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Predictive significance of the prognostic nutritional index for in-stent restenosis following carotid artery stenting

Short title: Carotid artery stenting and nutrition

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WHAT'S NEW?

The data obtained from our study indicate that the presence of malnutrition, as assessed by the Prognostic Nutritional Index, represents a risk factor for the development of in-stent restenosis following carotid artery stenting. Assessing the Prognostic Nutritional Index score of patients undergoing carotid artery stenting prior to non-urgent interventional procedures and administering nutritional supplements to these patients before and after the procedure may decrease the risk of in-stent restenosis development. In addition, it may enable patients with known malnutrition to be followed more carefully by physicians.

ABSTRACT

Background: Malnutrition and inflammation both have important impacts on the medical outcomes of individuals treated by carotid artery stenting (CAS). However, their impacts on the occurrence of carotid in-stent restenosis (ISR) are not sufficiently understood.

Aim: We explore the association of immune-nutritional status, as measured by the Prognostic Nutritional Index (PNI), with ISR among individuals who have undergone CAS.

Methods: This retrospective single-center study focused on individuals diagnosed with severe carotid artery disease who were treated with CAS in 2016–2021 at a tertiary healthcare facility. A total of 819 patients were considered in the analysis. Their cases were subdivided into groups in line with the presence or absence of ISR as confirmed by angiography conducted subsequent to ultrasonographic follow-up assessments.

Results: Over the course of 24 months of follow-up, ISR was observed angiographically in 35 patients (4.3%). Total cholesterol (odds ratio [OR], 1.011; 95% CI [confidence interval], 1.003–1.019; P = 0.009), stent overlap (OR, 5.424; 95% CI, 1.026–28.670; P = 0.047), residual stenosis (OR, 47.930; 95% CI, 16.280–141.110; P <0.001) and PNI (OR, 0.846; 95% CI, 0.782–0.915; P <0.001) independently served as predictors of ISR. Based on the results of receiver operating characteristic analysis, when the cut-off threshold of the PNI score is accepted as 39.5, it can predict ISR while providing sensitivity of 83% and specificity of 77%. (area under curve [AUC] 0.808; 95% CI, 0.754–0.869; P <0.001)

Conclusion: This research demonstrates the existence of a meaningful independent correlation between PNI and ISR in individuals treated with CAS. Malnutrition and inflammation, parameters easily evaluated with the help of the PNI, could be considered as simple and practical indicators for ISR in cases of CAS treatment.

Key words: carotid artery disease, carotid artery stenting, in-stent restenosis, malnutrition, Prognostic Nutritional Index

INTRODUCTION

Stroke constitutes a predominant cause of both disability and mortality on a global scale. Roughly 10%–15% of ischemic stroke cases are attributable to atherosclerotic stenosis within the carotid artery [1, 2]. Carotid artery stenting (CAS), established as a practical substitute for carotid endarterectomy, has emerged as a standard therapeutic modality for managing symptomatic or significantly asymptomatic carotid stenosis [3]. Despite extensive evidence elucidating the long-term outcomes following CAS, explorations of the potential risk factors influencing the protracted trajectory of the condition are still insufficient [4]. However, one critical determinant impacting the enduring efficacy and safety profile of CAS is known to be in-stent restenosis (ISR). ISR may manifest at varying rates, spanning from 3.3% to 21%, within

follow-up periods ranging from 6 months to 2 years after carotid artery stent placement [5, 6]. While early restenosis subsequent to CAS is correlated with neo-intimal hyperplasia, predominantly observed within the first year, late restenosis is associated with neo-atherosclerosis [7]. Neo-atherosclerosis mirrors the pathological attributes of conventional atherosclerosis, thus sharing common risk factors [8].

Malnutrition is another significant public health concern, impacting an estimated 30% to 70% of hospitalized individuals and correlating with unfavorable outcomes across various diseases [9, 10]. Evidence suggests that malnutrition exacerbates inflammation and fosters atherosclerosis, particularly in cases of heart failure or chronic renal failure [11, 12]. Numerous scoring systems have been proposed for identifying malnutrition, the most prominent of which include the Nutritional Risk Index, the Controlling Nutritional Status (CONUT) scoring system, and the Prognostic Nutritional Index (PNI) [13–15]. Furthermore, a wealth of recent evidence has underscored the significant place of both inflammation and malnutrition in driving the progression of carotid artery disease [16–18]. However, there exists insufficient information regarding the predictive significance of malnutrition and inflammation in the onset of ISR among patients undergoing CAS. We planned the present study with the intention of clarifying the impact of immune-nutritional status, as reflected by PNI scores, on the occurrence of carotid ISR.

MATERIAL AND METHODS

Design of the study and selection of the patient population

This retrospective research was undertaken in a single center and enrolled 819 patients who had presented at a tertiary healthcare facility with a diagnosis of atherosclerotic carotid artery disease between 2016 and 2021 and then underwent CAS. CAS was performed based on both the ESC guidelines and the experience of the medical team, considering morphological and clinical data, suitability, and the lowest periprocedural risk [19]. Patients with symptomatic carotid artery stenosis who had 50%–99% stenosis and patients with asymptomatic carotid artery stenosis who had 70% or greater stenosis underwent CAS. Those 819 individuals were subsequently subdivided into two groups, an ISR group and a non-ISR group, in light of the presence of restenosis as angiographically confirmed following ultrasonographic follow-up assessments. Exclusion criteria included the following: (1) insufficient data availability; (2) confirmed non-atherosclerotic arterial stenosis (for example, cerebral arteritis); (3) history of carotid endarterectomy; and (4) severe comorbidities including advanced lung, heart, and kidney diseases or malignancies expected to result in mortality during the 6-month follow-up

duration. Demographic information, clinical profiles, and laboratory results of all participants were obtained from the hospital's electronic health records. Baseline values for laboratory parameters were obtained from a national database, reflecting the patients' statuses before undergoing CAS procedures. All research described here complied in full with the principles outlined within the Declaration of Helsinki and received ethical approval from the relevant hospital. In light of the retrospective nature of this case-control study, which utilized patient medical record data, the relevant ethics committee confirmed that it was not necessary to obtain written informed consent from the analyzed patients.

Definitions

ISR was characterized using digital subtraction angiography and diagnosed in the event of the presence of ≥50% stenosis in the treated vessel, consistent with the NASCET guidelines. The diagnosis of hypertension was declared in the event of the presence of systolic pressure of ≥140 mm Hg and/or diastolic pressure of ≥90 mm Hg and/or usage of antihypertensive medications. The diagnosis of diabetes mellitus was made in line with the diagnostic criteria established by the American Diabetes Association, comprising a fasting plasma glucose value of ≥126 mg/dl, random plasma glucose value of ≥200 mg/dl, HbA1c value of ≥6.5%, or usage of antidiabetic medications. Finally, the diagnosis of hyperlipidemia was based on a total cholesterol value of >200 mg/dl, triglyceride value of >150 mg/dl, low-density lipoprotein cholesterol value of >116 mg/dl, or usage of lipid-lowering medications. Individuals who were current smokers or had a history of tobacco use were categorized as smokers.

Follow-up assessments

Patients attended regular follow-up appointments to be evaluated by duplex ultrasound in the outpatient clinic of the hospital at 3, 6, 12, and 24 months following their CAS procedures. Any patients with suspected ISR underwent further evaluations *via* digital subtraction angiography.

PNI and CONUT scores for malnutrition risk assessments

The PNI is a scoring system utilized for the assessment of malnutrition risk, calculated in light of serum albumin (SA) level and lymphocyte (LYM) count *via* application of the following equation: PNI was calculated as follows (10 × SA [g/dl] + 0.005 × total LYM count [mm^3] [20, 21]. Patients' initial SA values, LYM counts, and total cholesterol levels were utilized in computing their CONUT scores. Scores of 0, 1, 2, or 3 points were assigned based on the

severity of decreases in LYM counts and total cholesterol levels, while decreases in albumin levels were allocated 0, 2, 4, or 6 points.

Statistical analysis

Continuous variables that did not reflect a normal distribution were presented as median values with interquartile ranges. Categorical data were presented in the format of numerical values accompanied by percentages. To facilitate comparisons of independent groups of continuous data, the Mann–Whitney U test or the independent samples t-test was applied, and Pearson's χ^2 test or Fisher's exact test was applied to facilitate efforts to compare groups of categorical data. Cut-off values of the variables of interest were established *via* receiver operating characteristic (ROC) curve analysis, and ROC analysis facilitated the dichotomization of continuous variables, as well. Univariate and multivariable models were established with logistic regression to determine variables with the power to predict ISR. For predicting ISR, a baseline logistic regression model was constructed utilizing covariates identified as possessing associations with the occurrence of ISR in univariate analysis (P <0.05). This model was adjusted for traditional risk factors including sex and age. In all of these analytical procedures, two-tailed probability (P) values lower than 0.05 were recognized as signifying the presence of statistical significance. IBM SPSS Statistics 25 (IBM Corp., Armonk, NY, US), Jamovi, or R 4.3.2 software (R Foundation, Vienna, Austria) was used in all analyses.

RESULTS

The retrospective data of 819 patients were analyzed in this research; all of these individuals had undergone CAS placement in a single center. During 24 months of follow-up, ISR was observed angiographically in 35 patients (4.3%) (Figure 1). The demographic, clinical, and angiographic data of all analyzed patients, who were subdivided into groups in light of the absence or presence of ISR, are comprehensively detailed in Table 1. Hypertension was more prevalent in the group without ISR (P = 0.048), whereas rates of angiographically observed residual stenosis (P <0.001) and stent overlap (P <0.001) were seen to be higher among patients with ISR.

Table 2 illustrates comparisons of laboratory parameters in light of the occurrence of restenosis. Among individuals who experienced ISR, values of triglycerides and non-high-density lipoprotein cholesterol were seen to be elevated, reaching statistical significance (P <0.001; P = 0.006), whereas their LYM counts, alanine transaminase, albumin, high-density lipoprotein cholesterol and PNI scores were seen to be lower in comparison to those who had

not experienced ISR (P = 0.007; P = 0.047; P <0.001; P <0.001; P = 0.003 and P <0.001) (Figure 2).

The PNI and CONUT scores were individually added to the base model and two further models were created as a result (Table 4: model 1 and model 2, respectively). In model 1, total cholesterol, stent overlap, residual stenosis, and PNI score independently served as predictors of ISR (OR, 1.011; 95% CI, 1.003–1.019; P = 0.009; OR, 5.424; 95% CI, 1.026–28.670; P = 0.047; OR, 47.930; 95% CI, 16.280–141.110; P <0.001; and OR, 0.846; 95% CI, 0.782–0.915; P <0.001, respectively). In model 2 total cholesterol, stent overlap and residual stenosis independently served as predictors of ISR (OR, 1.012; 95% CI, 1.002–1.021; P = 0.02; OR, 4.578; 95% CI, 1.052–19.916; P = 0.04; and OR, 33.998; 95% CI, 13.405–86.230; P <0.001, respectively). However, the CONUT score proved unable to independently predict the occurrence of ISR (OR, 1.168; 95% CI, 0.897–1.521; P = 0.25). Based on the results of ROC analysis, when the cut-off threshold of the PNI score is accepted as 39.5, it can predict ISR while providing sensitivity of 83% and specificity of 77%. (AUC 0.808; 95% CI, 0.754–0.869; P <0.001) (Figure 3).

DISCUSSION

In this retrospective study, we conducted an investigation of the capability of PNI scores to predict the occurrence of ISR in individuals treated with CAS. The findings indicated that the PNI, as an indicator of immune-nutritional status, serves as an independent predictor for carotid ISR development.

Previous studies have demonstrated variability in the incidence of restenosis CAS, with reported rates ranging from 5% to 11% across different follow-up durations. The results of systematic reviews conducted by Wholey et al. [22] and Clavel et al. [23] included cumulative restenosis rates of 5.7% and 3.46%, respectively, within the first year. Our findings also confirm the relevance of ISR as a pertinent clinical issue, as it was observed in 4.03% of our study population during a 24-month follow-up period. These consistent results underscore the critical need to identify predictors of ISR for informing and optimizing clinical management strategies.

A variety of studies in the literature have identified various risk factors associated with ISR following CAS. One of these risk factors is stent design. Closed-cell stents, constructed with denser and more rigid materials, produce higher rates of restenosis in comparison to open-cell stents according to multiple studies [24, 25]. However, in our study, we did not obtain a statistical difference in ISR rates between cases treated with open-cell and closed-cell stents. This discrepancy might have arisen from the relatively shorter duration of follow-up in the

present study compared to most works in the currently available body of literature. The persistence of residual stenosis following stent placement was recognized as an independent risk factor for restenosis. This emphasizes the critical significance of employing meticulous procedural techniques during CAS to minimize the possibility of residual stenosis [26, 27]. Additionally, our study revealed that the presence of residual stenosis following stent placement independently increases the risk of ISR. In contrast, increasing the diameter of the post-dilatation balloon may aid in achieving maximum stent expansion and subsequently decrease the probability of long-term restenosis [28]. Diabetes mellitus was identified as another independent predictor of ISR in the present study, and Achim et al. similarly stated that their patients with the comorbidity of diabetes had a higher rate of ISR compared to individuals without diabetes, with the difference reaching the level of statistical significance [29]. Yılmaz et al. [30] conducted a study investigating the relationship between ISR and various non-traditional lipid parameters such as the atherogenic index and atherogenic index of plasma in patients undergoing CAS. Their findings indicated that several non-traditional lipid parameters had the power to independently predict carotid ISR [30]. This underscores the significance of lipid profile parameters after the placement of a carotid artery stent in terms of both treatment and follow-up strategies. In their study, Kadoglou et al. [31] highlight that statin therapy reduces carotid plaque vulnerability not just by lowering lipid levels but also through anti-inflammatory and other pleiotropic effects. Their review suggests that statins stabilize atherosclerotic plaques by decreasing inflammation and neovascularization, as confirmed by various imaging modalities and biomarkers. The present study has addressed the association of malnutrition with the occurrence of ISR following CAS, which was not previously described in the literature.

Malnutrition poses a significant public health concern, even in developed nations. The PNI serves as a critical indicator of malnutrition, calculated with an equation that utilizes the patient's LYM count and SA value. Albumin values are of great significance as hypoalbuminemia, often associated with malnutrition, serves as a reliable predictor of surgical risk and has been independently linked to various cardiovascular disorders that may include heart failure, stroke, and coronary artery disease. Albumin's significance particularly arises from its antioxidant, anti-inflammatory, and anticoagulant activities, in addition to its well-known impact on osmotic pressure regulation [32]. Lymphopenia, marked by decreased LYM counts, correlates with the occurrence of various adverse events in cases of atherosclerotic cardiovascular disease [33]. Furthermore, elevated values of the neutrophil/LYM ratio have prognostic predictive power in the follow-up of individuals treated with coronary artery bypass

grafts, with numerous studies supporting its predictive value [34]. The number of LYM, which affects the PNI value with fivefold power, also impacts this value significantly.

Initially utilized in cases of malignancy and gastrointestinal disorders, the PNI gradually found further applications in cases of cardiovascular conditions [35, 36]. The PNI correlates with diminished survival rates in cases of both chronic and acute heart failure, as well as hypertrophic cardiomyopathy cases [37–39]. Moreover, it successfully predicts mortality among individuals undergoing coronary artery bypass graft placement and those with ST-elevation myocardial infarction or acute coronary syndrome [40, 41].

Previous research has also addressed the relationships between PNI scores and both short-term and long-term prognoses after the application of CAS. For instance, Cakmak et al. considered the correlation between malnutrition and major adverse events experienced within the first 30 days after such procedures [42]. Their research demonstrated that continuous monitoring of CONUT, Nutritional Risk Index, and PNI scores allowed for the independent prediction of major adverse events within 30 days. In another study, Öcal et al. [43] considered the relationship between immune-nutritional status, reflected by the individual's PNI score, and 5-year outcomes among individuals who had undergone CAS. They revealed that PNI scores were able to independently predict the likelihood of both major stroke occurrences and long-term mortality in individuals undergoing CAS.

Limitations

Our study presents certain limitations that require careful consideration. First, its retrospective nature and reliance on medical record data may have introduced selection and information biases. Second, the follow-up duration for patients was confined to 24 months, potentially limiting the ability to predict long-term outcomes in the context of the association between PNI and carotid ISR. Extending this investigation to multiple centers with prospective patient enrollment would facilitate a more robust evaluation of the predictive power of the PNI in conjunction with carotid ISR over an extended follow-up period. Moreover, the assessment of nutritional status and malnutrition scores, although essential for patient management, was performed only once at admission for the PNI. Therefore, the obtained values may not reflect changes over time. Additionally, hormonal factors, which can influence nutritional status, were not evaluated in our study. Consequently, further research employing prospective designs and larger patient cohorts is warranted to validate our findings.

CONCLUSION

The findings of this research suggest that valuable prognostic insights can be derived from the findings of routine blood testing for patients undergoing CAS. Our investigation demonstrated that the PNI was independently correlated with ISR as an outcome seen in CAS patients. Thus, the PNI could be successfully applied as a simple and practical indicator for ISR in individuals undergoing CAS.

Article information

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Table 1. Comparison of baseline clinical, demographic and periprocedural features of carotid artery stenting of study population according to in-stent restenosis

Variables	**ISR (+)** **n = 35**	**ISR (-)** **n = 784**	***P*-value**
Age, years, median (IQR)	66.3 (59.4–71.2)	66.1 (61.2–71.3)	0.962
Sex, male, n (%)	27 (77%)	572 (72.9%)	0.407
BMI, median (IQR)	28.1 (25.5–30.2)	26.8 (24.8–29.2)	0.322
HT, n (%)	24 (68%)	650 (83%)	**0.048**
DM, n (%)	18 (51%)	321 (40.9%)	0.429
CAD, n (%)	26 (74.2%)	588 (75.0%)	0.759
HL, n (%)	26 (86.7%)	502 (73.6%)	0.110
CKD, n (%)	6 (17.1%)	132 (16.8%)	0.948
PAD, n (%)	11 (31.4%)	173 (22%)	0.303
Smoker, n (%)	25 (57.1%)	439 (56%)	0.916
Alcohol consumption, n (%)	2 (5.7%)	32 (4%)	0.647
Symptomatic stenting, n (%)	21 (71.4%)	431 (54.9%)	0.123
Contralateral disease, n (%)	28 (80%)	613 (78.1%)	0.769
Lesion type, n (%)			
Calcified lesion	22 (62.8%)	388 (49.4%)	0.134
Thrombotic lesion	8 (22.8%)	130 (16.5%)	0.368
Dissected lesion	1 (2.9%)	26 (3.3%)	0.403
Fibrotic lesion	28 (80%)	595 (75.8%)	0.524
Ulcerous lesion	5 (14.2%)	36 (5.7%)	0.062
Predilation, n (%)	1 (2.8%)	78 (9.9%)	0.076
Postdilation, n (%)	27 (77%)	608 (77.5%)	0.842

Stent overlap, n (%)	5 (14.2%)	23 (2.9%)	**<0.001**
Open-cell stent, n (%)	12 (34.2%)	182 (23.2%)	0.232
Residual stenosis, n (%)	15 (42.8%)	16 (2%)	**<0.001**
Stent length, mm, median (IQR)	35 (30–40)	30 (30–40)	0.839
Stent duration, median (IQR)	50.5 (36–57)	46 (34–57)	0.682
Dual antiplatelet usage, n (%)	13 (43.3%)	315 (46.2%)	0.759
Statin usage, n (%)	12 (40%)	252 (37%)	0.594

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CKD, chronic kidney disease; DM, diabetes mellitus; HL, hyperlipidemia; HT, hypertension; IQR, interquartile range; ISR+, in-stent restenosis; ISR–, non-in-stent restenosis; PAD, peripheric arterial disease

Table 2. Comparison of laboratory parameters in study population according to in-stent restenosis

Variables	**ISR (+)**	**ISR (–)**	***P*-value**
WBC, 10^9/l, median (IQR)	8.16 (7.57–8.2)	8.08 (6.86–9.09)	0.311
NEU, 10^9/l, median (IQR)	5.1 (4.58–5.5)	4.82 (3.78–5.9)	0.459
LYM, 10^9/l, median (IQR)	1.76 (1.35–2.4)	2.17 (1.76–2.55)	**0.007**
MONO, 10^9/l, median (IQR)	0.62 (0.49–0.8)	0.69 (0.54–0.88)	0.209
Hb, g/dl, median (IQR)	12.4 (11.1–14.6)	13.6 (11.8–15.2)	0.100
MCV, fl, median (IQR)	87.3 (84.2–89.6)	87.4 (83.5–90.5)	0.853
RDW, %, median (IQR)	13.4 (12.9–14.9)	13.5 (12.9–14.9)	0.919
MPV, fL, median (IQR)	10.5 (9.6–11.7)	10 (9.4–10.9)	0.119
PLT, 10^9/l, median (IQR)	238 (203–280)	253 (218–305)	0.160

PDW, fL, median (IQR)	12.8 (10.7–15.4)	12.4 (11–14.9)	0.951
BUN, mg/dl, median (IQR)	36.3 (30.6–41.9)	37.1 (30.3–45)	0.671
Cr, mg/dl, median (IQR)	0.9 (0.84–1.22)	0.96 (0.83–1.17)	0.772
Uric acid, mg/dl, median (IQR)	5.45 (4.1–7.55)	5.6 (4.5–6.9)	0.447
Na, (mmol/dl), median (IQR)	139 (138–140)	139 (138–141)	0.331
K, (mmol/dl), median (IQR)	4.55 (4.2–4.78)	4.61 (4.25–4.87)	0.380
AST, U/l, median (IQR)	17.8 (15.7–20.8)	17.2 (13.6–22)	0.327
ALT, U/l, median (IQR)	12.6 (8.72–18.2)	16.4 (12–22)	**0.047**
Tbil, mg/dl, median (IQR)	0.44 (0.32–0.49)	0.45 (0.3–0.6)	0.569
TC, (mg/dl), median (IQR)	189 (146–226)	166 (140–198)	0.064
HDL cholesterol, (mg/dl), median (IQR)	37 (24.7–39)	44.7 (39–51.3)	**<0.001**
TG, (mg/dl), median (IQR)	272 (240–287)	151 (106–181)	**<0.001**
LDL cholesterol, mg/dl, median (IQR)	100 (50.8–142)	86.6 (64.5–121)	0.521
Non-HDL, (mg/dl), median (IQR)	151 (108–193)	121 (91.6–153)	**0.006**
HbA1c, %, median (IQR)	6.2 (5.88–6.85)	6.2 (5.8–7.2)	0.834
ALB, g/dl, median (IQR)	3.9 (3.4–3.9)	4.4 (4–4.7)	**<0.001**

CRP, mg/l, median (IQR)	3.83 (2.31–11.5)	3.1 (1.14–5.7)	0.064
CONUT score, median (IQR)	1.5 (0–3)	1 (0–2)	0.078
PNI score, median (IQR)	39 (34–39)	44 (40–47)	**<0.001**

Abbreviations: ALB, albumin; ALT, alanine transaminase; AST, aspartate transaminase; BUN, blood urea nitrogen; CONUT, Controlling Nutritional Status; Cr, creatinine; CRP; C reactive protein; Hb, hemoglobin; HbA1c, glycated hemoglobin; HDL-C, high density lipoprotein cholesterol; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; LYM, lymphocytes; MCV, mean corpuscular volume; MONO, monocytes; MPV, mean platelet volume; NEU, neutrophils; non-HDL-C, non- high-density lipoprotein cholesterol; PDW, platelet distribution width; PLT, platelets; PNI, Prognostic Nutritional Index; RDW, red blood cell distribution width; Tbil, total serum bilirubin; TC, total cholesterol; TG, triglyceride; WBC, white blood cell; other — see Table 1

Table 3. Univariate logistic regression analysis for assessment of predictors of in-stent restenosis

	UNIVARIATE	
Variables	**OR (95% CI)**	***P*-value**
Age, years	1.002 (0.952–1.054)	0.937
Sex	1.467 (0.590–3.646)	0.409
DM	1.360 (0.654–2.826)	0.410
HT	0.454 (0.654–2.826)	**0.055**
Smoker	1.021 (0.654–2.826)	0.956
Hemoglobin, g/dl	0.859 (0.654–2.826)	**0.067**
Lymphocytes	0.422 (0.229–0.776)	**0.006**
ALT	0.987 (0.942–1.035)	0.601
Albumin	0.177 (0.093–0.340)	**<0.001**
Total cholesterol	1.008 (1.001–1.016)	**0.032**
HDL	0.827 (0.767–0.891)	**<0.001**
Triglyceride	1.014 (1.009–1.018)	**<0.001**
Non-HDL	1.012 **(**1.005–1.020)	**0.002**

CONUT score	1.340 (1.103–1.626)	**0.003**
PNI score	0.841 (0.788–0.898)	**<0.001**
Ulcerous lesion	2.761 (0.788–0.898)	**0.072**
Stent overlap	5.031 (0.788–0.898)	**0.006**
Residual stenosis	36.487 (14.904–89.326)	**<0.001**

Abbreviations: CI, confidence interval; OR, odds ratio; other — see Tables 1 and 2

Table 4. Multivariable model 1 — including PNI score and model 2 — including CONUT score for prediction of carotid in-stent restenosis

	Model 1			**Model 2**		
Variables	**OR**	**95% CI**	***P*-value**	**OR**	**95% CI**	***P*-value**
Age, years	0.983	0.925–1.044	0.575	0.971	0.913–1.033	0.346
Sex (male)	1.203	0.404–3.585	0.740	1.391	0.494–3.912	0.532
Total cholesterol	1.011	1.003–1.019	**0.009**	1.012	1.002–1.021	**0.019**
Stent overlap	5.424	1.026–28.670	**0.047**	4.578	1.052–19.916	**0.043**
Residual stenosis	47.930	16.280–141.110	**<0.001**	33.998	13.405–86.230	**<0.001**
CONUT score				1.168	0.897–1.521	0.248
PNI score	0.846	0.782–0.915	**<0.001**			

Abbreviations: see Table 2 and 3

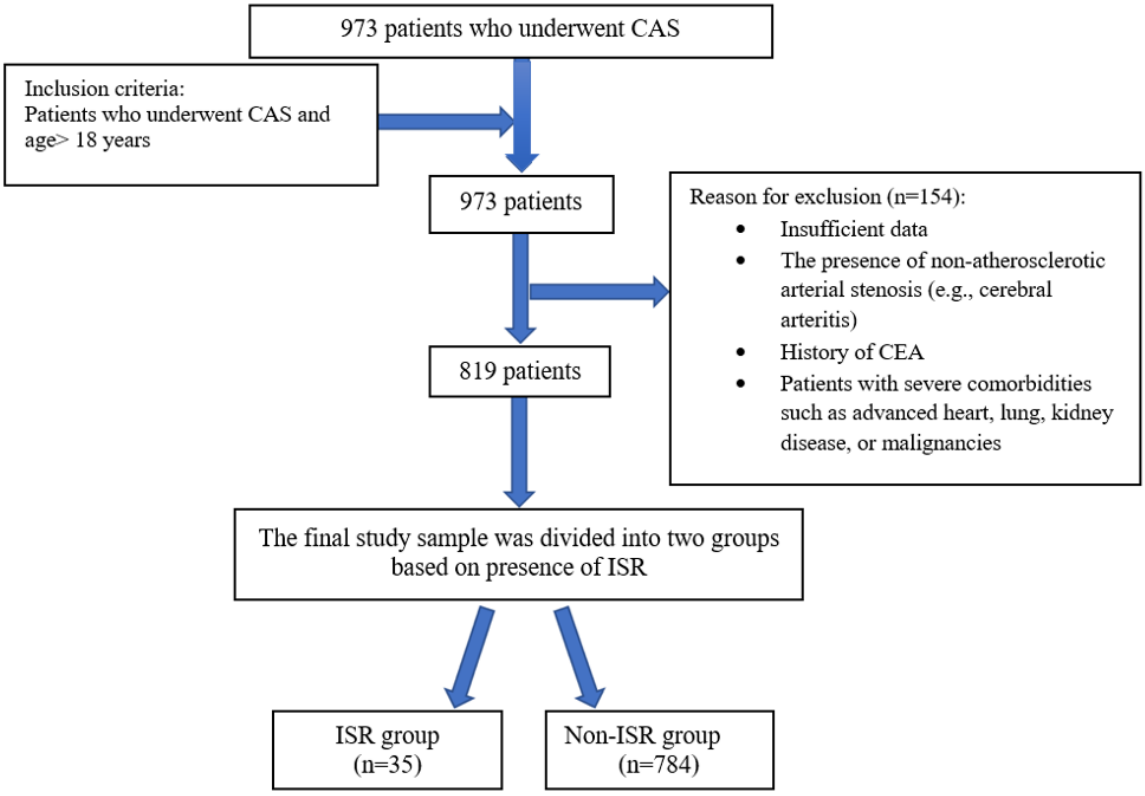

Figure 1. Consort flow diagram for inclusion in the study

Abbreviations: CAS, carotid artery stenting; CEA, carotid endarterectomy; ISR, in-stent restenosis

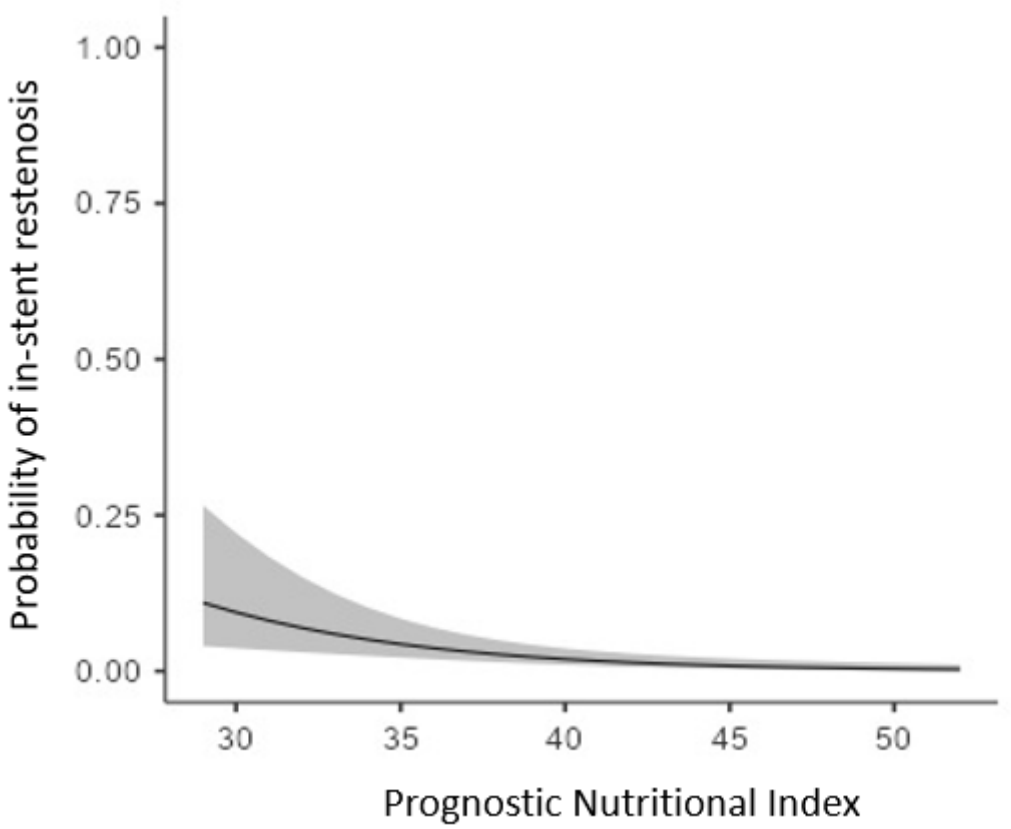

Figure 2. Marginal means plot showing the relationship between the probability of in-stent restenosis and Prognostic Nutritional Index

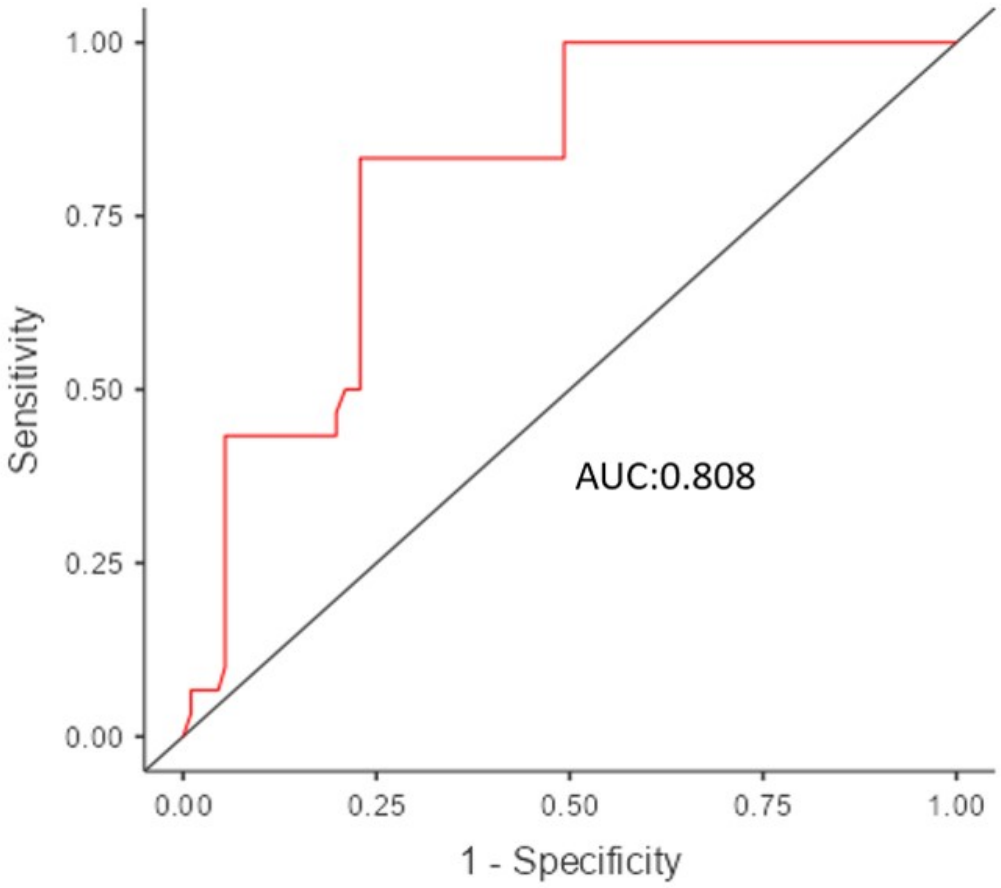

Figure 3. Receiver operating characteristic curves for Prognostic Nutritional Index score to predict the in-stent restenosis

Abbreviaton: AUC, area under curve