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

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ABSTRACT

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

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

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

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

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

INTRODUCTION

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

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

METHODS

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

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

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

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

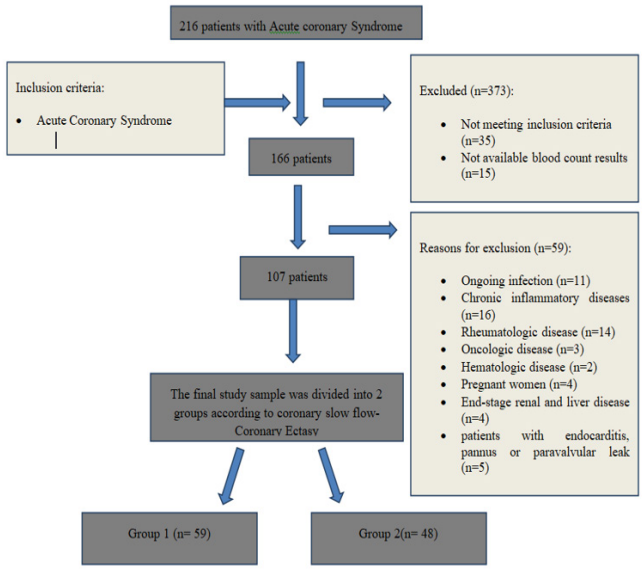

Figure 1. Flow chart of the study population

Adequate Nutrition Screening Tools

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

Statistical Analysis

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

RESULTS

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

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

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

Table 1. Baseline characteristics of study population

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

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

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

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

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

Table 3. BMI and nutritional indeces

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

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

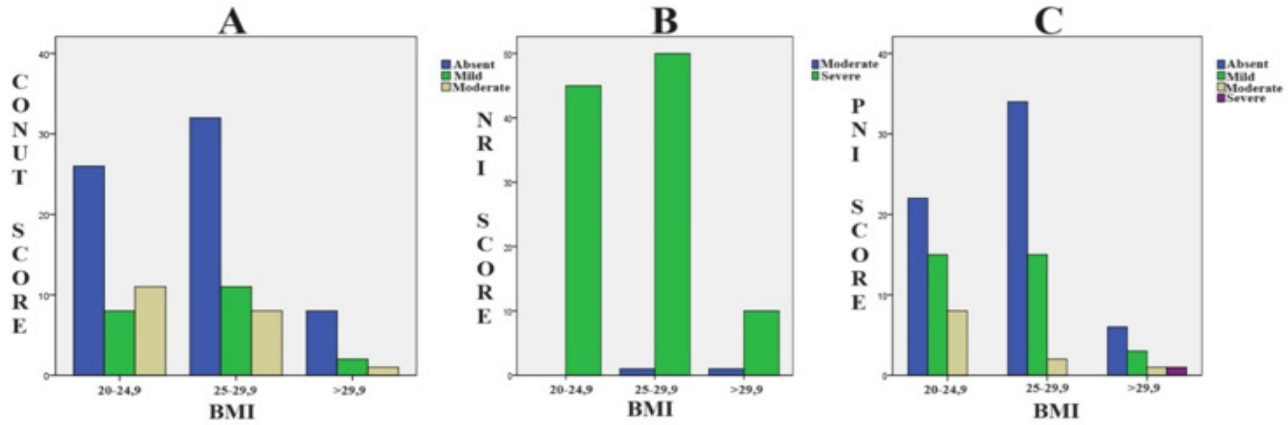

Figure 2. Malnutrition and body-mass index

Table 4. Body-mass index and gender

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

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

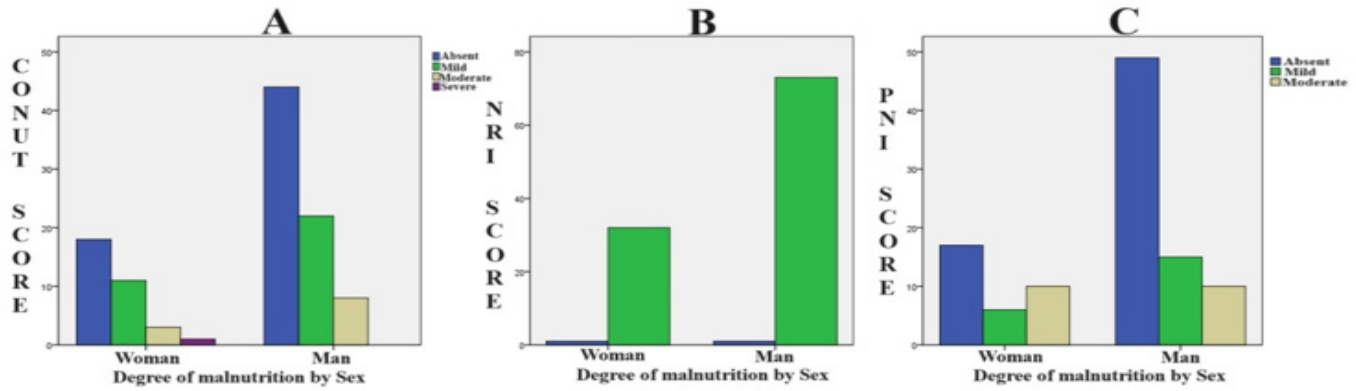

Figure 3. Malnutrition by gender

Tabel 5. Labaratory parameters

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

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

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

DISCUSSION

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

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

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

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

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

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

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

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

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

Table 6. Nutritional indeces

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

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

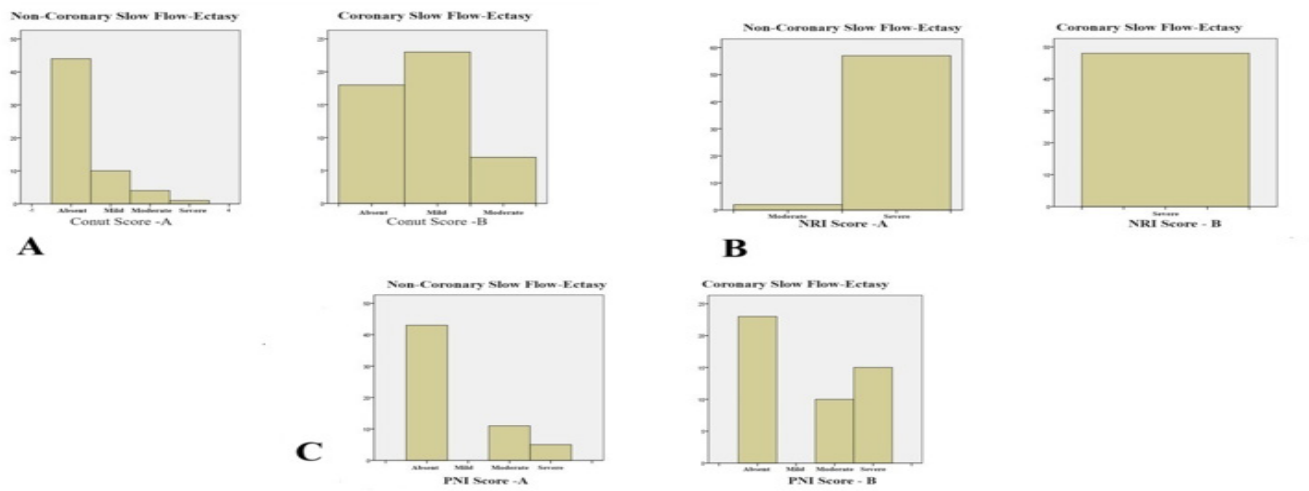

Figure 4. Box graphy coronary ectasy slow flow and non-coronary ectasy slow flow group

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

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

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

Limitations

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

CONCLUSION

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

ETHICAL DECLARATIONS

Ethics Committee Approval

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

Informed Consent

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

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

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

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