Nutritional status and severity of coronary artery disease

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Objective **The aim of this study is to evaluate the association between Nutritional Risk Index (NRI), a simple tool to assess nutritional status, and coronary artery disease severity and complexity in patients undergoing coronary angiography.**

Methods **This study is a retrospective analysis of 822 patients undergoing coronary angiography. Patients with previous revascularization were excluded. Gensini and SYNTAX scores were calculated according to the angiographic images to determine atherosclerosis severity. NRI was calculated as follows: NRI = [15.19 × serum albumin (g/dl)] + [41.7 × (body weight/ideal body weight)]. In patients ≥65 years of age, Geriatric NRI (GNRI) was used instead of NRI. GNRI was calculated as follows: GNRI = [14.89 × serum albumin (g/dl)] + [41.7 × (body weight/ideal body weight)]. Patients were then divided into three groups as previously reported: NRI < 92, NRI 92–98 and NRI > 98. Gensini and SYNTAX scores were compared between three groups.**

Results **The mean age of study population was 61.9 ± 11.1 years. NRI < 92, 92–98, and >98 was measured in 212, 321 and 289 patients, respectively. There was no difference regarding to sex, BMI, smoking, hypertension and diabetes mellitus between three groups. Patients with NRI < 92 had the highest mean Gensini score than the patients with NRI 92–98 and NRI > 98 (38.0 ± 40.6 vs. 31.17 ± 42.4 vs. 25.8 ± 38.4, *P* = 0.005). Also patients with NRI < 92 had the highest mean SYNTAX score than the patients with NRI 92–98 and NRI > 98 (11.8 ± 12.9 vs. 9.3 ± 12.4 vs. 7.7 ± 11.8, *P* = 0.001). Also, Gensini score of ≥20 and high SYNTAX score of ≥33 were associated with lower NRI (*P* < 0.001 and *P* < 0.001, respectively).**

Conclusion **In our study, nutritional status evaluated by the NRI was associated with more extensive and complex coronary atherosclerosis in patients undergoing coronary angiography.** ***Coron Artery Dis*** **XXX: 000–000**

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Keywords: atherosclerosis, coronary artery disease, malnutrition, Nutritional Risk Index

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Introduction

Malnutrition has been recognized as an independent risk factor for unfavorable events in hospitalized patients [1]. It is related to worse clinical outcomes in patients with cancer, renal failure or heart failure [2–4]. It is a common problem, especially in elderly patients and recently, it has been reported that adverse outcomes were increased when the atherosclerotic disease and malnutrition coexist [5,6]. Thus, assessing nutritional status could be important for risk stratification in both elderly and patients with atherosclerotic diseases.

Nutritional Risk Index (NRI) and its modified form Geriatric NRI (GNRI) which is calculated in elderly are easy and efficient screening tools for malnutrition. Although the association between nutritional status and clinical outcomes after ST-segment elevation myocardial infarction (STEMI) or percutaneous coronary intervention (PCI) has been shown, studies evaluating the association between nutritional status and severity and complexity of atherosclerosis are lacking. The aim of this study is to evaluate the association between nutritional status and coronary artery disease (CAD) severity and complexity in both patients younger than 65 years and elderly.

Methods

Study population

This retrospective study assessed the data of 1282 patients who had undergone coronary angiography between January 2017 and January 2019 in our angiography laboratory because of suspicion of stable CAD or non-ST-segment elevation acute coronary syndrome. Among these, 460 patients were excluded because of incomplete data, missing values for albumin, previous history of coronary revascularization, systemic inflammatory disease, renal or hepatic failure, severe heart failure, hypo/hyperthyroidism and malignancy. Finally, we evaluated the data of 822 patients in our analysis. The assessed clinical parameters were age, sex, weight and height, and coronary risk factors. Hypertension was defined as SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg or current medication with antihypertensive drugs. Patients were defined as diabetic if they had been informed of this diagnosis before and had been using oral antidiabetic drugs or insulin treatment on admission. BMI was calculated as body weight in kilograms divided by the squared value of body height in meters (kg/m^2).

The study was approved by the local Ethics Committee. Data from subjects were analyzed retrospectively.

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Angiographic evaluation

Baseline diagnostic angiograms of the patients were assessed independently by two experienced interventional cardiologists who were blinded to the patients' clinical or laboratory parameters. SYNTAX score for each patients was calculated by scoring all coronary lesions producing ≥50% diameter stenosis in vessels ≥1.5 mm, using the SYNTAX score algorithm which was available on the SYNTAX website. Gensini score was calculated by assigning a severity score to each coronary narrowing on the basis of the degree of luminal stenosis and its location [7]. Decreases in luminal diameter of 25, 50, 75, 90, 99% and total occlusion were given scores of 1, 2, 4, 8, 16 and 32, respectively. The score was then multiplied by a factor symbolizing the functional significance of the myocardial area supplied by that segment, that is five for the left main artery, 2.5 for the proximal left anterior descending artery or proximal circumflex artery, 1.5 for the mid-left anterior descending artery, one for the distal left anterior descending artery, right coronary artery and obtuse marginal artery, and 0.5 for all other areas. In cases of disagreement regarding the SYNTAX or Gensini score, an additional observer was consulted and the final decision was made by consensus. A low SYNTAX score was defined as ≤22, intermediate score as 23–32 and high SYNTAX score as ≥33 [8]. Patients with Gensini score of ≥20 were defined as having severe CAD, which was approximately equal to having a 70% stenosis or more in the proximal left anterior descending artery [9].

Nutritional Risk Index and Geriatric Nutritional Risk Index

The patients' serum albumin, body weight and height were measured before the coronary angiography. NRI was calculated for patients <65 years of age [10]. GNRI was calculated by modifying the NRI for elderly patients (≥65 years of age) in a manner previously reported [11,12].

The body weight/ideal body weight ratio was set to one when the patients' actual body weight exceeded their ideal body weight. The ideal body weight was defined as the value calculated from the patients' height and a BMI of 22 [13–15]. Patients were then divided into three groups based on previously published thresholds: NRI <92, 92 to ≤98, and >98 [6,11,16].

Statistical analysis

Continuous variables were expressed as mean ± SD; categorical variables were defined as numbers and percentages. Student's *t*-test or one-way analysis of variance were used to compare continuous variables, least significant difference test was performed for the binary comparisons among the groups. Pearson's correlation analysis was performed for investigating the relationship between two continuous variables. Partial correlation analysis was performed to measure the relationship between NRI and angiographic scores while controlling for multiple covariates such as age, sex, hypertension, diabetes mellitus, smoking and low-density lipoprotein cholesterol (LDL-C). Differences in the distribution of categorical variables were assessed by Pearson's chi-square test. A *P*-value of less than 0.05 was considered statistically significant. Data analyses were performed by using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, Illinois, USA).

Results

Baseline characteristics

The mean age of study population was 61.9 ± 11.1 years and 58.2% of the 822 patients were males. More than half of the patients had hypertension, one-third of the patients had diabetes mellitus and one-third of the patients had any smoking history. Sixty-three percent of the patients had stable angina pectoris, 22% had unstable angina pectoris and 15% had non-ST-elevation myocardial infarction. PCI was performed in 26% of the patients and coronary artery bypass grafting (CABG) was performed in 15% of the patients. Mean Gensini score was 31.1 ± 40.8 and mean SYNTAX score was 9.4 ± 12.4. Mean NRI was 95.7 ± 7.5. Number of the patients under 65 years of age was 456 (55.5%) and 366 patients (44.5%) were ≥65 years of age. Patients ≥65 years of age had lower NRI than patients younger than 65 years of age (92.8 ± 7.5 vs. 97.9 ± 6.7, $P < 0.001$). There was no correlation between BMI and albumin ($P = 0.740$).

NRI <92, 92–98 and >98 was measured in 212, 321 and 289 patients, respectively. Age, sex and CABG as a treatment modality choice after coronary angiography were significantly associated with NRI. There was no difference between groups regarding to BMI, hypertension, diabetes mellitus and any smoking history. Clinical and procedural characteristics of the patients stratified by NRI groups are listed in Table 1. NRI <92 was associated with decreased albumin, total cholesterol, LDL-C and triglyceride, and increased creatinine levels.

Coronary artery disease scores

Patients with NRI < 92 had the highest mean Gensini score than the patients with NRI 92–98 and NRI > 98 (38.0 ± 40.6 vs. 31.17 ± 42.4 vs. 25.8 ± 38.4, $P = 0.005$). Also patients with NRI < 92 had the highest mean SYNTAX score than the patients with NRI 92–98 and NRI > 98 (11.8 ± 12.9 vs. 9.3 ± 12.4 vs. 7.7 ± 11.8, $P = 0.001$) (Table 1). Patients with Gensini score ≥20 had lower NRI than patients with Gensini score <20 (94.3 ± 7.8 vs. 96.8 ± 6.9, $P < 0.001$). Patients with high SYNTAX score had the lowest NRI than the patients with low or intermediate SYNTAX score ($P < 0.001$ and $P = 0.017$, respectively). There was no association between BMI and Gensini and SYNTAX scores ($P = 0.126$ and $P = 0.115$, respectively). There was a negative association between NRI and Gensini and SYNTAX scores ($r = -0.140$, $P = 0.001$, $r = -0.155$, $P = 0.001$, respectively). NRI was negatively

Table 1 Baseline characteristics of patients

Variable	Overall ($n = 822$)	NRI <92 ($n = 212$)	NRI 92–98 ($n = 321$)	NRI >98 ($n = 289$)	*P*-value
Age (years)	61.9 ± 11.1	67.1 ± 9.6	62.5 ± 11	57.3 ± 10	**<0.001**[a,b,c]
Male (%)	58.2	52.6	59.9	63.2	**0.026**
Hypertension (%)	57.5	64.4	55.7	54.6	0.067
Diabetes mellitus (%)	32.9	37.6	32.6	29.9	0.205
Smoking (%)	32.3	29.3	30.4	36.5	0.158
BMI (kg/m^2)	29.1 ± 4	28.9 ± 5	29.3 ± 4	29.1 ± 4	0.651
Serum albumin (g/dl)	3.58 ± 0.3	2.96 ± 0.3	3.59 ± 0.1	4.05 ± 0.2	**<0.001**[a,b,c]
Total cholesterol (mg/dl)	192.4 ± 46	180.2 ± 44	193.7 ± 47	199.7 ± 46	**<0.001**[a,b]
LDL-cholesterol (mg/dl)	113.7 ± 37	104.8 ± 34	114.6 ± 38	119.1 ± 37	**<0.001**[a,b]
HDL-cholesterol (mg/dl)	41.8 ± 12	41.2 ± 13	41.9 ± 12	42.2 ± 11	0.631
Triglyceride (mg/dl)	165.6 ± 111	138.5 ± 78	171.2 ± 125	178.9 ± 110	**<0.001**[a,b]
Glucose (mg/dl)	117.7 ± 49	123.1 ± 63	116.8 ± 44	115.1 ± 41	0.181
Creatinine (mg/dl)	0.94 ± 0.3	1.03 ± 0.3	0.93 ± 0.3	0.89 ± 0.1	**<0.001**[a,b]
Uric acid (mg/dl)	5.7 ± 2.0	5.7 ± 2.2	5.7 ± 1.9	5.6 ± 1.8	0.685
Mean Gensini score	31.1 ± 40.8	38.0 ± 40.6	31.17 ± 42.4	25.8 ± 38.4	**0.005**[a,b]
Mean SYNTAX score	9.4 ± 12.4	11.8 ± 12.9	9.3 ± 12.4	7.7 ± 11.8	**0.001**[a,b]
Treatment modality (%)					**0.017**
Medical	58.6	50.7	57.9	65.3	
PCI	26.4	29.6	26.4	24.2	
CABG	15.0	19.7	15.8	10.6	

Data are expressed as percentage for categorical variables; chi-square test was used. Data are expressed as mean ± SD for continuous variables; one-way ANOVA was used; LSD test was performed for binary comparisons between groups and the *P*-value was set at 0.05. Bold indicates *P* values are significant.
ANOVA, analysis of variance; CABG, coronary artery bypass grafting; LDL, low-density lipoprotein; LSD, least significant difference; NRI, Nutritional Risk Index; PCI, percutaneous coronary intervention.
[a]Significant differences were found between <92 vs. 92–98.
[b]Significant differences were found between <92 vs. >98.
[c]Significant differences were found between 92–98 vs. >98.

Table 2 Nutritional Risk Index according to angiographic scores and age of patients

Variable	Gensini score ≥ 20	Gensini score < 20		*P*-value
NRI				
Patients <65 years ($n = 456$)	97.0 ± 7.2	98.6 ± 6.1		**0.014**
Patients ≥65 years ($n = 366$)	91.9 ± 7.6	93.7 ± 7.6		**0.023**
NRI	Low SYNTAX score	Intermediate SYNTAX score	High SYNTAX score	
Patients <65 years ($n = 456$)	98.3 ± 6.5	96.6 ± 7.3	95.2 ± 6.6	**0.028**
Patients ≥65 years ($n = 366$)	92.9 ± 7.4	89.1 ± 8.9	94.1 ± 6.2	**0.018**

Bold indicates *P* values are significant.
NRI, Nutritional Risk Index.

correlated with Gensini score in both females and males ($P < 0.001$ and $P = 0.003$, respectively) and NRI was also negatively correlated with SYNTAX score in both females and males ($P < 0.002$ and $P < 0.001$, respectively). Also, there was a negative weak association between NRI and Gensini and SYNTAX scores after controlling for confounding variables ($r_{partial} = -0.125$, $P = 0.001$, $r_{partial} = -0.132$, $P = 0.001$, respectively).

In patients younger than 65 years of age, NRI < 92 had the highest mean Gensini and SYNTAX scores than the patients with NRI 92–98 and NRI > 98 ($P = 0.021$ and $P = 0.017$, respectively). There was a negative weak association between NRI and Gensini and SYNTAX scores ($r = -0.145$, $P = 0.002$, $r = -0.143$, $P = 0.003$, respectively). Also, the associations between NRI and Gensini score and between NRI and SYNTAX score remain valid after controlling for confounding variables ($r_{partial} = -0.189$, $P = 0.001$, $r_{partial} = -0.187$, $P = 0.001$, respectively). Patients with Gensini score ≥20 had lower NRI than patients with Gensini score <20 ($P = 0.014$) (Table 2). Patients with high SYNTAX score had lowest NRI than patients with low or intermediate SYNTAX score ($P = 0.028$) (Table 2).

In patients ≥65 years of age, there was no difference regarding to Gensini and SYNTAX scores between groups NRI < 92, NRI 92–98 and NRI > 98 ($P = 0.880$ and $P = 0.565$, respectively). But patients with Gensini score ≥20 had lower NRI than patients with Gensini score <20 ($P = 0.023$) and patients with intermediate SYNTAX score had lowest NRI than patients with low or high SYNTAX score ($P = 0.018$) (Table 2).

Discussion

The present study showed that low NRI was significantly associated with higher Gensini and SYNTAX scores and especially Gensini score ≥20 was associated with low NRI in both patients younger than 65 years old and elderly. To the best of our knowledge, this is the first study to evaluate relationship between NRI and angiographic CAD severity. The findings of this study suggest that

evaluation of nutritional risk is important for predicting CAD severity and risk stratification of patients undergoing coronary angiography.

In previous studies, lower GNRI was associated with cardiac death and all-cause deaths in CAD patients after PCI [6,17,18]. In another study of geriatric patients with CAD, GNRI predicts all-cause death in a median follow-up of 27 months [19]. Also, it was reported that GNRI was strongly associated with presence of peripheral arterial disease in elderly CAD patients [20]. Unlike these studies, we did not include only elderly patients in our study. And we found a stronger relationship between nutritional status and atherosclerosis severity in patients younger than 65 years of age. But in routine clinical practice, there is a tendency to manage very old, fragile patients by conservative treatment without angiography and this may affect our results.

Some objective nutritional indices such as the Controlling Nutritional Status (CONUT) score and Prognostic Nutritional Index (PNI) are also studied in CAD patients. Recently, several clinical studies have shown that CONUT score and PNI were associated with long-term outcomes in stable CAD patients treated with PCI [18,21–23]. Also, both CONUT score and PNI were associated with increased mortality in patients with STEMI undergoing primary PCI [24,25]. Despite these observed associations between simple, objective nutritional indices and CAD prognosis, no single nutritional index to date has become a routine tool in clinical practice of CAD patients.

While studies suggest that poor nutritional status is related to worse prognosis once significant CAD develops, limited data are available on the contribution of poor nutritional status to coronary atherosclerosis characteristics. In previous studies, patients with poor nutritional status presented as lower GNRI, lower PNI and higher CONUT score, had higher proportion of multi-vessel disease [6,18,23]. In angiographic analysis, these nutritional indices were not associated with reference lumen diameter, diameter stenosis or stent size [6,18,23]. CONUT score and PNI were found to be correlated with post-PCI TIMI 3 flow in STEMI patients [24,25]. Unlike previous studies, we assessed coronary atherosclerosis in a more detailed fashion. We calculated both Gensini and SYNTAX scores and found that patients with lower NRI had more severe and extensive atherosclerosis. But further studies are required to clarify whether more complex and extensive coronary atherosclerosis may represent a mechanism for the increased mortality in patients with coexisting CAD and poor nutritional status.

In the present study, 26% of the patients undergoing coronary angiography had poor nutritional status represented as NRI < 92. Patients with lower NRI had similar proportions of traditional risk factors such as diabetes mellitus, hypertension, BMI and smoking compared to patients with higher NRI, but they tended to be older, have extensive CAD and have lower total cholesterol, lower LDL-C and lower triglyceride levels. Low blood lipid level has been shown as an indicator of malnutrition [26,27]. Studies evaluating nutritional status in CAD patients have reported that levels of total cholesterol, LDL-C and triglyceride were lower in patients with poor nutritional status [17,22]. Our findings were consistent with these studies. Having low lipid levels with advanced age may put the patients with poor nutritional status at an unfamiliar risk for atherosclerosis management. Beyond the conventional therapies for secondary management, new strategies may be required for this vulnerable patient group.

In the present study, NRI was associated with angiographic scores, but BMI was not associated with them. There are conflicting results about the association between BMI and angiographic severity of the CAD in previous studies. Both negative, positive or no association have been reported [28–30]. BMI was also not associated with albumin in our study. It has been reported that in patients with stable CAD, there is a subgroup of patients with apparently normal BMI and with poor nutritional status [22]. Also, this subgroup of patients had worse prognosis than patients with normal BMI and good nutritional status [22]. Body weight, BMI and nutritional status are all interrelated subjects but they are not equivalent. Our findings may underline the need for desirable tool to evaluate nutritional status in CAD patients.

NRI is an objective simple tool for nutrition assessment and serum albumin is one of the components of NRI. Albumin is widely used for nutrition assessment and it has been demonstrated that inflammation response lessens albumin levels [31,32]. Low albumin levels are associated with oxidative damage in atherosclerotic plaque [33]. There are several studies that tied malnutrition to the chronic inflammation [34,35]. Malnutrition, inflammation, atherosclerosis syndrome has been investigated in chronic kidney patients and helps to explain high mortality rates [36]. Tumor necrosis factor-α, interleukin (IL)-1 and IL-6 are key cytokines in the development of catabolism and have been implicated in pathogenesis and progression of atherosclerosis [34,37,38]. In addition, some studies demonstrated an association between malnutrition and arterial calcification [39,40]. Atherosclerosis is a multifactorial, immunoinflammatory disease process driven by lipids. Chronic inflammation may have a predominant role in atherosclerotic process in CAD patients with malnutrition. However, the pathophysiologic mechanisms underlying the association between poor nutritional status and extensive CAD and worse outcomes are not completely recognized.

Conclusion

In our study, nutritional status evaluated by the NRI was associated with more extensive and complex CAD in patients undergoing coronary angiography. No single nutritional index to date has been integrated into routine

clinical practice and this result suggest that NRI might be useful for risk stratification and identification of residual risk in CAD patients.

Study limitations

Several limitations of this study should be considered. It is a retrospective study and there is the possibility of bias from unmeasured cofounders such as dietary habits or undiagnosed systemic illness. The observational nature of this study did not allow us to make cause and effect explanation for the malnutrition that was associated with extensive CAD. Also, lack of comparison of an inflammatory parameter such as high sensitivity C-reactive protein between NRI groups is another limitation.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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