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The Usage of Prognostic Nutritional Index to Predict Postoperative Atrial Fibrillation Development

Postoperatif Atriyal Fibrilasyon Gelişimini Öngörmede Prognostik Nutrisyonel İndeks Kullanımı

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Abstract

Objective: Postoperative atrial fibrillation (POAF) is one of the most common complications of cardiac surgery and frequency varies according to the type of surgery. Prognostic nutritional index (PNI), has been shown to be associated with adverse outcomes in heart failure, stroke, chronic renal failure, coronary artery disease, and ST-segment elevation myocardial infarction. In this study, we aimed to evaluate the relationship between PNI and POAF development in patients with a diagnosis of chronic coronary syndrome who underwent coronary angiography and decided to be treated with coronary artery bypass graft (CABG) operation.

Method: Patients diagnosed with chronic coronary syndromes and decided to be treated by CABG surgery at our institution between March 2014 and 2019 were evaluated retrospectively.

Results: A total of 314 patients were included in the study. Two groups were formed according to POAF development. Fifty-eight patients constituted the POAF (+) and 256 patients formed the POAF (-) group. Age, body mass index (BMI), hypertension, coronary artery disease, chronic obstructive pulmonary disease, creatinine were significantly higher and hemoglobin, hematocrit, left ventricular ejection fraction (LVEF) and PNI were found lower in the POAF (+) group. Advanced age, high BMI and creatinine, low LVEF and PNI were determined as independent risk factors for the development of POAF. It was concluded that a cut-off value of 53.13 for PNI could predict the development of POAF with 70.9% sensitivity and 69.6% specificity.

Conclusion: POAF was observed more frequently in patients in lower PNI values. PNI is an easy to use, rapidly measured and widely available index and have good diagnostic accuracy in determining POAF development. Aggressive treatment of malnutrition will be important in addition to personalized dyslipidemia therapy in patients with stable coronary artery disease.

Keywords: Coronary artery bypass graft surgery, postoperative atrial fibrillation, prognostic nutritional index

Öz

Amaç: Postoperatif atriyal fibrilasyon (POAF), kalp cerrahisi sonrası en sık görülen komplikasyonlarından biridir. Kalp yetmezliği, inme, kronik böbrek yetmezliği, koroner arter hastalığı ve ST segment yükselmeli miyokard enfarktüsünde düşük prognostik nütrisyonel indeks (PNI) değerinin olumsuz sonuçlarla ilişkili olduğu gösterilmiştir. Bu çalışmada koroner anjiyografi yapılan ve koroner arter baypas greft operasyonu (KABG) yapılan kronik koroner sendrom tanılı hastalarda PNI ve POAF ilişkisini değerlendirmeyi amaçladık.

Yöntem: Mart 2014 ve 2019 tarihleri arasında hastanemizde, kronik koroner sendrom tanısıyla KABG cerrahisi kararı verilen hastalar geriye dönük olarak değerlendirildi.

Bulgular: Çalışmaya toplam 314 hasta dahil edildi. POAF gelişimine göre 2 grup oluşturuldu. Elli sekiz hasta POAF (+) ve 256 hasta POAF (-) grubunu oluşturdu. Yaş, vücut kitle indeksi (VKİ), hipertansiyon, koroner arter hastalığı, kronik obstrüktif akciğer hastalığı, kreatinin POAF (+) grupta istatistiksel olarak anlamlı yüksek ve hemoglobin, hematokrit, sol ventrikül ejeksiyon fraksiyonu (SVEF) ve PNI ise anlamlı olarak daha düşük saptandı. İleri yaş, yüksek VKİ ve kreatinin, düşük SVEF ve PNI ise POAF gelişimi için bağımsız risk faktörleri olarak saptandı. PNI için 53,13 eşik değerinin POAF gelişimini %70,9 duyarlılık ve %69,6 özgüllük ile öngördürebildiği sonucuna ulaşılmıştır.

Sonuç: Düşük PNI değerlerinde daha sık POAF geliştiği saptanmıştır. PNI, kullanımı kolay ve hızlı sonuç veren bir indeks olup inflamatuar ve nütrisyonel durumun birlikte değerlendirilebilmesini sağlamaktadır. Stabil koroner arter hastalığı olan hastalarda kişiye özel dislipidemi tedavisine ek olarak malnütrisyonun agresif tedavisi önemli olacaktır.

Anahtar kelimeler: Koroner arter bypass greft cerrahisi, postoperatif atriyal fibrilasyon, prognostik nütrisyonel indeks

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Introduction

Postoperative atrial fibrillation (POAF) is one of the most common complications of cardiac surgery and frequency varies according to the type of surgery. It may develop in 15-40% of the patients after coronary artery bypass graft (CABG), whereas its incidence may raise up to 33-49% after valvular surgery (1,2). Perioperative oxidative stress, inflammation, electrolyte disturbance, ischemia, electrical remodeling and pain are known triggers for POAF development (3,4). Since most of the episodes terminate spontaneously, POAF is occasionally linked with myocardial infarction, stroke and death and those patients who experienced POAF has a 4-5-fold risk of persistent atrial fibrillation (AF) occurrence in 5 years follow-up (5).

Lymphocytes and neutrophils play a central role in atherosclerotic plaque rupture via immune reactions. Furthermore, lymphocytes have important roles in modulating the inflammatory response at different stages of the atherosclerotic process. Association between POAF development and inflammatory biomarkers has been shown in many studies (6). On the other hand, malnutrition, accelerates the atherosclerosis development by triggering inflammation (7). Malnutrition can be evaluated with various scoring systems. Prognostic nutritional index (PNI), is an index revealed by calculating the lymphocyte, which is an indicator of inflammation, and albumin, which is an indicator of nutrition, with the formula [serum albumin (g/L) + 0.005x lymphocyte count/mm^3]. Moreover, PNI has been shown to be associated with adverse outcomes in heart failure, stroke, chronic renal failure, coronary artery disease, and ST-segment elevation myocardial infarction (8, 9).

In this study, we aimed to evaluate the relationship between PNI and POAF development in patients with a diagnosis of chronic coronary syndrome (CCS) who underwent coronary angiography and decided to be treated with coronary artery bypass grafting.

Materials and Methods

Patients diagnosed with CCSs and decided to be treated by CABG surgery at our tertiary center between March 2014 and March 2019 were evaluated retrospectively. All patients signed an informed consent form before operation. All transactions were carried out in agreement with the Declaration of Helsinki. Pre-, peri- and postoperative data were retrieved from hospital database and patients' files. Demographic, clinical and laboratory parameters were noted for each patient. The patients with preoperative AF rhythm or history of atrial arrhythmia, moderate to severe valvular disease, congenital heart disease, preoperative renal disease (serum creatinine >2 mg/dL), albuminuria and chronic liver disease, albumin replacement therapy in past 6 months, previous diagnosis of an autoimmune disease, endocrinologic disorders (hypo/hyperthyroidism), malignancy, systemic inflammatory diseases, hematologic diseases, left atrial enlargement (>4.5 cm in echocardiography), active infection, undergone emergency operations (e.g., acute myocardial infarction) were excluded from the study. Those with unavailable serum lymphocyte count or albumin levels were also excluded.

Routine preoperative blood tests before coronary angiography were used in the formula [serum albumin (g/L) + 0.005x lymphocyte count/mm^3] to calculate the PNI value. All 12-lead electrocardiography (ECG) (filter range 0.5 Hz_150 Hz, AC filter 60 Hz, 25 mm/s, 10 mm/mV) which were obtained daily as a routine follow-up procedure in postoperative period and those obtained due to patients' symptoms or abnormality suspected during telemetry monitoring were evaluated to define rhythm abnormalities or AF development during the hospital stay. A standard 12-lead ECG recording or a single-lead ECG tracing of ≥30 s showing heart rhythm with no discernible repeating P waves and irregular RR intervals (when atrioventricular conduction is not impaired) was regarded as diagnostic of clinical AF (2,10). POAF was defined as an episode of AF requiring treatment related to surgery that developed during hospitalization.

Patients were further grouped into 2 according to the POAF development; POAF developed as POAF (+) and POAF non-developed as POAF (-). The primary endpoint of the study was occurrence of the first documented AF episode during the hospital stay.

This study was approved by Ethical Committee of University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital (date: 05/07/2022 number: 2022/07/02/002). Patient consent was waived due to retrospective design of the study.

Statistical Analysis

The Statistical Package for the Social Sciences 25.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. The normality of the data was analyzed by Kolmogorov-Smirnov test. Continuous data are stated as mean ± standard deviation, and categorical data are stated as percentages. Chi-square test was applied to assess

differences in categorical variables between groups. Unpaired samples were compared by using Student's t-test or Mann-Whitney U, as needed. Independent variables of POAF were identified by using logistic regression analysis. Receiver operating characteristic (ROC) curve analyses were performed to evaluate diagnostic accuracy of PNI for POAF. Significance was expected at a 2-sided p<0.05.

Results

A total of 314 patients (234 male, 80 female) were included in this retrospective single center study. Mean age of all included patients was 59.8±10.2. POAF developed in 58 patients (18.5%) at a mean time of 2.31±1.47 days postoperatively. We formed 2 groups according to POAF development as defined in methodology. Fifty-eight patients formed POAF (+) and 256 patients formed POAF (-) group. Both groups were similar in terms of gender, presence of hyperlipidemia and history of cerebrovascular accident. Age (63.5±9.4 vs. 59.1±10.2; p=0.002), body mass index (BMI) (29.7±4.4 vs. 27.6±3.4; p<0.0001), hypertension (HT) (65.5% vs. 48.1%; p=0.016), chronic obstructive pulmonary disease (COPD) (41.4% vs. 17.2%; p<0.0001), diabetes mellitus (DM) (56.9% vs. 35.9%, p=0.003), history of coronary artery disease (CAD) (45.7% vs. 28.6%; p=0.013) and smoking status (70.7% vs. 44.9%; p<0.0001) were significantly higher in POAF (+) group. Regarding labaratory markers; creatinine (1.2±0.4 vs. 1.1±0.7; p=0.013) was significantly higher and preoperative haemoglobin (11.6±1.9 vs. 12.5±1.6; p=0.002), hematocrit (36.8±5.1 vs. 39.6±4.8, p=0.001), PNI (52.6±6.1 vs. 55.1±5.7; p=0.005) and left ventricular ejection fraction (46.1±7.8 vs. 50.4±8.3; p<0.0001) were lower in POAF (+) group. When the patients were assessed according to medical therapy on admission β-blocker (26.4% vs. 41.1%, p=0.047) usage were significantly lower in POAF (+) group. Moreover, length of intensive care unit (4.7±2.3 vs. 3.5±3.2; p=0.014) and total length of hospital stay (10.4±4.4 vs. 6.4±4.4; p<0.0001) stay was significantly higher in POAF (+) group. Demographical, baseline clinical, and biochemical characteristics of the cohort based on the presence or absence of POAF are presented in detail in Table 1.

To further evaluate individual risk factors for POAF development, we performed logistic regression analysis for age, BMI, smoking status, history of HT, COPD, DM, CAD, left ventricular ejection fraction, preoperative hemoglobin, creatinine and PNI, respectively. Logistic regression analysis revealed that age [p=0.026, β: 1.065, odds ratio (OR) [95% confidence interval (CI)]: 1.008-1.126], BMI [p=0.001, β: 1.265, OR (95% CI): 1.105-1.447], smoking status [p=0.003, β: 0.202, OR (95% CI): 0.070-0.581], left ventricular ejection fraction [p=0.007, β: 0.923, OR (95% CI): 0.871-0.979], creatinine [p=0.048, β: 1.839, OR (95% CI): 1.006-3.363] and PNI [p=0.038, β: 0.911, OR (95% CI): 0.834-0.995] were independent risk factors associated with POAF development (Table 2). ROC curve analysis was performed to identify the optimal cut-off value and area under the curve (AUC) for PNI. ROC curve for accuracy of PNI for predicting POAF development in CABG patients is shown in Figure 1. The AUC for PNI was 0.730 (95% CI: 0.616-0.844). A cut-off value of 53.13 for PNI was associated with 70.9% sensitivity and 69.6% specificity in prediction of POAF development.

Discussion

In this single-center retrospective study we sought to assess if PNI could predict POAF development in patients presenting with CCS and treated with isolated CABG. The prevalence of POAF was found 18.5% and our results determined low PNI as an independent predictor of POAF development. The results of this study suggest that preprocedural assessment of the PNI may raise suspicion to foresee the incidence of POAF in patients with CCS and treated with isolated CABG. The other independent predictors of POAF were advanced age, higher BMI, smoking, lower left ventricular ejection fraction, and creatinine levels. Consequently, close follow-up of patients with a PNI value <53.13 on admission as an additional clue to other risk factors may help to define patients under risk of POAF.

POAF is the most common arrhythmia after cardiac operations and its incidence may rise up to 40% and is unfavorable due to increased risk of mortality, heart failure, cerebrovascular events as well as financial burden on health care system (11). Valve disease, impaired left ventricular systolic function, left atrial enlargement, previous myocardial infarction, history of AF, advanced age, obesity, HT, DM, COPD, metabolic syndrome, ischemia, hypoxemia are known risk factors (12). In our study, advanced age, obesity, and lower left ventricular ejection fraction were found as independent predictors of POAF development in accordance with the literature. Although, HT, DM, COPD and history CAD were higher in POAF developed group, those were not detected as independent predictor.

Malnutrition is an important public health problem in developing countries. Serum albumin levels represent degree of nutritional status and on the other hand is known as a negative acute phase reactant decreasing

Table 1. Comparison of demographic, clinical and laboratory parameters between groups according to postoperative atrial fibrillation development

Variables	All (n=314)	POAF (-) (n=256)	POAF (+) (n=58)	p
Age (years)	59.8±10.2	59.1±10.2	63.5±9.4	0.002
Gender				0.282
Male, n (%)	234 (74.5)	194 (75.8)	40 (68.9)	
Female, n (%)	80(25.4)	62 (24.2)	18 (31.1)	
Body mass index	28.1±3.7	27.6±3.4	29.7±4.4	**<0.0001**
Hypertension, n (%)	161 (51.3)	123 (48.1)	38 (65.5)	0.016
Chronic obstructive pulmonary disease, n (%)	68 (21.7)	44 (17.2)	24 (41.4)	**<0.0001**
Diabetes mellitus, n (%)	125 (39.8)	92 (35.9)	33 (56.9)	0.003
Hyperlipidemia, n (%)	169 (53.8)	140 (54.7)	29 (50.0)	0.518
Cerebrovascular accident, n (%)	9 (2.9)	7 (2.7)	2 (3.4)	0.769
Coronary artery disease, n (%)	99 (31.5)	73 (28.6)	26 (45.7)	0.013
Smoking, n (%)	156 (49.7)	115 (44.9)	41 (70.7)	**<0.0001**
Left atrial diameter (mm)	36.4±4.4	36.6±4.8	35.6±3.9	0.128
Left ventricular ejection fraction, (%)	49.6±8.4	50.4±8.3	46.1±7.8	**<0.0001**
Thyroid stimulating hormone, (mU/L)	2.1±1.9	2.1±1.2	1.9±1.3	0.790
White blood cell, ($10^3/\mu L$)	7.9±1.9	7.9±1.9	7.9±2.1	0.908
Preoperative hemoglobin (g/dL)	12.3±1.7	12.5±1.6	11.6±1.9	0.002
Preoperative hematocrit (%)	38.9±5.1	39.6±4.8	36.8±5.1	0.001
Creatinine, (mg/dL)	1.1±0.7	1.1±0.7	1.2±0.4	0.013
C-reactive protein (mg/L)	12.2±8.2	13.2±8.5	14.3±6.7	0.361
HbA1c (%)	6.8±2.3	6.7±2.1	7.2±2.5	0.062
Prognostic nutritional index	55.0±5.9	55.1±5.7	52.6±6.1	0.005
Intensive care unit stay (days)	3.8±3.1	3.5±3.2	4.7±2.3	0.014
Total length of hospital stay (days)	7.2±4.7	6.4±4.4	10.4±4.4	**<0.0001**
Preoperative treatment, n (%)				
β-blockers	115 (36.6)	101 (41.1)	14 (26.4)	0.047
ACEI/ARB	139 (44.3)	118 (50.0)	21 (41.2)	0.253

ACEI: Angiotensin converting enzyme inhibitor, ARB: Angiotensin receptor block, POAF: Postoperative atrial fibrillation

Table 2. Logistic regression analysis for predictors of postoperative atrial fibrillation development

Variables	p	OR (95% CI)
Age	**0.026**	1.065 (1.008-1.126)
Body mass index	**0.001**	1.265 (1.105-1.447)
Hypertension	0.144	0.450 (0.154-1.314)
Chronic obstructive pulmonary disease	0.364	0.610 (0.210-1.774)
Diabetes mellitus	0.607	0.767 (0.280-2.105)
Coronary artery disease	0.193	0.483 (0.161-1.446)
Smoking	**0.003**	0.202 (0.070-0.581)
Left ventricular ejection fraction	**0.007**	0.923 (0.871-0.979)
Preoperative hemoglobin	0.131	0.439 (0.151-1.277)
Creatinine	**0.048**	1.839 (1.006-3.363)
Prognostic nutritional index	**0.038**	0.911 (0.834-0.995)

OR: Odds ratio, CI: Confidence interval

with inflammation. Moreover, as stated before, albumin has antiplatelet effect by modulating arachidonic acid metabolism and a protective effect by anti-oxidant property (13). Hypoalbuminemia, a good predictor of surgical risk, is closely associated with malnutrition. The relationship between hypoalbuminemia and acute coronary syndromes, cardiovascular ischemic disease, and stroke was reported previously (14,15). Besides, in atherosclerotic cardiovascular diseases, lymphopenia is reported to be associated with major adverse events (16). High neutrophil/lymphocyte ratio is widely used as an indicator of inflammation and have been widely studied in various cardiac conditions formerly (17-19). Both decreased lymphocyte count or increased neutrophil count may end up with an increased ratio. Thus, the 5xlymphocyte count used in the calculation of PNI seems to be a more reliable variable. PNI easily calculated and offers valuable information about nutritional status especially in hemodialysis and malignancy patients (20,21). The role of PNI was assessed in stable coronary patients who were treated by percutaneous coronary intervention (PCI) and PNI was established to be associated with long-term cardiovascular outcomes (8). On the other hand, its predictive usefulness for early outcomes after CABG was documented (22). In our study, PNI was documented as an independent predictor of POAF, which is one of the essential morbidities after CABG.

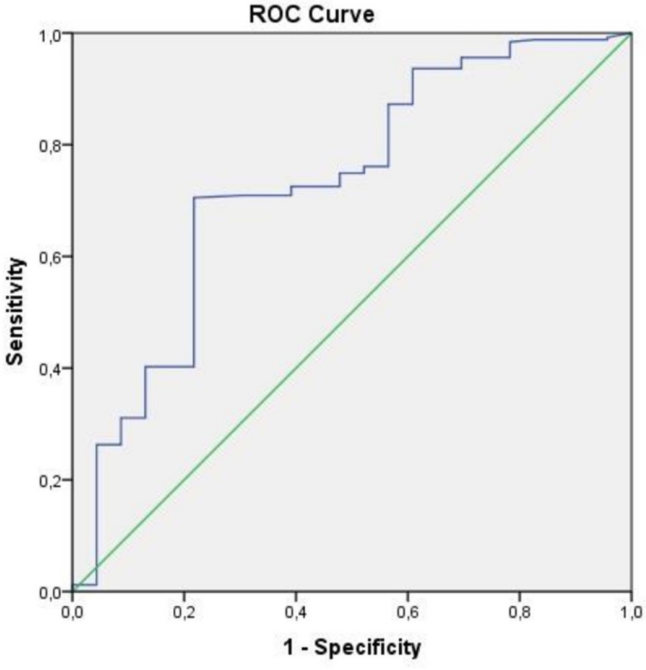

Figure 1. ROC curve for the diagnostic accuracy of prognostic nutritional index for predicting postoperative atrial fibrillation development

ROC: Receiver operating characteristic

Study Limitations

Retrospective and single center design with a relatively lower patient number are the main limitations of study. Moreover, comparison with other malnutrition and inflammation indices would give more reliable evidence. Also, our data is limited to in-hospital detection of POAF development where a longer duration would give better diagnostic ability. Although smoking is known to be associated with cardiovascular disorders, smoking was found as a negative predictor in our study. Relative small sample size may be related with this conflicting result, further studies are needed to evaluate the relation between smoking and POAF development.

Conclusion

This study demonstrated that malnutrition as evaluated using the PNI at admission may predict the POAF development in patients with stable coronary artery disease who underwent CABG for revascularization. POAF was observed more frequently in patients in lower PNI values. PNI is an easy to use, rapidly measured and widely available index and have good diagnostic accuracy in determining POAF development. As a result, aggressive treatment of malnutrition may be important in addition to personalized dyslipidemia therapy in patients with stable coronary artery disease. Further studies with longer follow-up and greater patient numbers are required to improve the clinical utility of PNI.

Ethics

Ethics Committee Approval: This study was approved by Ethical Committee of University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital (date: 05/07/2022 number: 2022/07/02/002).

Informed Consent: Patient consent waived due to retrospective design of the study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: S.Ö., E.D., E.O., İ.Ş., Design: S.Ö., E.D., E.O., İ.Ş., B.M., A.P., Data Collection or Processing: S.Ö., E.D., B.M., A.P., Analysis or Interpretation: S.Ö., E.D., Drafting Manuscript: S.Ö., E.D., Critical Revision of Manuscript: S.Ö., E.D., E.O., İ.Ş., Writing: S.Ö., E.D., E.O., İ.Ş., Final Approval and Accountability: S.Ö., E.D., E.O., İ.Ş., B.M., A.P.

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