, or any revascularization within 24 months following the index procedure, regardless of whether they were guided by FFR or IVUS.[15] In addition to determining hemodynamic significance, FFR also has prognostic predictive value. Tonino et al.[16] showed that routine FFR measurement in patients with multivessel CAD planning to undergo percutaneous coronary intervention reduced the rate of major adverse cardiac events in a 1-year follow-up. Earlier research indicated that in patients with

acute MI and multivessel disease, both FFR-guided PCI and angiography-guided PCI targeting non-IRA lesions to achieve complete revascularization markedly decrease adverse clinical outcomes compared to performing PCI solely on the IRA.[17] Therefore, in this study, FFR measurement was used to determine the functional significance of coronary lesion severity and its relationship with TG/HDL-C levels. We found that TG/HDL-C levels were significantly higher in patients with functionally significant lesions (FFR≤0.80) assessed by FFR measurement.

Oxidative stress and inflammation are central mechanisms in the development and progression of atherosclerosis.[18,19] Unlike larger, low-density lipoprotein cholesterol (LDL-C) particles, small and dense LDL-C particles are more prone to oxidative damage.[20] These particles are rapidly taken up by arterial tissue and thus cause oxidative damage.[21-23] Hypertriglyceridemia is associated with the presence of small, dense LDL-C particles that are more easily oxidized, have higher affinity for extracellular matrix, migrate more easily from arterial walls, and are highly retained in the subendothelial space.[20-24] Hypertriglyceridemia is generally associated with a decrease in HDL-C.[25] Lipoproteins rich in triglycerides have various properties, such as increasing the expression of endothelial adhesion molecules and stimulating macrophage chemotaxis.[26] HDL-C molecules reduce macrophage accumulation and support the removal of oxidized cholesterol from the arterial wall.[27,28] Recent studies have also shown that HDL-C can inhibit monocyte activation, adhesion, and inflammation.[29,30] HDL-C increases nitric oxide synthase expression in endothelial tissues and supports vasorelaxation, in addition to its antioxidative and anti-inflammatory effects.[31] Higher HDL-C levels are known to provide protection against atherosclerosis and are associated with a better prognosis in patients with atherosclerosis.[32] Therefore, a high TG/HDL-C ratio may reflect an increased atherogenic risk and may play a role in explaining our findings as discussed above. The studies revealed that an elevated TG/HDL-C ratio, after adjusting for established CVD risk factors, was linked to an increased risk of CVD.[33] Plasma's atherogenic lipoprotein profile is an important risk factor for CAD. It is characterized by a high LDL-C to HDL-C ratio and elevated TG levels.[34] Studies have shown that the TG/HDL-C ratio is strongly associated with major adverse cardiovascular events (MACE) in patients with acute coronary syndrome undergoing percutaneous coronary intervention.[35] The high TG/HDL-C ratio has been shown to be an independent risk factor for recurrent percutaneous coronary intervention.[36] In a study by Kundi et al.,[37] it was suggested that a high TG/HDL-C ratio could increase the risk of in-stent restenosis through increased insulin resistance, endothelial dysfunction, atherosclerosis, oxidative stress, proinflammatory state, and proliferation of vascular smooth muscle cells. In another study by Luz et al.,[38] it was found that the TG/HDL-C ratio is a strong independent predictor of widespread coronary artery disease. In yet another study, the TG/HDL-C ratio was found to be strongly associated with noninvasive parameters of coronary disease severity.[39] Our study also found a significant association between TG/HDL-C levels and coronary artery stenosis evaluated after adenosine-induced hyperemia. All these literature data clearly demonstrate that patients with hemodynamically significant coronary lesions have a poor prognosis and are closely associated with increased TG/HDL-C.

Furthermore, white blood cell (WBC) and neutrophil counts were significantly higher in Group 2 patients. Studies have shown that total WBC counts are higher in patients with critical lumen narrowing compared to those with non-critical lumen narrowing.[40] However, in our study, WBC and neutrophil elevation were not identified as independent predictors in multivariate analysis.

It is noteworthy that coronary artery risk factors such as diabetes mellitus, hypertension, hyperlipidemia, smoking, and male gender were similar between Groups 1 and 2 in our study. It would be expected that one or more of these risk factors would be significantly higher in Group 2 patients. The reason for this may be the inadequacy of the sample size. Therefore, larger studies with larger sample sizes are needed.

Limitations

This study has some limitations. Firstly, the study has a retrospective design with a limited number of patients. Secondly, our study analyses are based on a single TG/HDL-C value, and we did not follow up on temporal changes and variations in TG/HDL-C. Lastly, our study does not provide a mechanistic explanation for the effect of specific TG and HDL-C subgroups on CAD severity and TG/HDL-C.

CONCLUSION

This study demonstrated that TG/HDL-C levels were independently associated with the functional significance of coronary artery stenosis assessed by FFR measurements. Lipid panels are widely used and cost-effective. Therefore, TG/HDL-C values can be easily determined in clinical settings to predict the likelihood of hemodynamically significant coronary artery stenosis. Larger sample sizes and prospective designs are needed in future studies.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Bursa City Hospital Clinical Researches Ethics Committee (Date: 20.12.2023, Decision No: 2023-21/15).

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.

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Original Article

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The characteristics of patients undergoing endobronchial ultrasonography-guided transbronchial needle aspiration (EBUS-TBNA): single-center experience

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ABSTRACT

Aims: We aimed to present the features of our Endobronchial ultrasonography-guided transbronchial needle aspiration (EBUS-TBNA) cases, the lymph nodes that were biopsied, their pathological diagnoses, and the complications that developed due to the procedure.

Methods: All cases who underwent EBUS-TBNA between January 2016 and December 2023 in the chest diseases clinic of a training and research hospital were retrospectively screened. The patients who underwent the procedure (n=274) were included in the study. Cases in which fine needle aspiration biopsy was performed with EBUS-TBNA and the material obtained was not diagnostic (n=3) or in which the pathology result could not be obtained in the files (n=9) were excluded from the study. The design of our study was cross-sectional and planned as a descriptive study.

Results: Of the 262 patients included in the analysis, 66.4% (n=174) were male and the average age of the population was 60.8±11.4 years. When EBUS-TBNA indications were evaluated, the procedure was performed for diagnostic purposes in 96.9% (n=254) and for re-evaluation after chemotherapy in 3.1%. EBUS-TBNA procedure was performed in 16.8% (n=44) patients due to mediastinal mass and in 83.2% (n=218) patients due to mediastinal lymphadenopathy. The most common stations where biopsy is performed with the EBUS-TBNA process are the subcarinal (7) and lower right paratracheal (4R) lymph node stations. When the biopsy results were evaluated, malignancy was reported in 54.6% (n=143) of the patients. The complications related to the EBUS-TBNA procedure were generally mild and trancient .

Conclusion: EBUS-TBNA is a minimally invasive method used in the diagnosis and staging of lung cancer, the evaluation of non-endobronchial lesions, the diagnosis of benign diseases of the mediastinum, and the diagnosis of mediastinal metastases of extrathoracic malignancies. In experienced centers like our clinic, the diagnostic value of the procedure is high and the complication rates are very low.

Keywords: EBUS, lung cancer, metastasis

INTRODUCTION

Endobronchial ultrasonography-guided transbronchial needle aspiration (EBUS-TBNA) plays an important role in the diagnosis and staging of lung cancer, mediastinal restaging after lung cancer treatment, evaluation of possible mediastinal lymph node metastases of extrathoracic primary cancers, diagnosis of lymphoma, infectious and granulomatous diseases, and determination of nodal localizations.[1-3] In addition, in recent years, cytopathological sampling for genotyping and immunohistochemical analysis in targeted therapies in lung cancer has been recommended many guidelines as the first choice diagnostic tool.[4]

EBUS-TBNA is a minimally invasive procedure that enables direct bronchoscope imaging and sampling of mediastinal and hilar lymph nodes and masses adjacent to the trachea and bronchi, and provides equivalent diagnostic accuracy and reliable patient safety when compared to traditional invasive techniques such as mediastinoscopy and thoracoscopy.[5]

When EBUS-TBNA is performed by experienced physicians, its diagnostic value is high and procedure complications are observed less frequently. In addition, the recovery time to return daily life after the procedure is much shorter than surgical procedures, and the loss of labor per working days is significantly shorter. The EBUS-TBNA process is reproducible, does not cause any permanent anatomical changes, and is advantageous compared to surgical biopsies. Some of these advantages include the absence of many factors that reduce

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the quality of life, such as wound healing after the procedure, dressing requirements, surgical site infections, and post-surgical pain.

We have been performing EBUS-TBNA procedures for approximately 8 years by experienced chest diseases specialists in our center, which started in a chest diseases branch hospital and grew as a training and research hospital. We aimed to present the features of our EBUS-TBNA cases, which we thought would contribute to national data, the lymph nodes that were biopsied, pathological diagnoses, and complications related to the procedure.

METHODS

This study was carried out with the approval of the Samsun University Clinical Researches Ethics Committee (Date: 18,10,2023, Decision No: 2023/19/2). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

All cases who underwent EBUS-TBNA at the Chest Diseases Clinic of Samsun Training and Research Hospital between January 2016 and December 2023 were retrospectively screened . The patients who underwent the procedure (n=274) were included in the study. Cases in which fine needle aspiration biopsy was performed with EBUS-TBNA and the obtained material was not diagnostic (n=3) or in which the pathology result could not be reached in the records (n=9) were excluded from the study (Figure). The design of our study is descriptive study.

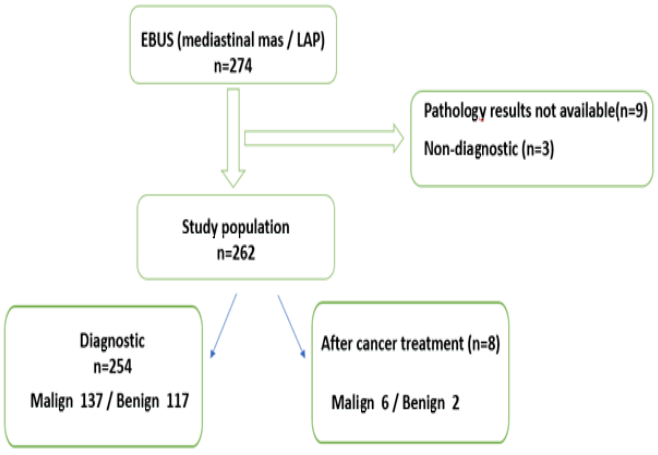

Figure. Patient's flowchart

The data were evaluated and, the main EBUS-TBNA indication was the presence of mediastinal lymphadenopathy or mass lesion on computed thorax tomography. The second indication was incidentally found lesions on PET-CT performed for screening purposes. The cases in which the short axis of any lymph node was larger than 1 cm and/or any involvement at the level of malignancy (SUVmax≥2.5) were evaluated by EBUS-TBNA.

The written informed consent forms were obtained from all patients before the EBUS-TBNA procedure. The EBUS-TBNA procedure was performed orally in the operating room under sedation with propofol, in a supine position with spontaneous breathing.

EBUS-TBNA is performed using thorax computed tomography or PET-CT, where the short axis is greater than 1 cm and/or involvement at the level of malignancy is reported on PET-CT, or the short axis is not reported on CT and PET-CT but detected by EBUS over 0.5 cm. At least two biopsies were taken from each focus on lymph node stations (4R, 4L, 7, 10R, 10L, 11R, 11L) and mediastinal masses using Fujifilm's EB-530US EBUS device and a 22-gauge disposable needle. Aspirates were spread on glass slides, air dried, and fixed with 95% alcohol. Histological aspirate tissues were fixed with 10% neutral buffered formalin for pathological examination. Rapid on-site evaluation (ROSE) was not performed during the procedure. In this study, demographic data of the patients, foci biopsied with EBUS-TBNA, pathological diagnoses and procedure-related complications were recorded.

Statistical Analysis

All data were analyzed with SPSS V 23 Windows statistical program (SPSS Inc., Chicago, IL, USA). Frequencies and percentage values of categorical variables; Mean and standard deviation values of numerical variables were calculated.

RESULTS

Of the 262 patients included in the analysis, 66.4% (n=174) were male and the mean age of the entire population was 60.8±11.4 years. When EBUS-TBNA indications were evaluated, the procedure was performed for diagnostic purposes in 96.9% (n=254) and for re-evaluation after chemotherapy in 3.1%. The average age of the cases was 60.8±11.4 years. The mean age of women in the population was lower than men (59.2±11.6 vs 61.5±11.3).

EBUS-TBNA procedure was performed in 16.8% (n=44) patients due to mediastinal mass and in 83.2% (n=218) patients due to mediastinal lymphadenopathy. The most common stations where biopsy is performed with the EBUS-TBNA process are the subcarinal (7) and lower right paratracheal (4R) lymph node stations (Table 1).

When the biopsy results were evaluated, malignancy was reported in 54.6% of the patients (n=143) (Figure). In patients with malignant pathology, the most common subtype was adenocarcinoma (n=50), followed by small cell carcinoma (n=31) and squamous cell carcinoma (n=24), respectively. The most common extrathoracic malignancy metastases were breast (n=5) and bladder (n=2) carcinoma. Among non-malignant findings, normal lymph node cytopathology (n=59) was most frequently reported. The most common benign pathology was sarcoidosis (n=41), followed by anthracosis (n=11) (Table 2).

Complications related to the EBUS-TBNA procedure were generally mild and trancient . Mild hemorrhage, which was controlled during the procedure, was observed in 10 (0.07%) patients. Short-term desaturation due to general anesthesia which was recovered with oxygen support, was observed in 12 (0.04%) patients. After the end of the procedure, no complications requiring treatment or hospitalization or prolonging hospital stay were observed.

Table 1. Demographic data of patients who underwent EBUS procedure	
Age; year (mean±SD)	60.8 ± 11.4
Gender	n (%)
Male	174 (66.4)
Female	88 (33.6)
Stations with EBUS	(%)
Lymph node	218 (83.2)
4 R	44 (16.8)
4 L	1 (0.4)
7	133 (50.8)
11 R	19 (7.3)
11 L	21 (8)
Mass	44 (16.8)
Procedure-related complications	n (%)
Hemorrhage (mild)	10 (0.07)
Desaturation	12(0.04)

R: Right, L: Left, SD: Standard deviation, EBUS: Endobronchial ultrasonography

Table 2. EBUS pathology diagnoses	
Pathology	**n (%)**
MALIGN	143 (54.6)
NSCLC	
Adenocarcinoma	50 (19.1)
Squamous cell carcinoma	24 (9.2)
Non-small cell carcinoma (type indistinguishable)	20 (7.6)
large cell carcinoma	1 (0.4)
SCLC	31 (11.8)
Lymphoma	6 (2.3)
Breast carcinoma metastasis	5 (1.9)
Bladder carcinoma metastasis	2 (0.8)
Cervix carcinoma metastasis	2 (0.8)
Renal cell carcinoma metastasis	1 (0.4)
Pleomorphic adenoma	1 (0.4)
BENING	119 (45.4)
Normal cytology	59 (22.5)
Sarcoidosis	41 (15.6)
Anthracosis	11 (4.2)
Tuberculosis	5 (1.9)
Pneumoconiosis	2 (0.8)
Invasive pulmonary aspergillosis	1 (0.4)

NSCLC: Non-small cell lung cancer, SCLC: Small cell lung cancer, EBUS: Endobronchial ultrasonography

DISCUSSION

Lung cancer is one of the leading causes of cancer-related deaths. According to WHO data, it is the most common cancer in men and the third most common in women, is often diagnosed in advanced stages, and is largely preventable because it is directly related to tobacco exposure.[6] In addition, the lungs and mediastinal lymph nodes are areas where extrathoracic malignancies frequently metastasize. Therefore, rapid diagnosis and accurate staging are very important in primary lung cancer or metastatic mass and lymph node metastases. Mediastinal lymph node involvement is the most important parameter to determine the type of treatment and staging before surgery, and deciding whether surgery will be recommended to the patient or not. EBUS-TBNA has a very important role in the diagnosis and staging of lung cancer. In the study by Torre et al. in which EBUS-TBNA results were evaluated including 456 cases, it was found that EBUS-TBNA had an accuracy rate of 97.1% in the diagnosis of primary lung cancer and 96.2% in the diagnosis of malignancy. In this study, the distribution of malignant diseases were 46.3% adenocarcinoma, 11.5% large cell, 10.4% squamous cell, and 10.7% small cell carcinoma.[7]

In Yılmaz et al.'s[8] study, EBUS-TBNA performed for mediastinal staging in 37 patients diagnosed with lung cancer and 37 patients for diagnostic purposes, sensitivity was found to be 83%, specificity was 100%, positive predictive value was 100%, negative predictive value was 70%, and accuracy was 88%. The diagnostic distribution of 37 cases biopsied with EBUS-TBNA was as follows: 19 cases were diagnosed with lung cancer, 5 cases with extra-thoracic cancer metastasis, 5 cases with sarcoidosis, 2 cases with tuberculosis, and 6 cases with benign lymph adenomegaly. The distribution of malignant diseases in our study population was as follows: 50 cases of adenocarcinoma, 31 cases of small cell carcinoma, 24 cases of squamous cell carcinoma, 20 cases of undifferentiated non-small cell carcinoma, and 1 case of large cell carcinoma. In our study, unlike other studies, EBUS-TBNA was also performed on masses adjacent to the trachea and bronchi.

The surgically treated lung cancer patients are followed-up radiologically for recurrence or second primary occurrence. Again, treatment response evaluation of lung cancer cases which are still under treatment is done by radiological methods. One of the most common clinical problems for clinicians in the follow-up of such patients is an emergence of a mediastinal lymph node whose diameter increase exceeds the limits or a lymph node with uptake slightly above the limit on control PET-CT. In these cases, especially those who have undergone thoracotomy or mediastinoscopy, repeated surgical biopsy is almost impossible due to postoperative adhesions, altered anatomy, and possible fibrosis after radiotherapy or surgery. In these cases, EBUS-TBNA provides significant advantages in both the ability to obtain reproducible biopsies and the ability to perform characteristic examination of the lymph node with ultrasonography. Additionally, another area where EBUS-TBNA is used is the restaging of lung cancer. In their study by Öztürk et al.,[9] in which they restaged patients who underwent chemoradiotherapy (n=26) and radical surgery (n=74), EBUS-TBNA had high diagnostic accuracy (93.2% after surgery, 100% after chemoradiotherapy). They reported that the sensitivity after surgery was 84.8% and, 100% after chemoradiotherapy. In our study, EBUS-TBNA

was performed on 8 patients who received treatment for lung cancer. Malignancy recurrence was reported in 6 patients, normal lymph node cytopathology was reported in 2 patients.

Apart from malignancies, EBUS-TBNA is frequently used in the detection of benign pathologies that cause mediastinal lymphadenopathy, especially in the diagnosis of granulomatous diseases such as tuberculosis and sarcoidosis.[9] In their study, Batum et al.[10] reported that EBUS-TBNA had a specificity of 86.6% and sensitivity of 98.3% in benign diseases, specificity of 100% and sensitivity of tuberculosis as 81.9%, and specificity of 100% and sensitivity of 95% in sarcoidosis. In their study, 590 patients were evaluated and the final diagnoses of the patients were reported as 62.7% non-granulomatous benign disease (n=370), 28.8% sarcoidosis (n=170), and 8.4% tuberculosis (n=50). In the study of Ortaköylü et al.[11] which data included from Turkey, the diagnostic distribution of the cases which reported benign disease was reported as 27% sarcoidosis and 8.8% tuberculosis. In our study, benign pathologies (n=119) were reported as sarcoidosis in 15.6%, anthracosis in 4.2%, and tuberculosis in 1.9%. Additionally, the pathological result was reported as normal lymph node cytopathology in 22.5% (n=59) of our cases. While the majority of these cases were followed up clinically and radiologically, some suspicious cases were referred to the thoracic surgery clinic for mediastinoscopy.

The role of EBUS-TBNA in the investigation of mediastinal lymph node metastases of extrapulmonary malignancies has not been widely studied. Mediastinal and hilar lesions are common findings on imaging in patients with extrathoracic primary cancers. Distant metastasis, disease recurrence and second primary malignancy can be diagnosed in a newly diagnosed patient. It may also indicate granulomatous disease in a previously diagnosed and treated patient. The role of EBUS-TBNA has previously been evaluated in several clinical studies, with reported sensitivity values (81-95%) and negative predictive values falling on a highly variable spectrum. While metastasis was detected in approximately 50% of these cases, a second primary malignancy, most commonly in the lung, was reported in 25%. Additionally, granulomatous inflammation such as tuberculosis and sarcoidosis was detected in a significant number of patients.3 As one of the largest studies published in our country, Demirdöğen et al.[12] evaluated the EBUS-TBNA results of a large number of patients with extrathoracic malignancies. Accordingly, it was reported that metastases were detected in 14.7% (n=16) of 109 patients with extrathoracic malignancy in EBUS-TBNA. In other studies, the most common extrathoracic malignancies were found to be head and neck malignancies, breast carcinomas, urological malignancies and gastrointestinal system tumors.[13-16] In our study, the most common disease with extrathoracic mediastinal metastasis was breast carcinoma, followed by urological malignancies.

Rapid pathological evaluation (ROSE) can be performed per case by a cytopathologist during the EBUS procedure. Although there is no difference in the final pathological diagnosis between cases in which ROSE was performed and those in which it was not performed, there are studies proving that it shortens the procedure time, reduces anesthesia-related complications, and allows adequate sample collection with fewer lymph node accesses.[17] Since there are not enough cytopathologists in our hospital, ROSE cannot be performed in EBUS-TBNA cases. Despite this, among our cases, the number of cases in which we reoperated due to insufficient cytopathological material was only.[3]

In the literature, most complications related to the EBUS-TBNA procedure are reported as case reports, and no deaths have been reported. In a meta-analysis in which 1299 patients were evaluated, the complication rate was reported as 0.15%,[18] and in another multicenter study in which 3123 patients were evaluated, the major complication rate was reported as 0.16%.[19] The most common complications include infection (mediastinitis, pneumonia or pericarditis), bleeding, pneumothorax, mediastinal emphysema and vocal cord damage. In our cases, complications related to the EBUS-TBNA procedure were generally mild and trancient. Mild hemorrhage, which was controlled during the procedure, was observed in 0.07% (n=10). During general anesthesia, short-term desaturation was observed due to sedation, which was recovered with oxygen support at a rate of 0.04% (n=12). After the end of the procedure, no complications requiring treatment or hospitalization or prolonging hospital stay were observed.

Limitations

The limitations of our study are that it is single-center and retrospective. Apart from this, follow-up results cannot be obtained because most of the malignant patients are followed up in oncological follow-up in another center from the moment of diagnosis.

CONCLUSION

EBUS-TBNA is a minimally invasive method used in the practice of the department of Chest Diseases in the diagnosis and staging of lung cancer, the diagnosis of non-endobronchial lesions, the diagnosis of benign diseases of the mediastinum and the diagnosis of mediastinal metastases of extrathoracic malignancies. In experienced centers like our clinic, the diagnostic value of the procedure results is high and the complication rates are very low.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Samsun University Clinical Researches Ethics Committee (Date: 18,10,2023, Decision No: 2023/19/2).

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
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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.

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Original Article

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Perioperative risk factors for acute kidney ınjury in major abdominal surgeries: a retrospective observatioal study

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ABSTRACT

Aims: Acute kidney injury (AKI), particularly as a postoperative complication related to surgery, has been independently associated with morbidity and mortality. AKI also develops at a significant rate after major abdominal surgery. In this study, it was aimed to identify the risk factors contributing to the development of AKI following major abdominal surgery.

Methods: The study was retrospectively planned. Patients who underwent major abdominal surgery were included in the study. Patients' demographic data, preoperative laboratory data, intraoperative data, and postoperative data were recorded from patient files. The diagnosis and severity of postoperative acute kidney injury (PO-AKI) were assessed using serum creatinine and/or urine output criteria in accordance with the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines. The patients were divided into two groups: AKI and non-AKI.

Results: A total of 64 patients with complete data were included in the study. Among these patients, 6 developed AKI (9.3%). The mean age in the AKI group was found to be statistically significantly higher (p: 0.043). The Frailty index was significantly higher in the AKI group (p: 0.020). Additionally, it was observed that the use of aspirin and angiotensin-converting enzyme inhibitor (ACEI) / angiotensin receptor blocker (ARB) was statistically significantly higher in the AKI group (p: 0.022, p: 0.044, respectively). When patients were evaluated in terms of intraoperative parameters, the amount of colloid used, the amount of ES used, and vasopressor usage were found to be statistically significantly higher in the AKI group (p<0.001, p: 0.036, p: 0.022, respectively). Lastly, vasopressor usage and diuretic usage were found to be statistically significantly higher in the AKI group for postoperative period (p: 0.002, p: 0.044, respectively)

Conclusion: Many parameters covering the perioperative period can cause PO-AKI. Especially in elderly patients, frailty and age are significant factors that must be kept in mind.

Keywords: Abdominal surgery; acute kidney injury; perioperative; postoperative; risk factors

INTRODUCTION

Recent studies have shown that major noncardiac surgery is associated with significanst morbidity and mortality. The development of acute kidney injury (AKI), particularly as a postoperative complication related to surgery, has been independently associated with morbidity and mortality. Even if a patient's kidney function improves, AKI has been associated with long-term adverse events, including the development of chronic kidney disease (CKD) and late mortality.[1,2]

AKI is a common condition among hospitalized patients and has various adverse effects on patient outcomes.[3,4] These effects can be listed as increased in-hospital mortality, prolonged length of hospital stay, increased healthcare costs, progression of CKD, and increased cardiovascular events.[5,6] The relationship between postoperative AKI and cardiovascular surgery has been extensively researched (11% to 31%). Factors such as the type of surgery (coronary artery bypass grafting, valve repair or replacement), advanced age, congestive heart failure, chronic obstructive pulmonary disease (COPD), longer cardiopulmonary bypass duration, and pre-existing CKD have been identified as risk factors for AKI.[7] There are fewer studies related to AKI following abdominal surgery. The incidence of AKI in major abdominal surgery has been reported to vary between 0.8% and 22.4%. This variability may be attributed to differences in case populations across studies and variations in diagnostic criteria for AKI. Additionally, changes in intraabdominal pressure and renal perfusion pressure during and after abdominal surgery lead to various pathophysiological mechanisms. Considering this, it can

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be said that the risk factors for AKI after major noncardiac surgery may not be similar to those after cardiovascular surgery.[5,7]

In recent years, the definition of AKI has evolved from the old term acute renal failure to a set of uniform criteria that combine small changes in creatinine and urine output, ultimately defining AKI. Initially, the risk, injury, failure, loss, and end-stage kidney disease (RIFLE) classification was used for AKI, followed by the Acute Kidney Injury Network (AKIN) classification. In recent years, the RIFLE and AKIN classifications have been integrated into the Kidney Disease: Improving Global Outcomes (KDIGO) classification. This consolidation aims to provide simpler and more cohesive criteria that can be applied in clinical practice, research, and public health surveillance. As a result, AKI is defined as an increase in serum creatinine (SCr) of ≥0.3 mg/dl (≥26.5 µmol/l) within 48 hours; or an increase in SCr≥1.5 times the baseline value known or presumed to have occurred within the previous 7 days; or a urine volume 0.5 ml/kg/hour for 6 hours.[3,8-10]

The hypothesis of this study is that if the risk factors for postoperative AKI (PO-AKI) can be identified more specifically, necessary measures can be taken to reduce the incidence of PO-AKI. As a result of all these, this study aimed to identify the risk factors contributing to the development of PO-AKI following major abdominal surgery.

METHODS

The study was retrospectively planned at Ankara Bilkent City Hospital. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. After obtaining approval from Ankara Bilkent City Hospital Clinical Researches Ethics Committee (Date: 17.03.2021, Decision No: E1/1605/2021), patients who underwent major abdominal surgery between 2020 and 2021 were included in the study. Patients aged between 18 and 80 years, classified as American Society of Anesthesiologists (ASA) I-III, with normal preoperative serum creatinine levels (Normal value: 1.2 mg/dl) and preoperative glomerular filtration rate (GFR) values, without a history of kidney failure - liver failure - heart failure, scheduled for elective surgery, under general anesthesia with inhalation, and with complete data available in the patient files, were included in the study.

Patients' demographic data (*age, gender, body mass index (BMI), comorbidities, medication history*), Geriatric Nutritional Risk Index (GNRI) score,[11] Prognostic Nutritional Index (PNI) score,[12,13] Frailty Index,[14] Model for End-Stage Liver Disease (MELD) score,[15] preoperative laboratory data (serum creatinine, hematocrit, albumin, lymphocyte count, bilirubin, international normalized ratio (INR), sodium), intraoperative data (anesthesia duration, amount of crystalloid, colloid volume, Erythrocyte Suspension (ES) volume, Fresh frozen plasma (FFP) volume, amount of bleeding, urine output, vasopressor usage, nephrotoxic agent usage, diuretic usage), and postoperative data (Acute Physiology and Chronic Health Evaluation (APACHE)-II score, vasopressor usage, diuretic usage, presence of complications, length of stay in intensive care unit (ICU), creatinine at ICU discharge, length of hospital stay, creatinine at hospital discharge, hospital mortality, and three-month mortality) were recorded from patient files.

Patients underwent anesthesia induction with 0.3 mg/kg midazolam, 0.25-0.50 µg/kg remifentanil, 1.5-2 mg/kg 2% propofol, and 0.6 mg/kg rocuronium intravenous (iv) bolus. They were then intubated with an appropriate endotracheal tube (7-8.0 cuffed). Anesthesia maintenance was achieved with Desflurane at 1.0-1.2 MAC, a continuous infusion of 0.5 µg/kg/h remifentanil, and additional doses of rocuronium as needed.

The diagnosis and severity of PO-AKI were assessed using serum creatinine and/or urine output criteria in accordance with the KDIGO guidelines.[8,16] The most recent serum creatinine level before surgery was considered as the baseline value. Serum creatinine levels were monitored at least once daily during the initial 3 days post-surgery.Patients were staged with KDIGO according to Serum creatinine and Urine output status[16,17](Table 1).

Table 1. Staging of acute kidney injury

Stage	Serum creatinine	Urine output
1	1.5 to 1.9 times baseline or ≥0.3 mg/dl (≥26.5 µmol/l) increase	<0.5 ml/kg/hour for 6 to 12 hours
2	2.0 to 2.9 times baseline	<0.5 ml/kg/hour for ≥12 hours
3	3.0 times baseline or increase in serum creatinine to ≥4.0 mg/dl (≥353.6 µmol/l) or initiation of renal replacement therapy	<0.3 ml/kg/hour for ≥24 hours or anuria for ≥12 hours

Statistical Analysis

Data analyses were performed by using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL, United States). Whether the distribution of continuous variables was normal or not was determined by the Kolmogorov-Smirnov test. The Levene test was used for the evaluation of homogeneity of variances. Unless specified otherwise, continuous data were described as mean±standard deviation (SD) for normal distributions, and median (Q_1; 25th percentile - Q_3; 75th percentile) for skewed distributions. Categorical data were described as several cases (%). Statistical analysis differences in normally distributed variables between two independent groups were compared by Student's t-test, Mann-Whitney U test was applied for comparisons of the not normally distributed data. Categorical variables were compared using Pearson's chi-square test or Fisher's exact test was accepted p-value <0.05 as a significant level on all statistical analysis.

RESULTS

Between 2020 and 2021, a total of 64 patients with complete data were included in the study. Among these patients, 6 developed AKI (9.3%). Four of these patients were classified as KDIGO Stage I, and 2 as KDIGO Stage II. The demographic data of the patients are presented in Table 2. The mean age in

the AKI group was found to be statistically significantly higher (p: 0.043). ASA score was statistically significantly higher in patients in the AKI group (p: 0.002). Additionally, The Frailty Index was significantly higher in the AKI group (p: 0.020). Lastly, it was observed that the use of aspirin and aniotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB) was statistically significantly higher in the AKI group (p: 0.022, p: 0.044, respectively) Table 2.

Table 2. Demographic data of the patients

Parameter		Non-AKI n=58	AKI n=6	p
Age, year		57 (43-62)	67 (58-70)	0.043
Gender	Female	36 (62.1)	4 (66.7)	1.000
	Male	22 (37.9)	2 (33.3)	
BMI (kg/m²)		26.3 (22.3-29)	25.0 (24.4-29)	0.927
Frailty index	Yes	18 (31.0)	5 (83.3)	0.020
	No	40 (69.0)	1 (16.7)	
GNRI score		114 (104-122)	108 (107-116)	0.557
PNI score		42.5 (38.3-46)	41 (41-41)	0.225
MELD score		21.7 (20.2-24.4)	20 (19.3-21.5)	0.264
HT	Yes	17 (29.3)	3 (50.0)	0.366
	No	41 (70.7)	3 (50.0)	
CAD	Yes	4 (6.9)	0	1.000
	No	54 (93.1)	6 (100.0)	
CHF	Yes	3 (5.2)	0	1.000
	No	55 (94.8)	6 (100.0)	
DM	Yes	13 (22.4)	3 (50.0)	0.159
	No	45 (77.6)	3 (50.0)	
COPD	Yes	4 (6.9)	0	1.000
	No	54 (93.1)	6 (100.0)	
ASA	II	48 (82.7)	1 (16.7)	0.002
	III	10 (17.3)	5 (83.3)	
Aspirin usage	Yes	5 (8.6)	3 (50.0)	0.022
	No	53 (91.4)	3 (50.0)	
ACEI/ARB usage	Yes	7 (12.1 %)	3 (50.0)	0.044
	No	51 (87.9 %)	3 (50.0)	
Beta-blocker usage	Yes	8 (13.8)	2 (33.3)	0.234
	No	50 (86.2)	4 (66.7)	
Diuretic usage	Yes	3 (5.2)	0	1.000
	No	55 (94.8)	6 (100.0)	
Statin usage	Yes	2 (3.4)	0	1.000
	No	56 (96.6)	6 (100.0)	

Continuous variables are expressed as either the median (Q1; 25th percentile - Q3; 75th percentile), and categorical variables are expressed as either frequency (n) or percentage (%). Continuous variables were compared with the Mann-Whitney U test, and categorical variables were compared using Pearson's chi-square test or Fisher exact test. Statistically significant p-values are in bold.
AKI: Acute kidney injury; ASA: American Society of Anesthesiologists ; ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; BMI: Body mass index; GNRI: Geriatric Nutritional Risk Index; PNI: Prognostic Nutritional Index; MELD: Model for End-Stage Liver Disease; MELD-NA: Model for End-stage Liver Disease sodium; HT: Hypertension; CHF: Congestive heart failure; DM: Diabetes mellitus; COPD: chronic obstructive pulmonary disease

There was no significant difference between the groups in terms of patients' preoperative laboratory values Table 3. When patients were evaluated in terms of intraoperative parameters, the amount of colloid used, the amount of ES used, and vasopressor usage were found to be statistically significantly higher in the AKI group (p<.001, p: 0.036, p: 0.022, respectively) (Table 4).

When patients were evaluated in terms of postoperative parameters, vasopressor usage and diuretic usage were found to be statistically significantly higher in the AKI group (p: 0.002, p: 0.044, respectively) Table 5.

Table 3. Patients' preoperative laboratory values

Parameter	Non-AKIn=58	AKIn=6	p
Serum creatinine (mg/dl)	0.77 (0.66-0.92)	0.65 (0.62-0.80)	0.433
Hematocrit (%)	41 (35-44)	38 (32.5-42)	0.374
Serum albumin (g/L)	42.5 (38.3-46)	41 (41-41)	0.248
Lymphocyte (10^9/L))	1.58 (1.12-1.98)	1.66 (1.45-1.97)	0.917
Bilirubin (mg/dl)	0.58 (0.4-0.94)	0.6 (0.45-0.60)	0.945
(INR)	1 (1-1.1)	1 (1-1)	0.902
Sodium (mEq/L)	139 (137-141)	139 (136-141)	0.954

Continuous variables are expressed as either the median (Q1; 25th percentile - Q3; 75th percentile). Continuous variables were compared with the Mann-Whitney U test. Statistically significant p-values are in bold. AKI: Acute kidney injury, INR: International normalized ratio

Table 4. Intraoperative parameters

Parameter		Non-AKI n=58	AKIn=6	p
Surgical operation				
Colorectal resection		18 (31.0)	2 (33.3)	0.105
Operation whipple		17 (29.3)	1 (16.7)	
Liver resection		14 (24.1)	0	
Gastric resection		6 (10.3)	1 (16.7)	
Intestinal resection		3 (5.3)	2 (33.3)	
Anesthesia duration, min		420 (288-493)	450 (259-495)	0.991
Crystalloid amount, ml		2950 (2000-4375)	4250 (2250-5875)	0.222
Colloid usage	Yes	49 (84.5)	6 (100)	0.582
	No	9 (15.5)	-	
Colloid amount, ml		500 (500-600)	850 (625-1000)	<.001
ES replacement	Yes	48 (82.8)	3 (50.0)	0.092
	No	10 (17.2)	3 (50.0)	
ES amount, ml		0 (0-0)	150 (0-975)	0.036
FFP amount, ml		0 (0-188)	250 (0-500)	0.122
Amount of intraoperative bleeding, ml		375 (150-688)	1250 (400-2100)	0.116
Intraoperative urine output amount, ml		625 (400-1313)	650 (275-763)	0.496
Intraoperative vasopressor usage	Yes	5 (8.6)	3 (50.0)	0.022
	No	53 (91.4)	3 (50.0)	
Nephrotoxic agents usage	Yes	50 (86.2)	6 (100)	1.000
	No	8 (13.8)	-	
Diuretic usage	Yes	15 (25.9)	1 (16.7)	1.000
	No	43 (74.1)	5 (83.3)	

Continuous variables are expressed as either the median (Q1; 25th percentile - Q3; 75th percentile), and categorical variables are expressed as either frequency (n) or percentage (%). Continuous variables were compared with the Mann-Whitneyww U test, and categorical variables were compared using Pearson's chi-square test or Fisher exact test. Statistically significant p-values are in bold.
AKI: Acute kidney injury; ES: Erythrocyte Suspension; FFP: Fresh frozen plasma

Table 5. Postoperative parameters

Parameter		Non-AKI n=58	AKI n=6	p
APACHE-II score		5 (3-6)	6 (5.25-6.75)	0.110
Postoperative vasopressor usage	Yes	1 (1.7)	3 (50.0)	0.002
	No	57 (98.3)	3 (50.0)	
Postoperative diuretic usage	Yes	7 (12.1)	3 (50.0)	0.044
	No	51 (87.9)	3 (50.0)	
Postoperative complication	Yes	15 (25.9)	3 (50.0)	0.338
	No	43 (74.1)	3 (50.0)	
Length of stay in ICU, days		3 (2-4)	3 (2-13)	0.440
Creatinine at ICU discharge		0.57 (0.48-0.69)	0.9 (0.49-1.03)	0.150
Length of hospital stay, days		12 (10-18)	18 (9-23)	0.481
Creatinine at hospital discharge		0.65 (0.51-0.73)	0.78 (0.71-0.87)	0.064
Hospital mortality	Yes	1 (1.7)	-	1.000
	No	57 (98.3)	6 (100)	
Three-month mortality	Yes	2 (3.4)	1 (16.7)	0.259
	No	56 (96.6)	5 (83.3)	

Continuous variables are expressed as either the median (Q1; 25th percentile - Q3; 75th percentile), and categorical variables are expressed as either frequency (n) or percentage (%). Continuous variables were compared with the Mann-Whitney U test, and categorical variables were compared using Pearson's Chi-Square test or Fisher exact test. Statistically significant p-values are in bold.
AKI: Acute kidney injury; APACHE-II: Acute Physiology and Chronic Health Evaluation II skoru; ICU: Intensive care unit.

DISCUSSION

In this study evaluating factors influencing the development of AKI in patients undergoing major abdominal surgery, advanced age, ACEI/ARB usage, aspirin usage, and frailty index, along with intraoperative vasopressor usage, ES usage, colloid usage, and postoperative vasopressor and diuretic usage, were observed to be significant risk factors. These findings suggest that during the perioperative period of major abdominal surgeries, various demographic and clinical parameters play a role in the development of AKI.

AKI is a serious health issue and among the leading causes of morbidity and mortality. Moreover, the presence of multiple risk factors requires a detailed analysis of these factors. In recent years, the increase in the elderly population and the consequent proliferation of comorbidities have led to encountering patient groups requiring surgical interventions at an advanced age more frequently.[18,19] In major abdominal surgeries, not only non-modifiable factors such as age but also modifiable factors (such as vasopressor, colloid, diuretic usage, etc.) necessitate a comprehensive perioperative analysis. An increase in the frailty index and the consequent rise in AKI incidence, particularly in the postoperative period, can be a commonly encountered situation.[20] In our study, we demonstrated that there is no correlation between the GNRI score and the PNI score with AKI in major abdominal surgeries where nutritional deficiency may be observed. However, several aspects including preoperative frailty, intraoperative management and events, and postoperative care may influence the risk of developing postoperative complications.[21] Therefore, we believe that the frailty index, which encompasses more than just nutrition, may be a more suitable prognostic factor for AKI in major abdominal surgeries. In our study, an increase in advanced age and frailty index was observed to be effective factors in the development of AKI. Therefore, comprehensive and multidisciplinary evaluation, especially in the frail patient population, is crucially important.

Another important factor is the inevitable need for polypharmacy in this patient group due to comorbidities.[22] Especially the negative effects of ACEI/ARB, NSAIDs, and diuretic usage on renal functions are a well-known fact. This effect can lead to adverse outcomes both intraoperatively and postoperatively. However, there is no consensus on the mechanisms by which these drugs are associated with the risk of AKI development.[23,24] Adding multiple risk factors arising from major surgeries and significant, uncontrolled surgical stress response to this situation can further adversely affect already problematic renal functions. The results of this study suggest that ACEI/ARB usage in the preoperative period and diuretic usage in the postoperative period may be a risk factor for the development of AKI.

An interesting finding in our study is the positive correlation between aspirin usage and the development of AKI. Although aspirin use in cardiac surgery has been noted to limit increase bleeding risk in patients, it has also been suggested to reduce the incidence of AKI development and intraoperative myocardial infarction.[25-27] However, research investigating the relationship between aspirin usage and AKI is predominantly focused on cardiovascular surgery. Contrary to these studies, there is a need for more comprehensive research to understand why such a result was encountered in this study.

AKI development is largely attributed to reduced renal perfusion due to volume depletion, which is a significant concern, especially in major surgeries. Therefore, effective perioperative fluid management aiming to maintain renal perfusion is crucial. In recent years, goal-directed fluid therapy has gained significant importance. This practice is also among the main objectives of Enhanced Recovery After Surgery (ERAS) protocols, which have become increasingly important in recent years.[28] Perioperative fluid management plays a crucial role in preventing organ hypoperfusion. This process should begin with optimal fasting duration in the preoperative period and continue with a positive fluid balance consisting of crystalloids and colloids during the intraoperative period. In the postoperative period, it should be completed with early oral hydration and nutrient intake. Additionally, vasopressor usage should be considered if necessary. However, there are studies indicating that colloid usage may be associated with AKI, and therefore its usage should be limited.[29] In our study, the higher use of colloids during the intraoperative period in patients who developed AKI may suggest this, but it should be noted that this remains a topic of ongoing significant debate.

In a study, it was indicated that blood transfusion is associated with allergic reactions and may increase the incidence of AKI. Additionally, an increase in AKI incidence has been observed in patients receiving ES. This may be attributed to the kidneys being more sensitive to the inflammatory process associated with transfusion.[30] Additionally, patients undergoing surgery involving the use of blood and blood products may experience significant fluid shifts. These large fluid shifts can lead to hemodynamic instability, which in turn can cause AKI. The

higher incidence of AKI development in patients receiving transfusions in this study is consistent with this result.

Limitations

The study has several limitations. Firstly, it was conducted at a single center and retrospectively. Due to the limited number of patients in the study, multicenter and prospective studies are needed to determine more precise results. Additionally, including only abdominal surgeries in the study may limit generalization.

CONCLUSION

The development of AKI following major abdominal surgeries is not only a significant cause of morbidity and mortality but also leads to substantial resource utilization. Detailed analysis of risks that may affect the perioperative period and efforts to limit them is crucial in reducing AKI incidence. Especially in elderly patients, frailty and age are significant factors that must be kept in mind. In addition, polypharmacy and perioperative medications can significantly impact renal function in patients undergoing major abdominal surgery. It is crucial to conduct a detailed evaluation of the drug treatments and consider potential dose adjustments to mitigate these effects. We believe that more comprehensive studies in this regard will be important in uncovering specific and potential risk factors for subgroups.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was initiated with the approval of the Ankara Bilkent City Hospital Clinical Researches Ethics Committee (Date: 17.03.2021, Decision No: E1/1605/2021).

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.

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Original Article

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The power of serum albumin levels in predicting mortality in critical patients

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ABSTRACT

Aims: Given the presence of comorbidities and critical illnesses in patients admitted to the intensive care unit (ICU), it is imperative to accurately forecast their prognosis and mortality in order to effectively plan and administer their therapies. Decreased serum albumin level is associated with adverse clinical outcomes. We designed this study to evaluate the prognostic value of decreased serum albumin level and its association with age in critically ill patients based on data obtained from the intensive care unit (ICU).

Methods: Data of patients followed between June 2022 and December 2023 in the Internal Medicine ICU of Akdeniz University Hospital were retrospectively reviewed. Albumin, C-reactive protein (CRP), Sequential Organ Failure Assessment (SOFA), and Acute Physiology and Chronic Health Evaluation II (APACHE-II) scores were documented within the initial 24 hours following admission to the ICU. Delta Albumin expression was used to express the changes between albumin values. The relationship between the obtained data and age was examined and compared between the surviving and deceased patient groups.

Results: 300 patients were included in the study. Albumin levels were significantly lower at admission compared to discharge in both the survival and deceased groups (both p<0.001). Changes in albumin levels were significantly associated with ICU mortality independently of age, gender, SOFA, and APACHE changes. Lower albumin levels were associated with worse survival (Hazard ratio: 0.80; 95% Confidence interval: 0.69-0.92; p=0.001).

Conclusion: Changes in albumin levels were significantly associated with ICU mortality independently of age, gender, SOFA, and APACHE changes.

Keywords: Intensive care, albumin level, mortality

INTRODUCTION

In humans, albumin constitutes the most abundant plasma protein, accounting for approximately 55-60% of the measured serum protein.[1] Unlike synthetic colloids, albumin binds reversibly to drugs, hormones, bilirubin, and metal ions, among other substances, affecting their metabolism in hypoalbuminemic critically ill patients.[2] The distrubiton of albumin in the body is variable and interesting. The initial approach in the pharmacokinetics of albumin involves the intercompartmental movement and the exchange between plasma and extravascular space, which is faster than metabolic changes.

Exchange rate between departments is assumed to be approximately 1 day, while the overall exchange rate is assumed to be approximately 25 days.[3] In this cycle, the kidneys account for around 6% of the clearance, the gastrointestinal system accounts for approximately 10%, and catabolism accounts for 84%, while the liver has a synthesis rate of 10.5 g/day for albumin.[4] The second approach is uncompartmental and assumes that the effective albumin concentration. in the metabolic region is equal to the plasma concentration.[5]

The synthesis rate of albumin is also significantly decreased in critically ill patients. Trauma, inflammation, or sepsis-induced acute phase response lead to an increase in gene transcription rates for positive acute phase proteins such as C-reactive protein, while they cause a decrease in albumin mRNA transcription and consequently synthesis rates.[6] A continuous inflammatory response in critical illness can lead to prolonged inhibition of albumin synthesis. Both interleukin-6 and tumor necrosis factor-alpha show gene transcription-reducing effects.[7] Scoring systems in critical care medicine aim to measure the severity of diseases and evaluate patient groups based on objective criteria.[8] The Acute Physiology and

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Chronic Health Evaluation II (APACHE-II) score, calculated using data collected within the first 24 hours of admission to the intensive care unit, predicts in-hospital mortality; an increase in the score is associated with increased mortality risk. The Sequential Organ Failure Assessment (SOFA) score evaluates disease-related organ failure and can be recalculated repeatedly during intensive care unit (ICU) stay to monitor disease progression. High values are associated with increased organ system failure (neurological, respiratory, cardiovascular, renal, hepatic, and hematological).[9]

Considering the comorbidities and critical conditions of patients admitted to the ICU, prognosis and mortality prediction, and accordingly the adjustment of treatments, are crucial for these patients. Moreover, it is believed that the results obtained from this and similar studies will provide significant benefits for improving the follow-up and treatment processes of critically ill elderly patients in future intensive care services, thus reducing morbidity and mortality rates.

This study aimed to identify and predict factors that influence the prognosis of patients during their ICU follow-ups.

METHODS

This study was conducted at the Internal Medicine Intensive Care Unit of Akdeniz University Hospital between June 2022 and December 2023. Prior to the study, approval was obtained from the Akdeniz University Medical Scientific Researches Ethics Committee (Date: 25.04.2024, Decision No: KAEK-274, Annex 1). The study was conducted in accordance with the principles outlined in the Helsinki Declaration.

Method of Sudy t

The research is a retrospective clinical study based on the collection of retrospective data. The study has an observational research nature.s

Scope of the Research

Patients followed in the Internal Medicine Intensive Care Unit of Akdeniz University, who were monitored for at least 24 hours in the intensive care unit, were included in the study. Patients who were referred to an external center during hospitalization, patients monitored in the postoperative intensive care unit, and patients for whom any of the study parameters could not be calculated (due to inability to perform necessary tests, data inadequacy) were excluded from the study. Patients who presented to the intensive care unit multiple times during the study period were only included in the study at their initial presentation.

Data Collection Methods

The necessary data for this study were obtained from intensive care patient follow-up records, hospital electronic database, physician daily observation notes, nurse observation notes, test results, and evaluations performed in the department where the patient was admitted. Retrospective demographic and clinical data were collected from all patients. Patients were classified as survivors or deceased based on the outcomes of their ICU stay.

The APACHE II score was compiled using the worst values of 12 acute physiological variables (temperature, blood pressure, heart rate, respiratory rate) obtained during the first 24 hours in the intensive care unit. Missing data were assumed to be normal. The SOFA score was compiled from arterial oxygen saturation, fraction of inspired oxygen, serum creatinine, total bilirubin, platelet count, detailed Glasgow Coma Scale (GCS) score, mean arterial pressure, and the use of vasopressors such as dopamine, dobutamine, adrenaline, and noradrenaline. The albumin values measured within the first 24 hours of admission to the intensive care unit were referred to as 'entry values,' while those measured within the last 24 hours before discharge from intensive care or before death were referred to as 'exit values.' ΔAlbumin values were defined to represent the change in albumin score obtained.

Statistical Analysis

The data obtained in the study were statistically analyzed using IBM SPSS Statistics 24.0 software (IBM Co., Armonk, NY, USA). Visual and statistical tests for normality were conducted. Categorical variables were expressed as number (n) and percentage (%), while continuous variables were expressed as median [interquartile range (IQR)] for normally distributed data, and as mean±standard deviation (SD) values otherwise. The Chi-square test was used to assess relationships between categorical variables. Student's t-test was used for comparing normally distributed numerical parameters between two independent groups, while the Mann-Whitney U test was used for comparing parameters that did not follow normal distribution. One-way analysis of variance (ANOVA) for repeated measurements was used for normally distributed data with homogeneous variances, and the Wilcoxon signed-rank test was used for non-normally distributed data. Cox regression analysis was conducted to evaluate factors affecting mortality risk, and model fit was assessed with the Concordance Index. A significance level of $p<0.05$ was accepted in the study for statistical significance.

RESULTS

A total of 300 patients who were admitted to the intensive care unit (ICU) and followed were included in the study.. The mean age of the deceased patients was 64.0±13.6 years, while the mean age of the surviving patients was 59.4±19.5 years, and the difference was found to be statistically significant (p=0.017). The distribution of gender was also statistically different between the two groups, with a significantly higher proportion of males among the deceased patients compared to the surviving patients (p=0.008). The burden of chronic diseases, regular medication use, and other basic characteristics were similar between the groups. The majority of deceased patients, accounting for 87.2%, were admitted from the ward, while this rate was seen to be 73.8% for surviving patients (p=0.005).

The median duration of ICU follow-up was significantly longer in deceased patients compared to surviving patients (p=0.002). The history of steroid use and the need for platelet replacement were significantly higher in deceased patients, but there was no significant difference between the groups

in terms of the need for erythrocyte replacement. He most common indication for ICU admission among both groups was acute respiratory failure. However, this indication was significantly more prevalent among deceased patients compared to those who survived (40.2% vs. 28.4%, p=0.035). Septicemia was identified as the second most common reason for ICU admission. A statistically significant difference was also observed between the survived and deceased groups, with septicemia occurring in 35.0% of deceased patients compared to 16.4% of survived patients (p<0.001).The need for Mechanical Ventilation (MV) was significantly higher in deceased patients in the intensive care unit (p<0.001). The basic and clinical characteristics of the patients are detailed in **Table 1**.

Table 1. Examination of basic and demographic characteristics of patients followed in the intensive care unit according to survival status

	Survival (n=183)	Deceased (n=117)	p
Age, years	59.4±19.5	64.0±13.6	0.017
Gender			
Female	86 (47.0%)	37 (31.6%)	0.008
Male	97 (53.0%)	80 (68.4%)	
Hospitalization in the ICU			
Sepsis	30 (16.4)	41 (35.0)	<0.001
Acute resp failure	52 (28.4)	47 (40.2)	0.035
Acute renal failure	2 (1.1)	6 (5.1)	0.060
Pancreatitis	2 (1.1)	4 (3.4)	0.21
Trauma	8 (4.4)	2 (1.7)	0.33
Septic shock	7 (3.8)	8 (6.8)	0.28
Other	82 (44.8)	10 (8.5)	<0.001
Presence of chronic disease	95 (51.9%)	59 (50.4%)	0.87
Alcohol	7 (3.8%)	2 (1.7%)	0.42
Multimorbidity	72 (39.3%)	40 (34.2%)	0.37
Pre-ICU service admission	135 (73.8%)	102 (87.2%)	0.005
Service admission duration, days	4.0 (13.0)	8.0 (15.0)	0.013
ICU stay duration, days	3.0 (4.0)	4.5 (8.0)	0.002
Steroid treatment	57 (31.1%)	54 (46.2%)	<0.001
Platelet Replacement	5 (2,7)	17 (14,5)	<0.001
Erythrocyte Replacement	36 (19,7)	28 (23,9)	0,055
Need for MV, at admission	15 (8.2%)	12 (10.3%)	0.15
Need for ICU MV	9 (4.9%)	51 (43.6%)	<0.001

Variables are expressed as number (%), mean ± standard deviation, and median [interquartile range]. MV: Mechanical ventilation, ICU: Intensive care unit

The entry and exit laboratory values, as well as organ function scores of patients requiring intensive care monitoring, are shown in **Table 2**. The CRP levels in the deceased group were significantly higher compared to the living group (p<0.001), however the change in CRP during ICU monitoring did not have any significance. Both the SOFA score and the APACHE score showed a significant increase in the values between admission and discharge in the deceased group, with a p-value of less than (p<0.001).

Regarding albumin values, significantly higher levels were observed in both intensive care entry and exit in the survival group. During intensive care monitoring, albumin values significantly decreased more in the deceased group (p<0.001).

The changes in CRP, albumin, SOFA score and APACHE scores during intensive care follow-up in the survival and death groups are presented in Table 3.CRP levels did not show a statistically significant difference between the survival and death groups at discharge (p=0.25 and p=0.88, respectively). Albumin levels were found to be significantly lower at the time of admission in both the survival group and the deceased group (p<0.001 for both). While the SOFA score increased significantly in the deceased group, it decreased significantly in the survival group (p<0.001 for both). APACHE score was also significantly higher in the deceased group at discharge compared to admission (p<0.001). In the survival group, however, a significant decrease in the APACHE score was observed (p<0.001).

Changes in albumin levels were found to be significantly associated with ICU mortality independent of age, sex, SOFA, and APACHE changes. Lower albumin levels were associated with worse survival (Hazard ratio: 0.80; 95% confidence interval: 0.69-0.92, p=0.001).Table 4

Table 2. Examination of laboratory values according to survival status of patients followed up in the intensive care unit

	Survival (n=183)	Deceased (n=117)	p
CRP entry	58.3(120.8)	142.5 (159.6)	<0.001
CRP exit	58.4 (92.2)	136.6 (164.5)	<0.001
CRP change	-0.32 (86.1)	9.1 (104.2)	0.31
Albumin entry	31.3 ±7.0	26.9 ±5.6	<0.001
Albumin exit	30.0±6.2	22.9 ±5.0	0.001
Albumin change	-1.3 (4.8)	-3.4 (7.1)	<0.001
SOFA entry	1.0 (1.0)	6.0 (3.0)	<0.001
SOFA exit	0.0 (1.0)	6.0 (4.59)	<0.001
SOFA change	0.0 (1.0)	3.0 (3.0)	<0.001
APACHE entry	18.0 (12.0)	29.0 (14.0)	<0.001
APACHE exit	10.0 (4.0)	55.0 (15.09	<0.001
APACHE change	-6.0 (10.0)	22.0 (16.0)	<0.001

Variables are Expressed as mean±standard Deviation and Median [interquartile range]. CRP: C-reactive protein, SOFA: Sequential Organ Failure Assessment, APACHE: Acute Physiology and Chronic Health Evaluation

Table 3. Changes of inflammatory indicators and prognostic indices upon entry and exit from intensive care unit according to survival status of patients

	Survival (n=183)			Deceased (n=117)		
	ICU entry	Exit	p	ICU entry	Exit	p
CRP	58.3(120.8)	58.4 (92.2)	0.25	142.5 (159.6)	136.6 (164.5)	088
Albumin	31.3±7.0	30.0±6.2	<0.001	26.9 ±5.6	22.9±5.0	<0.001
SOFA	1.0 (1.0)	0.0 (1.0)	<0.001	6.0 (3.0)	6.0 (4.5)	<0.001
APACHE	18.0 (12.0)	10.0 (4.0)	<0.001	29.0 (14.0)	55.0 (15.0)	<0.001

Variables are expressed as mean±standard deviation and median [interquartile range]. ICU: Intensive care unit, CRP: C-reactive protein, SOFA: Sequential organ failure assessment, APACHE: Acute Physiology and Chronic Health Evaluation

Table 4. Evaluation of risk factors affecting mortality according to survival status of patients monitored in intensive care

	Hazard ratio	95% Confidence interval	p
Age, year	1.01	0.98-1.05	0.50
Gender, male	0.41	0.08-1.70	0.20
Difference in albumin	0.80	0.69-0.92	0.001
Difference in SOFA	1.77	1.14-2.75	0.011
Difference in APACHE	1.32	1.21-1.44	<0.001

SOFA: Sequential organ failure assessment, APACHE: Acute physiology and chronic health evaluation

DISCUSSION

Albumin levels decrease in critically ill patients, both in those who survive and those who die in intensive care. A decrease in albumin levels can predict mortality independently of intensive care scoring systems and is an independent risk factor affecting mortality.

We observed a high mortality rate in patients receiving steroid treatment. Studies have shown that the use of corticosteroids is associated with infection, increased mechanical ventilation duration, and increased mortality.[10] The current findings can be attributed to the immunosuppressive effects of corticosteroids and their ability to alter infection rates. The use of corticosteroids should be closely monitored in intensive care units, and the risk-benefit ratio should be carefully reviewed.

In our study, platelet replacement was found to be significant for mortality, but the number of red blood cell replacements was deemed insignificant. In a prospective, multicenter, observational study conducted by Corwin and colleagues, the increasing number of erythrocyte transfusions received by patients was associated with longer durations of intensive care and hospital stays, as well as an increase in mortality.

It was concluded that increased number of red blood cell transfusions was an independent predictor of worse clinical outcomes.[11] The data was consistent with our study, and in a study involving 32,842 patients, intensive care unit and in-hospital platelet transfusion were not associated with increased mortality.[12]

In adults, serum albumin contributes sensitively to the regulation of osmotic pressure and vascular permeability and also contributes to physiological functions.[13] Additionally, albumin levels serve as an indicator to sensitively and effectively reflect the status of nutrition, organ function, and physical activity.[14]

Our research revealed that albumin levels were significantly associated with poor prognosis in critically ill patients. The decrease in albumin in intensive care patients can be explained by many mechanisms.

Our study demonstrated that albumin levels in critically ill patients are significantly associated with poor prognosis. The decrease in albumin levels in intensive care patients can be explained by various mechanisms. The presence of infection affects albumin balance in intensive care, particularly inflammatory processes such as sepsis, can impair vascular endothelial function, increase vascular permeability, and significantly increase systemic inflammatory factors. Increased cytokine levels can affect the gene expression and catabolism of albumin and also decrease plasma albumin concentration. This increase leads to the leakage of albumin out of the vessels, resulting in a decrease in plasma albumin levels.[15,16] The transcapillary escape of albumin is 300% in patients with septic shock and this rate increases by 100% after cardiac surgery.[17] The rate of albumin synthesis can vary significantly in critically ill patients,[17] which will exacerbate the deficit in critically ill patients.

In our study, the decrease in albumin levels was evident in both the deceased and surviving groups. This change was more pronounced in the deceased group compared to the surviving group and increased mortality. The literature supports our study. A study involving 5357 patients diagnosed with sepsis demonstrated a nonlinear relationship between albumin levels and mortality.[18] McCluskey;[19] in their study, found that serum albumin concentrations were lower in non-survivors upon admission to the intensive care unit, and serum albumin concentrations decreased more rapidly within the first 24-48 hours. In our study, albumin levels decreased in all patient groups. Kendall et al.,[20] in their study involving 577 patients, showed a strong negative trend with serum albumin levels, where survival, initially at 70.6%, decreased to 63.4% when serum albumin was ≤2.45 g/dl and further to 76.4% when the lowest serum albumin was ≤1.45 g/dl.

Studies have considered albumin levels. In a retrospective cohort study involving 18,353 patients monitored in intensive care, Jin et al.[21] found that decreasing serum albumin levels were associated with an increased risk of death. In the study, intensive care unit mortality was higher in patients with serum albumin levels <30 g/L compared to those with serum albumin levels ≥30 g/L. Serial measurement of serum albumin can provide information on the clinical prognosis of critical patients. A serum albumin level of 30 g/L has been widely accepted as the threshold and treatment target for hypoalbuminemia in clinical trials investigating the effect of albumin administration on the prognosis of critically ill patients.[22]

Despite all these data, the use of albumin in intensive care remains controversial. Serum albumin concentration will generally decrease dramatically from the early stages of a critical illness and will not usually return until the disease recovery stage, and the kinetics of administered albumin will vary greatly between critically ill patients and healthy subjects. Considering the important functions of albumin in health, it would be expected that exogenous albumin administration to increase intravascular albumin concentration would be beneficial during critical illness. However, studies have not demonstrated any benefit of albumin compared to other colloidal therapies in adults.[23] A meta-analysis reviewing 32 randomized controlled trials showed that albumin use resulted in an additional six deaths per 100 patients.[24] Recommendations by Vincent et al.[25] suggested that while the use of albumin may have a low probability of harm in most patients, it should be reserved for specific patient groups with evidence of benefit.

Limitations

The first limitation of our study is its retrospective study design, and there may be unmeasured potential confounding factors. Furthermore, the long half-life of the record also creates a limitation in terms of its marker. Therefore, when evaluating the main results of our study, it should be taken into account that the risk of type-2 error is high.

Well-designed and adequately powered controlled prospective studies are needed in the future to comprehensively identify the presence of underlying confounding factors.

CONCLUSION

We observed that albumin levels were significantly low in critically ill patients admitted to the ICU and correlated with mortality. In addition to scoring systems like APACHE II and SOFA, we believe that albumin levels could serve as an important marker. Albumin levels, being easily accessible, could be a valuable indicator in clinical monitoring and predicting mortality.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Akdeniz University Medical Scientific Researches Ethics Committee (Date: 25.04.2024, Decision No: KAEK-274).

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.

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Original Article

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The frequency of structural causes (PALM) according to figo palm-coein classification in patients undergoing hysterectomy for abnormal uterine bleeding

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ABSTRACT

Aims: We aimed to determine the frequency of the PALM group in the FIGO PALM-COEIN system of patients who were operated for AUB, and to evaluate and analyze our data in our clinic.

Methods: In a retrospective study, data were obtained for nonpregnant women aged 18–55 years who underwent hysterectomy for AUB at a center in Turkey in 2017-2022. The patients were retrospectively classified according to the PALM-COEIN system.

Results: A total of 847 women were included. Leiomyoma was the most common pathology result in only 377 (44.5%) patients. The second most common pathology result was adenomyosis and leiomyoma coexistence in 132 (15.6%) patients. The third most common pathology result was 62 (7.3%) adenomyosis.

Conclusion: In addition to the combined use of FİGO AUB system 1 and 2 in AUB, the notation grouping may be useful for clinicians in the management of AUB.

Keywords: Abnormal uterine bleeding, PALM-COEIN, notation

INTRODUCTION

Abnormal uterine hemorrhage (AUB) is a disease with a prevalence of 10-30% in women of reproductive age.[1] Due to its high incidence, it is a health problem that has been studied extensively. Various terminologies have been defined to identify the symptoms and causes of AUB, such as metrorrhagia, menorrhagia, menometrorrhagia, polymenorrhea, hypermenorrhea, and dysfunctional uterine bleeding.[2] The terms that make up the classical terminology of AUB have been used over the years and their use is no longer recommended.[3] For example, there are some contradictions even as to whether menorrhagia is a symptom or a diagnosis. In the study, in which 100 studies were examined, menorrhagia was accepted as a symptom in 3/4 of the studies, while it was accepted as a diagnosis in the others.[4] Due to these situations, there are long-term studies on the classification system accepted all over the world for AUB. One of the biggest reasons for this is that terms such as menorrhagia and metrorrhagia used in classical terminology cannot give clear information about the underlying pathologies. In addition, these terms are not sufficient to fully cover the situation encountered, both as a condition experienced by women and as medical diagnoses made by clinicians.[5]

AUB can be a symptom of many pathologies in women of reproductive age. Various terms and symptoms such as menorrhagia, metrorrhagia, polymenorrhea, hypermenorrhea, oligomenorrhea, and dysfunctional uterine bleeding have been used to describe AUB. Many of these terms are considered to be confusing and inadequate for identifying and classifying etiologies.[6] The etiology of AUB is not described by the physicians with the same terminology or the presence of more than one possible cause in a patient; This makes it difficult to reach a consensus on this issue both among clinicians and in the literature.

There is consensus that some traditional AUB terms should be abandoned because they are confusing and/

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or poorly defined.[6-8] Because of this confusion, FIGO first co-published the FIGO AUB System 1 for the identification of symptoms in normal and AUB patients in reproductive years and the FIGO AUB System 2-PALM-COEIN for the identification of the reasons of AUB in 2011.[9] classification was established in 2011 by the International Federation of Gynecology and Obstetrics (FIGO) Menstrual Disorders Group (FMDG) with the support of researchers from 6 continents and over 17 countries in order to standardize the terminology used in AUB in non-pregnant women in reproductive age.[5] In our study, we aimed to determine the frequency of the PALM group in the FIGO PALM-COEIN system of patients who were operated for AUB, and to evaluate and analyze our data in our clinic.

FIGO Abnormal Uterine Bleeding in 2011; It is classified as Terminology and Definitions (FIGO-AUB System 1). He classified the reasons as PALM-COEIN system (FIGO-AUB System 2). Later, in 2018, the classifications remained the same, but their contents were revised. In this revision of FIGO AUB System 1, the definition of irregularity has been changed . In this revision of FIGO AUB system 2 The basic/core classification system is almost unchanged and is presented. Category N has undergone a change from "not yet classified" to "not otherwise classified" as we cannot be certain which, if any, of these entities will ultimately be placed in a unique category.[11] The aim of our study is to determine the frequency of organic pathologies that cause abnormal uterine bleeding and to determine how often they combine.

METHODS

This study was approved by University of Health Sciences Adana City Training and Research Hospital Clinical Researches Ethics Committee (Date: 03.11.2022, Decision No:2225). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Since our study was retrospective, we did not obtain informed consent.

In this retrospective study, the data of 1158 patients aged 18-55 years who were operated for hysterectomy at Health Sciences University Adana City Training and Research Hospital between December 1, 2017 and December 1, 2022 were analyzed. Of 1158 patients, 847 patients had undergone hysterectomy due to PALM, and 311 patients had undergone hysterectomy due to COEIN. Since the FIGO PALM COEIN Classification examines abnormal uterine bleeding in women of reproductive age, patients with postmenopausal bleeding were not included in the study. Patients in the COEIN bleeding disorder class, such as women using systemic hormonal contraception or other hormonal therapy, were not included in the study.

Statistical Analysis

Demographic data of patients such as age, gravida, parity, body mass index was recorded. Then, Patients' data were scanned for structural pathologies classified according to the PALM group. Adana City Hospital data system was used to collect retrospective data. IBM SPSS V23 was used to analyze data. The comparison of categorical variables according to groups was analyzed with the chi-square test. Descriptive statistics were performed for all variables. Because the data were not normally distributed, the median was reported as [Q1-Q3]. The results of the analysis were used frequency (percent) for categorical variables. We took significance level as $p<0.050$.

RESULTS

During the study period, 1158 hysterectomies were performed. Among these, 847 patients had undergone hysterectomy for PALM and was enrolled in the research. The mean age of the participants was 45.44±3.89 years, the mean gravida was 2.84±1.65 and the mean parity was 2 2.16±1.88. The mean BMI was 29.33±5.13 kg/m^2 (Table 1).

Table 1: The Sociodemographic and obstetric characteristics of the study participants

Maternal age (years) (mean ± SD)	45.44 ± 3.89
Body-mass index (kg/m^2) (mean ± SD)	29.33 ± 5.13
Gravida (mean ± SD)	2.84±1.65
Parity (mean ± SD)	2.16 ± 1.88

Myoma incidence was found to be the most common pathology with 75.44%. Adenomyosis was evaluated as the second most common pathology with 31.28%. Polyp was found as the third most common pathology with 20.66% (Table 2). The prevalence of structural causes in pathology results are shown in Table 3.

When the pathology results of 847 patients who had hysterectomy were analyzed about coexistence of pathology results, leiomyoma was the most common pathology result in only 377 (44.5%) patients. The second most common pathology result was adenomyosis and leiomyoma coexistence in 132 (15.6%) patients. The third most common pathology result was 62 (7.3%) adenomyosis. When the other pathology results were examined: Polyp in 63 (7.5%) patients; polyp and malignancy coexistence in 14 (1.7%) patients; polyp

and leiomyoma coexistence in 53 (6.4%) patients; polyp and adenomyosis coexistence in 16 (1.9%) patients; polyp, leiomyoma and malignancy coexistence in 4 (0.5%) patients; polyps, adenomyosis and malignancy coexistence in 1 (0.1%) patient; polyp, adenomyosis and leiomyoma coexistence in 22 (2.6%) patients; polyps, adenomyosis and leiomyoma and malignancy coexistence in 2 (0.2%) patients; adenomyosis and malignancy coexistence in 15 (1.8%) patients; adenomyosis, leiomyoma and malignancy coexistence in 15 (1.8%) patients; leiomyoma and malignancy coexistence in 34 (4%) patients and malignancy in 37 (4.4%) patients was detected (Table 3).

Table 2. Distribution of coexistence of pathology results according to the PALM-COEIN system.-1

	n=847 (%)
P	63 (7.5%)
PM	14 (1.7%)
PL	53 (6.3%)
PA	16 (1.9%)
PLM	4 (0.5%)
PAM	1 (0.1%)
PAL	22 (2.6%)
PALM	2 (0.2%)
A	62 (7.3%)
AL	132 (15.6%)
AM	15 (1.8%)
ALM	15 (1.8%)
L	377 (44.5%)
LM	34 (4%)
M	37 (4.4%)

Abbreviations: P, polyp. A, adenomyosis; L, leiomyoma; M, malignancy and hyperplasia. a Values are given as number (percentage).

Table 3. Frequency of structural causes in patients with hysterectoy.

	n (%)
Polyp	175 (20.66%)
Adenomyosis	265 (31.28%)
Leiomyoma	639 (71.44%)
Malignancy and hyperplasia	122 (14.4%)

DISCUSSION

In AUB FİGO 1 system, the four parameters used to define normal uterine bleeding are frequency, regularity, duration, and volume.[7,8,10,11] The FIGO AUB System 2 enables the differentiation of potential causes contributing to the patient's AUB symptoms. It consists of two parts: structural (PALM) and unstructured (COEIN).[10] PALM classification, in which structural pathologies are classified, is performed by imaging method and/or histopathological. We also analyzed hysterectomy operations performed for structural reasons in our clinic according to PALM classification.

Uterine leiomyomas are cited as the most common indication in approximately one-third of all hysterectomies.[12] In our study, leiomyoma was the most common pathology result in only 377 (44.5%) patients. The most common pelvic neoplasms in women are leiomyomas.[13,14] The most common complaints in women with fibroids are AUB and cramps.[15] In our study, the second most common pathology result was adenomyosis and leiomyoma coexistence in 132 (15.6%) patients. In the study of Ferraz et al.,[16] adenomyosis and leiomyoma were mostly coexisted with 65.4% in hysterectomy materials. We found that leiomyoma and malignancy coexistence was in 34 (4%) patients. Studziński et al.[17] also found that leiomyoma was coexistence with endometrial cancer in 22 cases. In our study, polyp and leiomyoma coexistence was found in 53 (6.4%) patients. In the study of Kınay et al.,[18] the incidence of endometrial polyps in cases with leiomyoma was found to be 20.1% (n=155). The frequent association of leiomyoma with other pathologies shows that it is important to investigate other organic pathologies in patients with leiomyoma.

The lifetime prevalence of endometrial polyps ranges from 8% to 35%, and the incidence increases with age.[19] Similarly, polyps were detected in 20.66% (n=175) of the patients included in our study, and it is seen as the third most common cause of structural AUB after leiomyomas and adenomyosis. Although polyps are usually asymptomatic, they can be the cause of AUB. We think that endometrial polyp is common and attention should be paid to its investigation.

The prevalence of adenomyosis varies between 5% and 70% and its relationship with AUB is not clear.[20] In our study, adenomyosis was detected in 31.28% (n=265) of the patients who were operated for AUB. The fact that adenomyosis is common both alone and frequently accompanied by leimyoma shows that clinicians should suspect adenomyosis in patients with abnormal uterine bleeding.

Many premalignant conditions (hyperplasia) and malignancies can cause AUB. While the rate of malignancy or hyperplasia was 6% in the histopathological examination of patients with AUB in the study of Wynants et al.,[21] this rate was 26% in the study of Vijayaraghavan et al.[22] In our study, 122 women

with hyperplasia or malignancy were identified. It was seen in 14.40% of our patients included in the study as a percentage. It should be kept in mind that malignancy or hyperplasia may frequently occur in patients with abnormal uterine bleeding.

AUB in women of reproductive age is a symptom of any of several pathological conditions. The accepted method for classifying such patients in the literature were FIGO System 1 and the PALM-COEIN classifications. In our study, we also grouped hysterectomy materials performed for structural reasons in our clinic according to the palm classification, but in most cases, there was no single pathology result. The limitations of our study were that it was retrospective and only the data were analyzed based on the pathology results. In addition to the combined use of FIGO AUB system 1 and 2 in AUB, we think that the notation grouping suggested by Munro et al.[9] may be useful for clinicians in the management of AUB.

CONCLUSION

When we examined the structural causes of abnormal uterine bleeding, it was observed that the cause of bleeding in the patients in our study was generally due to more than one organic cause. In other words, even if we detect an organic cause in a patient with abnormal uterine bleeding, we must keep in mind that we may encounter another organic cause.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was initiated with the approval of the University of Health Sciences Adana City Training and Research Hospital Clinical Researches Ethics Committee (Date: 03.11.2022, Decision No:2225).

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.

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Original Article

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Effect of vitamin D deficiency on uric acid/HDL cholesterol ratio

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ABSTRACT

Aims: It has been suggested that vitamin D deficiency is involved in the etiology of cardiovascular diseases. High uric acid and low HDL cholesterol levels are critical risk factors for cardiovascular diseases. High uric acid levels, high total cholesterol and triglyceride levels, and low HDL-C levels are often encountered in cases with vitamin D deficiency. Our study aimed to investigate the relationship between vitamin D levels and uric acid /HDL-C (UHR) and plasma atherogenic index (PAI, triglyceride /HDL-C) in patients with vitamin D deficiency.

Methods: This retrospective study included patients whose vitamin D levels were checked in our clinic. The subjects were divided into two groups according to their vitamin D levels and the relationship between laboratory variables, such as uric acid, HDL cholesterol, UHR, and plasma atherogenic index, was examined.

Results: A total of 675 patients, 167 (24.7%) males and 508 (75.3%) females, were included in the study. The mean age of the patients was 53.6±15.2 years. It was found that patients with vitamin D deficiency had high UHR and PAI levels and low HDL-C levels (p=0.001, p=0.025; p=0.032, p=0.016).

Conclusion Our results suggest that vitamin D deficiency has a positive correlation with HDL cholesterol levels and an impact on the risk of cardiovascular diseases by increasing the uric acid/HDL ratio and plasma atherogenic index..

Keywords: Vitamin D deficiency on uric acid/HDL cholesterol ratio

INTRODUCTION

Vitamin D is taken with food in the form of ergocalciferol and cholecalciferol. It is actually formed through a process where 7-dehydrocholesterol in the skin absorbs solar ultraviolet-B ray photons and it is converted into previtamin D3 or cholecalciferol.[1] The active form of vitamin D is 1.25-dihydroxy vitamin D (1.25 (OH) 2D), which is produced by the 1α-hydroxylase enzyme in the renal proximal tubules, and its well-known impact is to ensure bone mineralization by increasing the absorption of calcium from the intestines.[2] The mechanism of 1.25 (OH) 2D works by binding to vitamin D receptors (VDR) found in many cells of the body, including cardiomyocytes, endothelium, and vascular smooth muscles. In addition, there are studies in the literature showing that VDR is present in many tissues and that vitamin D deficiency and insufficiency have an impact on common cancers, immune system diseases, metabolic syndrome, dermatological diseases, cardiovascular diseases, and lipid metabolism.[3-5] There is available data that 1.25(OH) 2D regulates the renin-angiotensin-aldosterone system. It has been experimentally observed that 1α-hydroxylase deficiency leads to the development of high-renin hypertension. In light of these studies, it is thought that vitamin D has a protective effect against cardiovascular diseases.[6]

It has been observed that high uric acid is associated with diabetes, hypertension, metabolic syndrome, insulin resistance, stroke, and cardiovascular events.[7,8] In addition to unclear data in the literature, there are many studies supporting the association of hyperuricemia and vitamin D deficiency.[9,10] In a meta-analysis of 32 studies by Isnuwardana et al.,[11,12] the likelihood of hyperuricemia due to vitamin D deficiency was determined to be approximately 1.5 times the normal level of vitamin D. It has been suggested that serum uric acid may reduce the conversion of 25-hydroxyvitamin D (25-OHD) to the active VIT D form of 1.25-di hydroxyl vitamin D (1,25-(OH)2D) by suppressing the 1-alpha-hydroxylase enzyme. It is considered that vitamin D deficiency may result in hyperuricemia by causing secondary hyperparathyroidism.

When the literature is reviewed, it can be seen that there is an inverse correlation between serum levels of 25(OH)D

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and serum lipid levels. In a study involving 8,592 patients, individuals with low 25(OH)D levels had higher levels of total cholesterol (TC), triglycerides (TGs), and low-density lipoprotein cholesterol (LDL-C) but lower levels of high-density lipoprotein cholesterol (HDL-C).[13] In another study, it was suggested that serum 25(OH)D levels had a negative correlation with total cholesterol, triglyceride, and LDL-cholesterol and a positive correlation with HDL cholesterol.[14] Lipid/lipoprotein abnormalities, which mean high uric acid, TC, TG, LDL-C, triglyceride/HDL cholesterol, uric acid/HDL cholesterol levels, and decreased HDL-C levels, are critical risk factors for atherosclerosis and CVDs. The TG/HDL cholesterol ratio (plasma atherogenic index-PIA), which best shows us small and dense LDL (sdLDL), which accumulates more easily in the artery wall than LDL cholesterol, has also become a guiding marker for atherosclerosis and coronary artery disease.[15]

In our study, we aimed to examine the relationship of 25(OH) vitamin D deficiency with the uric acid/HDL ratio, a marker for cardiovascular diseases, and TG/HDL cholesterol ratio (plasma atherogenic index).

METHODS

This investigation received authorization from the Hitit University Clinical Research Ethics Committee (April 30, 2024, approval 2024-11) and all protocols undertaken in investigations involving human subjects were conducted in strict compliance with the ethical guidelines outlined by the institutional and/or national research governing body, the 1964 Declaration of Helsinki, and its subsequent revisions or analogous ethical criteria. The present study is a retrospective multicenter study. Patients who applied to the internal medicine clinic between January 1, 2020 and January 30, 2023 were, a total of 675 patients, 167 men and 508 women, were included in the study. The patients who were <18 years old; who had Type 1 or Type 2 Diabetes mellitus, prediabetes or those who were on metformin therapy; who were pregnant; who had chronic diseases such as hypertension, chronic renal disease, liver diseases. The patients who were <18 years old; who had Type 1 or Type 2 Diabetes mellitus, prediabetes or those who were on metformin therapy; who were pregnant; who had chronic diseases such as hypertension, chronic renal disease, liver diseases, hypertension, cardiac insufficiency; who had active infection; who had hematological or immunological diseases or malignancies; who had primary hyperparathyroidism; and who were on medications for calcium and lipid metabolism and those using antihypertensive medications were excluded from the study. The demographics and anthropometric data of the patients were recorded. Vitamin D levels (ng/ml), triglyceride (mg/dl), total cholesterol (mg/dl), high-density lipoprotein cholesterol (HDL-C) (mg/dl), low-density lipoprotein cholesterol (LDL-C) (mg/dl) and uric acid levels (mg/dl) of all patients who met the inclusion criteria for the study were recorded from the hospital automation system. Patients with vitamin D levels <10 (ng/ml) were classified as group-1, patients with vitamin D levels between 10-20 (ng/ml) were classified as group-2, patients with 20-30 (ng/ml) were classified as group-3, and patients with >30 (ng/ml) were classified as group-4. The correlation between uric acid/HDL-C, tgl/HDL-C levels according to the patients' vitamin D levels was evaluated.

Statistical Analysis

The data were analyzed on the IBM SPSS Statistics Standard Concurrent User V 29 software (IBM Corp., Armonk, New York, USA). Summary statistics were given as numbers (n) and percentages (%) for categorical variables and arithmetic mean, standard deviation, standard error, median, and interquartile range values according to the distribution of the data for numerical variables. The normality of the data of numerical variables was evaluated with the Shapiro-Wilk normality test. The Levene test was employed to analyze the homogeneity of the variance of the groups. Comparisons between two groups of numerical variables were made with independent samples t-test for normally distributed data and with the Mann-Whitney U test for non-normally distributed data. One-way analysis of covariance was employed to compare age-adjusted uric acid/HDL ratios according to vitamin D groups. The bonferroni test was used as a multiple comparison test. Pearson chi-square test was utilized to compare groups with categorical variables. A value of $p<0.05$ was considered statistically significant.

RESULTS

A total of 675 patients, 167 (24.7%) males and 508 (75.3%) females, were included in the study. The age range of the patients was 18 to 85 years, with the mean age being 53.6±15.2 years.

As seen in Table 1, vitamin D deficiency was observed in 63.5% of male patients and 68.5% of female patients. There was no statistically significant difference between the vitamin D distributions of male and female patients. Age, creatinine, HDL, and aspartat transaminaz (AST) values of patients with vitamin D deficiency were statistically low. Total cholesterol, LDL, uric acid, uric acid/HDL ratio, glucose, alanin aminotransferaz (ALT), triglyceride values, and TGL/HDL ratio were not statistically different by vitamin D groups.

According to the comparisons in Table 1, since the ages of the patients were statistically different in the vitamin D groups, considering that the age variable could be a confounding factor, the uric acid/HDL and TGL/HDL ratios were adjusted for age and compared again. As seen in Table 2, uric acid/HDL and TGL/HDL ratios in patients with vitamin D deficiency were statistically higher than in patients without deficiency.

As seen in Table 3, uric acid/HDL ratios showed statistical differences in vitamin D groups. Patients with vitamin D<10 (ng/ml) had statistically higher uric acid/HDL ratios than those with vitamin D>30(ng/ml). Differences between other groups were not statistically significant. TGL/HDL ratios showed statistical differences in vitamin D groups. Patients with vitamin D>30(ng/ml) had statistically lower TGL/HDL ratios than other groups. TGL/HDL ratios of other vitamin D groups were not statistically different.

Table 1. Comparison of demographic and laboratory values of patients with vitamin D levels below and above 20 ng/mL

	Vitamin D		Test Statistics	
	<20 (ng/ml) n=454	≥20(ng/ml) n=221	Test value	p value
Gender. n (%)				
Male	106 (63.5)	61 (36.5)	1.445	0.229‡
Female	348 (68.5)	160 (31.5)		
Age. (year)	52.4±15.3	55.6±14.8	2.550	0.010†
Creatinine	0.70±0.18	0.74±0.20	2.360	0.019†
Total cholesterol	188.71±37.44	192.83±39.00	1.325	0.186†
LDL	104.67±30.35	106.78±31.27	0.840	0.401†
HDL	54.68±10.73	57.96±12.91	3.270	0.001†
Uric acid	4.64±1.24	4.79±1.30	1.422	0.155†
Uric acid/ HDL ratio	9.00±3.13	8.78±3.49	0.823	0.411†
Glucose	93.00 (19.00)	95.00 (21.00)	1.504	0.133&
AST	19.00 (6.00)	20.00 (5.50)	2.057	0.040&
ALT	17.00 (9.00)	18.00 (10.50)	1.606	0.108&
TGL	130.50 (96.25)	120.00 (88.00)	0.955	0.340&
TGL/HDL	2.84±1.73	2.61±1.63	1.685	0.093†

n: Number of patients, %: Row percentage, Data were presented as mean±standard deviation or median (interquartile range) values. ‡: Pearson chi-square test, †: Independent samples t test, &: Mann-Whitney U test ,AST: aspartat transaminaz ,ALT: alanin aminotransferaz

Table 2: Comparison of uric acid/HDL and TGL/HDL ratios in vitamin D groups for adjusted age

	Vitamin D		Test Statistics	
	<20(ng/ml) n=454	≥20(ng/ml) n=221	test value	p value
Uric acid/HDL	9.03±0.16	8.82±0.22	5.073	0.025¥
TGL/HDL	2.86±0.07	2.56±0.11	4.606	0.032¥

Data were summarized as mean±standard error estimate. ¥: One-way covariance analysis, TGL: Trigliserid

Table 3: Comparison of uric acid/HDL ratios in four vitamin D groups for adjusted age

	Vitamin D				Test Statistics	
	<10 (ng/ml) n=165	10-20 (ng/ml) n=289	20-30 (ng/ml) n=146	>30 (ng/ml) n=75	Test value	p value
Uric acid/ HDL	9.12±0.27a	8.98±0.19ab	9.08±0.27ab	9.08±0.27ab	3.788	0.010¥
TGL/ HDL	2.79±0.13a	2.89±0.10a	2.75±0.13a	2.75±0.13a	3.463	0.016¥

Data were summarized as mean±standard error estimates. ¥: One-way analysis of covariance; Superscripts a and b indicate the difference between groups. There was no statistically significant difference between groups containing the same superscript

DISCUSSION

Uric acid/HDL cholesterol and triglyceride/HDL cholesterol levels were high in patients with 25(OH)D below 20 (ng/ml). Our study is the first in the investigation of uric acid/HDL cholesterol and plasma atherogenic index simultaneously in patients with vitamin D deficiency.

Some studies have shown that vitamin D deficiency is a new risk factor for cardiovascular diseases.[4] It has been found that vitamin D levels are lower in conditions that increase the risk of cardiovascular disease, such as metabolic syndrome, diabetes mellitus, and hypertension.[16] Patients with low vitamin D face more cardiovascular mortality than individuals with normal vitamin D levels.[17]

There are some studies in the literature suggesting that high uric acid levels and low levels of HDL cholesterol may have synergistic negative effects on the cardiovascular system through insulin resistance and oxidative damage to endothelial cells.[18,19] Hu et al.[20] showed that high serum UA levels had an effect on carotid atherosclerosis of HDL-C. In a meta-analysis conducted by Yang et al.[21] in 480 patients with acute myocardial infarction, high uric acid and low HDL cholesterol levels were found as risk factors for AMI.

In a study conducted by Lupton et al.[22] on 20,360 individuals, it was observed that HDL cholesterol was low and LDL-cholesterol, total cholesterol, and triglyceride levels were significantly higher in individuals with low vitamin D. In a study conducted by Mashahit et al.,[23] it was observed that serum 25(OH)D was inversely associated with high TG and low HDL cholesterol levels in both diabetic and control groups.Ray Chaudhuri et al.[24] reported that 25-hydroxy vitamin D deficiency was significantly associated with dyslipidemia (P=0.0001) in the Indian population. There are some studies in the literature supporting that vitamin D deficiency is associated with dyslipidemia, as well as meta-analyses showing no association.[25,26] Data supporting literature findings were obtained in our study. It was observed in our study that HDL cholesterol levels were significantly lower in individuals with low vitamin D. However, supporting the studies in the literature, no significant relationship was detected in terms of total cholesterol, triglyceride, LDL-Cholesterol levels, and vitamin D deficiency.

In a study that included 18,596 patients, Hang Y. et al.[27] found a negative relationship between vitamin D and hyperuricemia. A study conducted in 2013 showed that vitamin D deficiency was significantly associated with high uric acid among postmenopausal Chinese women but not in premenopausal women.[28] It was observed that the uric acid levels of the patients with prediabetes and vitamin D deficiency, whose uric acid level was above 6 mg/dl, decreased after vitamin D supplementation.[29] On the other hand, there are some other studies that have not detected any relationship between vitamin D deficiency and hyperuricemia.[30] In our study, no significant relationship was found between uric acid and vitamin D deficiency.

There are studies in the literature indicating that high uric acid/HDL cholesterol levels may have synergistic harmful effects on the cardiovascular system by increasing endothelial oxidative damage and insulin resistance.[31-33] In our study, we found that vitamin D deficiency had a significant relationship with high uric acid/HDL cholesterol levels ($p>0.025$, $p<0.010$). In light of this study, we think that vitamin D deficiency may be a risk factor for cardiovascular diseases by increasing the uric acid/HDL cholesterol level. Plasma atherogenic index (PAI-TG/HDL cholesterol) is an important noninvasive biomarker used in the diagnosis of atherosclerotic coronary heart disease in recent years. In the KERCADR study conducted by Mahmodii et al.,[34] it was determined that there was an inverse relationship between PAI and vitamin D levels in healthy men. In the same study, it was stated that an improvement in vitamin D levels would cause a significant decrease in PAI to reduce the risk of

cardiovascular disease in individuals with a normal body mass index. In a case-control study in the literature, it was observed that vitamin D level and PAI were inversely proportional in patients with metabolic syndrome.[35] In our study, PAI was found to be statistically higher in patients with vitamin D deficiency than in patients without deficiency (p=0.032, p=0.016). As a result of our study, we think that the uric acid/HDL cholesterol ratio and PAI can help predict the risk of cardiovascular disease in individuals with vitamin D deficiency and that we can also reduce cardiovascular risk with vitamin D supplementation.

CONCLUSION

This is the first study in the literature simultaneously showing the relationship between UHR and PAI, which are used as biomarkers for cardiovascular risk, and vitamin D. We think that vitamin D deficiency and UHR and PAI increased by the deficiency may be a risk factor for cardiovascular events.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethics committee approval was obtained from Hitit University Clinical Researchs Ethics Committee (Date: 30.04.2024, Decision No: 11).

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.

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Original Article

MEDICINE PALLIATIVE CARE

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The role of cardiothoracic ratio in predicting coronary artery atherosclerosis in young adult patients

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ABSTRACT

Aims: This study aimed to determine the role of cardiothoracic ratio in predicting coronary atherosclerosis in young adult patients.

Methods: In this single-center retrospective study, young adult patients who underwent coronary computed tomography angiography (CTA) with suspicion of coronary artery disease between October 2022 and May 2024 were included. Demographic and clinical histories of all patients were determined from the medical record system. Coronary artery calcium scores (CACSc) and cardiothoracic ratios (CTR) of the patients in question were calculated and recorded from the coronary CTA images.

Result: A total of 264 young adult patients under the age of 45, with an average age of 42.2±3.1 years, were included in this study. The patients included in the study were divided into two groups according to the presence of atherosclerotic calcific plaque in coronary CTA. Smoking history, hyperlipidemia, hypertension and diabetes mellitus history were significantly different in the two patient groups (for all, $p<0.05$). In univariate regression analysis, hyperlipidemia, diabetes mellitus, hypertension, smoking history and high CTR values were determined as risk factors for coronary atherosclerotic calcific plaque.

Conclusion: Our findings show that the risk of coronary atherosclerosis is high in young adult patients with CTR values above 0.5150.

Keywords: Cardiothoracic ratio, coronary artery calcium score, atherosclerotic plaque, coronary computed tomography angiography

INTRODUCTION

Coronary artery disease (CAD) is among the leading causes of mortality and morbidity worldwide.[1] Atherosclerosis is the most important cause of the disease in its pathophysiological process, and coronary artery calcification is a risk marker for subclinical atherosclerosis.[2,3] Acute coronary events may be the first sign of coronary artery disease in asymptomatic individuals.[4] Therefore, identifying patients at risk before these events occur will significantly reduce cardiovascular mortality rates. Coronary computed tomography angiography (CTA) or coronary angiography, which has a high diagnostic rate, can be used to detect these patients. However, the use of these examinations as a screening method is limited due to reasons such as cost, radiation and potential kidney damage.[5] This has increased the interest in non-invasive screening methods for the detection of potential CAD patients.

Cardiothoracic ratio (CTR) is a radiographic parameter that evaluates heart size and functions, which was first described in 1919.[6] Normal values are between 0.42 and 0.50, and a value above 0.50 is considered cardiomegaly.[7] Studies conducted with the widespread use of computed tomography (CT) have found high correlations and minimal differences between CTR measured by CT and CTR measured by radiographs.[8] CTR has been used in the diagnosis and follow-up of many respiratory and cardiovascular diseases and has even been found to be one of the prognostic factors in terms of cardiovascular mortality.[9]

This study aimed to determine the role of cardiothoracic ratio in predicting coronary atherosclerosis in young adult patients.

METHODS

The study was carried out with the permission of the Siirt University Faculty of Medicine Non-invasive Ethics Committe(Date:04.04.2024, Decision No: 105146).

This single-center retrospective study included young adult patients under 45 years of age who underwent coronary CTA with suspected coronary artery disease between October 2022 and May 2024. The demographic characteristics (age and gender), body-mass index (BMI), diabetes mellitus, hypertension, hyperlipidemia and smoking history of the patients in question before coronary CTA were scanned in the medical record system and recorded. The inclusion criteria

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for diabetes mellitus, hypertension and hyperlipidemia were defined as being diagnosed and/or receiving medication for these diseases. For smoking, the criterion was determined as smoking at least 10 cigarettes per day for at least 1 year. BMI (kg/m^2) was calculated as weight (kg) divided by the square of height (m). Individuals with known or detected respiratory disease and any cardiac disease other than CAD were excluded.

To calculate the calcium load in all patients, the thorax area from the bottom of the tracheal carina to the heart base was imaged without intravenous contrast administration. Imaging was performed with a 128-slice CT device (General Electric Revolution EVO, GE Medical Systems, Milwaukee, WI, USA). The imaging protocol for coronary calcium scoring was as follows: gantry rotation time 0.35 seconds, tube voltage 120 kv, 100 mAs, and slice thickness 2.5 mm. The total coronary artery calcium score (CACSc) of all patients was obtained by summing the calcium values obtained from all coronary artery tracings and Agatston scoring was used.[10]

Coronary CTA images were reconstructed to create a maximum scanning field of view (SFOV). CTR was obtained by dividing the longest transverse heart diameter measured from the outer myocardium to the outer myocardium at the level of the diaphragmatic dome in SFOV axial sections by the longest transverse thoracic diameter measured from the inner thoracic wall to the inner thoracic wall (Figure 1).[8,11]

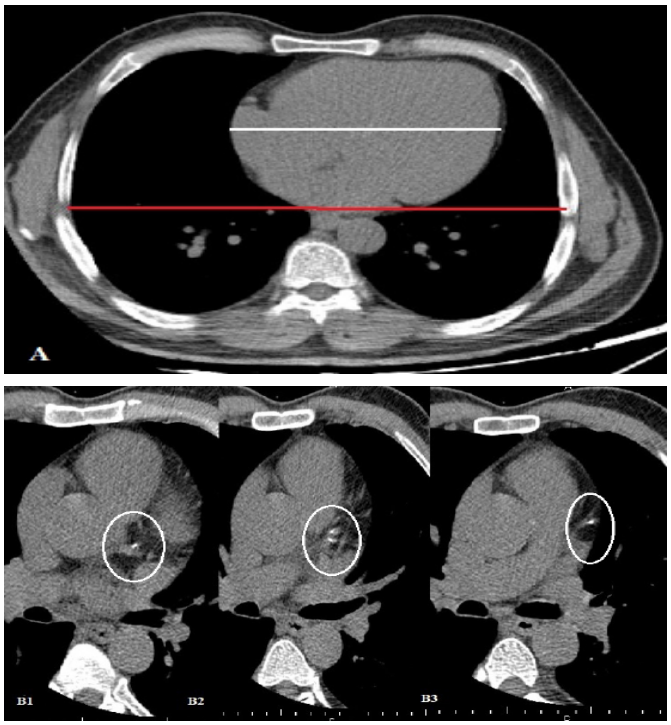

Figure 1 (A-B): Case example of a 44-year-old male patient with a history of smoking and hyperlipidemia, cardiotoxic index of 0.57 and coronary artery calcium score of 61. (A) Axial images of coronary CTA maximum scanning field of view (SFOV) showing measurement of cardiac indices. CT-derived cardiothoracic ratio: The white arrow depicts the greatest transverse cardiac diameter and the red arrow indicates the greatest transverse thoracic diameter (It has been included at this level only to simulate the measurement and to complete the figure). Calcific plaques are observed in the proximal (B1), middle (B2) and distal (B3) segments of the left descending coronary artery on non-contrast CT images.

Statistical Analysis

Data analyzes of our study were determined using SPSS 20.0 software (Statistical Package for the Social Sciences, Chicago, IL). Variables related to qualitative data are expressed as number (n) and percentage (%), and variables related to quantitative data are expressed as mean ± standard deviation (SD).In the evaluation of the study data, Student's t test was used for intergroup comparisons of normally distributed variables and mann-whitney U test was used for intergroup comparisons of non-normally distributed parameters. Chi-square test or Fisher's exact test was applied for the comparison of categorical variables depending on the sample size. univariate and multivariate binary logistic regression analyzes were used to determine the risk factors affecting coronary atherosclerosis. ROC (Receiver Operating Characteristic) curve analysis was used to determine whether CTR was a prognostic indicator in predicting coronary atherosclerosis and to determine optimal cut-off values. The significance level for statistical results was accepted as $p<0.05$.

RESULTS

A total of 264 young adult patients with an average age of 42.2±3.1 years were included in this study. Of all patients, 14.8% had hypertension, 15.9% had hyperlipidemia, 12.5% had diabetes mellitus and 36.8% had a history of smoking. CACSc values of patients with a history of hyperlipidemia, diabetes mellitus, hypertension and smoking were significantly higher than those without ($p<0.05$) (Table 1). A significant strong positive correlation was found between CTR and CACSc values ($r=0.757$, $p<0.001$) (Figure 2).

Table 1. Comparison of clinical variables and coronary artery calcium score values.

Parameters	CACSc	p values
Smoking		
No	4.4±9.6	0.001a
Yes	20.6±32.9	
Hypertension		
No	9.2±19.9	0.009a
Yes	19.6±35.6	
Hyperlipidemia		
No	8.9±22.1	0.005a
Yes	19.8±26.1	
Diabetes mellitus		
No	8.1±17.7	0.001a
Yes	28.3±42.1	

Notes: aMann Whitney U-test with median ± interquartile range (IQR). Statistically significant results ($p < 0.05$).
Abbreviations: CACSc, Coronary artery calcium scoring

The patients included in the study were divided into two groups according to the presence of atherosclerotic calcific plaque in coronary CTA. Group 1 included patients without coronary atherosclerotic calcific plaque and group 2 included patients with coronary atherosclerotic calcific plaque.

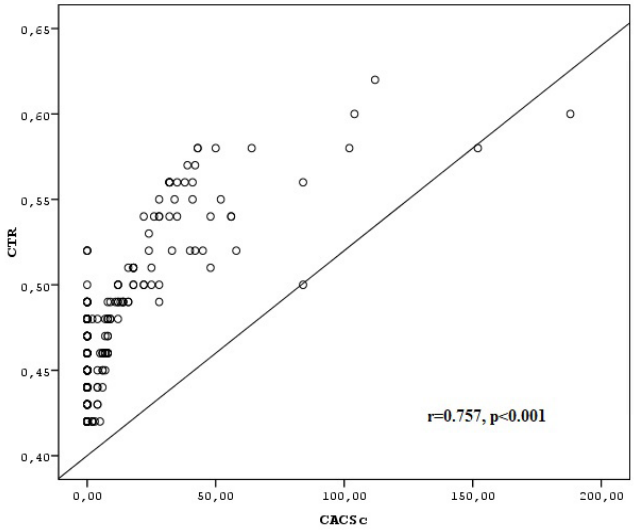

Figure 2. Correlation between coronary artery calcium score and cardiothoracic ratio in patients. Circles are data points, and diagonal lines are means.

No statistically significant difference was found between the two groups in terms of age and BMI (for all, p>0.05). However, smoking, hyperlipidemia, hypertension and diabetes mellitus history were significantly different in the two patient groups (for all, p<0.05). CTR values were statistically higher in group 2 patients (p<0.001, Figure 3). Demographic and clinical characteristics and CTR values between both groups are compared in Table 2.

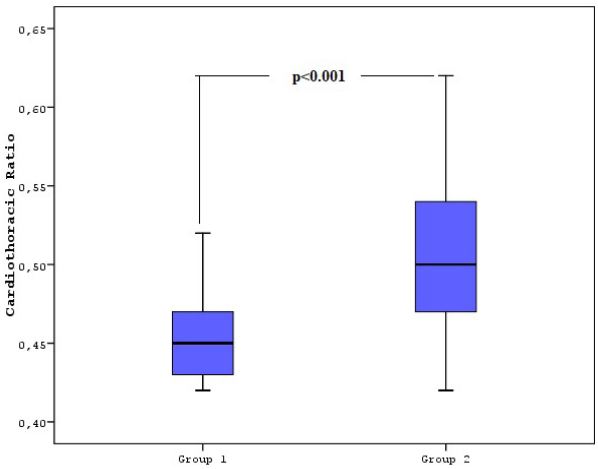

Figure 3. Boxplot of the distribution of cardiothoracic ratio among groups. The horizontal lines inside each box represent the mean values and the lower and upper rows of each box represent the minimum and maximum values, respectively.

In the receiver operating characteristics (ROC) curve analysis test of CTR values, the AUC values were determined as 0.836 (0.783-0.889) with a 95% confidence interval and therefore were considered statistically significant (p <0.001, Figure 4). Accordingly, when the cut-off value of CTR was taken as ≥ 0.5150 in predicting the presence of coronary atherosclerotic calcific plaque, its sensitivity was determined as 80.4% and its specificity was determined as 68.8%.

Regression analysis was used to determine effective parameters in predicting the presence of coronary atherosclerotic calcific plaque. In univariate regression analysis, hyperlipidemia (yes or no), diabetes mellitus (yes or no), hypertension (yes or no), smoking history (yes or no) and high CTR values (≥ 0.5150) were identified as risk factors for coronary atherosclerotic calcific plaque. In multivariate regression analysis, smoking history (p=0.001, OR: 1.55; 95% confidence interval (CI), 0.819-2.93) and CTR values above 0.5150 (p<0.001, OR: 45.8; 95% confidence interval (CI), 14.5-144.4) were independently associated with coronary atherosclerotic calcific plaque (Table 3).

Table 2: Baseline characteristics and comparison of variables among groups

Parameters	Group 1 (n=158)	Group 2 (n=106)	Total (n=264)	p values
Age (years)	42.3±2.8	42.1±3.5	42,2±3,1	0.739a
BMI (kg/m²)	25.3±4.1	25.4±4	25.4±4.1	0.797a
CACSc	0	26.7±30.2	10.7±23.1	<0.001a
Smoking, n (%)				
No	112 (70.9%)	50 (49.1%)	162 (63.2%)	0.001b
Yes	46 (29.1%)	56 (50.9%)	102 (36.8%)	
Hypertension, n (%)				
No	140 (88.6%)	85 (80.2%)	225(85.2%)	0.044b
Yes	18 (11.4%)	21 (19.8%)	39 (14.8%)	
Hyperlipidemia, n (%)				
No	139 (87.9%)	83 (78.3%)	222 (84.1%)	0.04b
Yes	19 (12.1%)	23 (21.7%)	42 (15.9%)	
Diabetes mellitus, n (%)				
No	144 (91.1%)	87 (82.1%)	231 (87.5%)	0.037c
Yes	14 (8.9%)	19 (17.9%)	33 (12.5%)	
CTR	0.4518±0.023	0.5039±0.046	0.4727±0.043	<0.001d

Notes: aStudent's t-test with mean ± standard deviation (SD). bFisher's Exact test with n (%). cChi-Square with n (%).dMann Whitney U-test with median ± interquartile range (IQR). Statistically significant results (p < 0.05).
Abbreviations: CACSc, Coronary artery calcium scoring; BMI, Body Mass Index; CTR, Cardiothoracic ratio

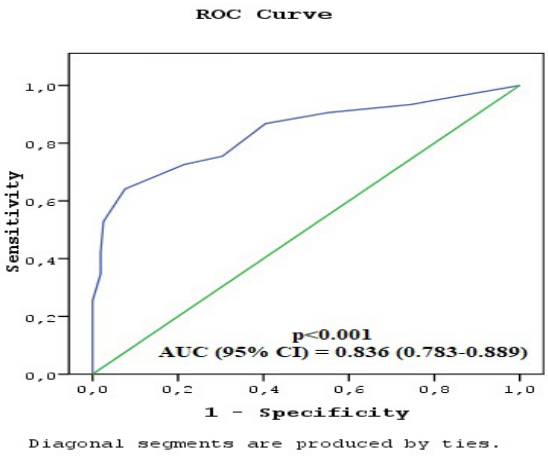

Figure 4. The receiver operating characteristic (ROC) curve and the area under the ROC (AUC) of cardiothoracic ratio in predicting the presence of coronary atherosclerotic calcific plaque

Table 3. Univariate and multivariate binary logistic regression analysis results for determining risk factors for coronary atherosclerotic calcific plaque

	Univariate		Multivariate	
	p values	OR (CI 95%)	p values	OR (CI 95%)
Smoking Yes, against no	<0.001	2.72 (1.63-4.55)	0.001	1.55 (0.819-2.93)
Hyperlipidemia Yes, against no	0.037	2.02 (1.04-3.94)	ns	
Diabetes mellitus Yes, against no	0.032	2.24 (1.07-4.70)	ns	
Hypertension Yes, against no	0.013	1.01 (1.003-1.027)	ns	
CTR ≥0.5150 against <0.5150	<0.001	43.12 (14.88-124.87)	<0.001	45.86 (14.56144.42)

Note: Statistically significant results (p < 0.05).
Abbreviations: ns, not significant; OR, Odds ratio; CI, Confidence interval; CTR, Cardiothoracic ratio

DISCUSSION

CAD is one of the most common causes of death, usually occurring due to atherosclerosis in the coronary arteries. Coronary artery calcification detected by coronary CTA is a highly specific indicator of atherosclerosis.[12] Coronary CTA has become a standard imaging modality for the diagnosis of CAD in symptomatic patients with recent technological advances. However, reasons such as radiation, cost and contrast material requirement prevent this method from being a screening method in asymptomatic individuals.[13] For this reason, many tests such as high-sensitivity C-reactive protein (hs-CRP), carotid intima-media thickness, aortic pulse wave velocity, and ankle-brachial index have been recommended and used to determine subclinical atherosclerosis.[14-20] However, we have not found a comprehensive study in the literature examining the relationship between CTR and coronary artery calcification in young patients. The most important finding of this study was that increased CTR values were independently associated with coronary artery calcification.

Many heart diseases such as cardiomyopathy, pericardiac effusion, heart failure, heart valve diseases, cardiomegaly and congenital heart anomalies can cause an increase in heart size.[21] Ischemic cardiomyopathy is one of the most important causes of heart failure worldwide, resulting from obstructive coronary artery disease.[22] As a result of myocardial damage caused by ischemia, ventricular dysfunction, adverse cardiac remodeling and heart failure may develop.[23] Changes in heart size play an important role in early detection and determining the severity of these diseases.

CTR is a simple and rapid method that reflects functional and morphological changes in the heart.[24] This method has been used as a prognostic factor in many disease groups. During a 4-year follow-up period in hemodialysis patients, high CRT values have been shown to be associated with an increased risk of cardiovascular disease independent of other risk factors.[9] It has also been determined that CTR values above 0.55 are one of the most important independent risk factors affecting mortality rates in hemodialysis patients.[25] In the 4-year follow-up of patients who underwent rheumatic heart valve surgery, it was shown that patients with high CTR values were associated with poor prognosis.[26] Eslami et al.[27] reported that increased CTR values are a strong indicator of mortality in hospitalized patients due to COVID-19 infection. Wilhelmsen et al.[28] argued that increased CRT values could predict CAD mortality independently of other traditional risk factors in a study conducted in middle-aged men. Treasure et al.[29] reported that endothelial dysfunction, which is an early indicator of atherosclerotic coronary artery disease, is associated with increased left ventricular volume. To our knowledge, this is the first study to examine the role of CRT in predicting the presence of coronary artery calcification in young patients. In our study, CRT was significantly higher in the group with coronary artery calcification, and the cut-off value in the ROC analysis was 0.5150. CRT above this value emerged as an independent risk factor for coronary artery calcification in multivariable logistic regression analysis. Therefore, our findings show that CRT levels may be an effective and reliable parameter that can be used to predict coronary artery calcification.

Hypertension, hyperglycemia, dyslipidemia and smoking are the most important known risk factors for CAD.[30] Smoking increases the risk of complications of both the primary pathogenesis of cardiovascular diseases and other etiological causes.[31] The most common risk factor found in young patients with coronary artery disease is smoking with a rate of up to 60%.[32] In this study, consistent with the literature, the most common risk factor detected in young patients with coronary atherosclerosis was smoking, with a rate of 50.9%. Numerous studies show that smoking is independently associated with coronary atherosclerosis.[33-35] In our study, smoking was significantly higher in the group with coronary atherosclerosis and emerged as an independent risk factor in multivariate logistic regression analysis.

Hyperglycemia is a strong risk factor that causes atherosclerosis both directly and indirectly.[36,37] Many studies have found that the risk of coronary atherosclerosis is increased in young patients with diabetes.[36-38] One of the most important risk factors leading to the emergence, progression and complication of atherosclerosis is dyslipidemia.[39-41] Stone et al.[42] found that the risk of atherosclerosis increased with increasing exposure time in young adults with dyslipidemia. Many studies have shown that dyslipidemic status is an independent risk factor for coronary atherosclerosis in all age groups.[43,44] Hypertension is an important risk factor for CAD independent of other risk factors.[33,45] It has been determined that the risk of CAD in hypertensive individuals increases 2-3 times compared to normotensive individuals.[46] Kang et al.[47] reported a gradual increase in the risk of coronary atherosclerosis with increases in systolic blood pressure in young patients in a large-scale study. In our study, consistent with the literature, CACSc values were significantly higher in patients with a history of diabetes, dyslipidemia and hypertension, and they emerged as risk factors in univariate logistic regression analysis.

Limitations

The primary limitation of our study is that it is single-center and retrospectively designed. Second, the patients included in the study were selected patients with clinically suspected coronary artery disease, which reduces the generalizability of the study findings. Third, information about familial CAD history, which is an important risk factor for atherosclerosis, could not be included in the statistical analysis because it was not sufficient in the registry system.

CONCLUSION

In conclusion, our findings show that the risk of coronary atherosclerosis is high in young adult patients with CTR values above 0.5150. Therefore, determining CRT levels at admission may help identify patients at high risk for coronary atherosclerosis. In fact, CTR, which is a simple, non-invasive and rapid method, may be a candidate parameter to be a screening method for the detection of coronary atherosclerosis in the young population.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Siirt University Faculty of Medicine Non-invasive Ethics Committe(Date:04.04.2024, Decision No: 105146).

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.

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