J Turgut Ozal Med Cent
DOI: 10.5455/jtomc.2018.01.07 2018;25(1):145-7

Original Article

N-terminal pro-brain natriuretic peptide predicts instent restenosis in patients with stable coronary artery disease

Adil Bayramoglu

Ordu University, School of Medicine, Department of Cardiology, Ordu, Turkey

Abstract

Aim: Instent restenosis is associated with a poor outcomes in coronary artery disease patients. There are many factors and mechanisms that contribute to the development of IRS. Some of clinical trials have been shown that N-Terminal –pro Brain Nnatriuretic Peptide has an important prognostic value in coronary artery disease. we aimed to evaluate the relationship between stent restenosis and N-Terminal–pro Brain Nnatriuretic Peptide in patients of stable coronary artery disease undergo percutaneous coronary intervention.

Material and Methods: 411 patients with stent implantation due to stable coronary artery disease were evaluated and eighty patients underwent re-coronary angiography because of recurrent angına. NT-proBNP measured before coronary intervention. The patients were divided into two groups of instent restenosis developed and undeveloped.

Results: In the multivariate regression analysis; Age (OR = 1.067; 95% CI 1.002-1136, P = 0.042) and NT-proBNP (OR = 1.023, 95% CI 1.008-1.038.p = 0.002).) have been shown that they were independent predictors of IRS. The optimal threshold NT-pro BNP value for predicting IRS was >111, with a 56.5% sensitivity and 92% specificity (area under the curve [AUC]: 0.749, 95% CI: 0.639-0.840, P <0.001).

Conclusion: Measurement of NT-proBNP ın stable coronary artery disease patients used to predict IRS; may help physicians to estimate the presence of IRS.

Keywords: NT-Pro BNP; Coronary Artery Disease; Instent Restenosis.

INTRODUCTION

Coronary heart disease, results in reduced blood flow to the myocardium due to coronary atherosclerosis. This disease is among the causes of mortality and morbidity in our country as well as all over the world (1,2).

In-stent restenosis (ISR) is an undesirable condition seen after percutaneous coronary intervention and is an important cause of recurrence of coronary morbidity and revascularization after coronary surgery (3,4). Increasingly, in the treatment of more complex lesions and although it uses stents for its widespread use intra-stent restenosis is between 10-20% (5).

Brain natriuretic peptide (BNP) is synthesized by cardiac myocytes against increased ventricular wall stress. After secretion as prohormone it is separated into NT-proBNP, which contains the biologically active brain natriuretic peptide and the inactive N-terminal part. Even if NT-proBNP is not myonecrosis, ischemic events can be increased by the consequence of systolic and diastolic dysfunction. In a large number of clinical trials, it has been shown that NT-proBNP has an important prognostic value in acute coronary syndromes (6,7).

Although the association between NT-proBNP and coronary artery disease has been shown in previous studies the relationship between long-term follow-up stent restenosis after revascularization of patients with stable coronary artery disease was not studied (8). On follow-up of stable coronary artery patients who were revascularized in our study ,we aimed to evaluate the relationship between stent restenosis and NT-proBNP.

MATERIAL and METHODS

Between 2015 and 2016, 411 patients with stent implantation due to stable coronary artery disease were evaluated retrospectively. 80 patients underwent repeated angiography as a result of recurrent angina symptoms. 80 patients who were found to have a high risk of stable coronary artery disease and who underwent re-coronary angiography for this reason were included in the study. Written or verbal informed consent was received from all patients, and the study protocol was approved by the hospital's local ethics committee in accordance with the Helsinki Declaration and Good Clinical Practice Guidelines.

Received: 08.01.2018 **Accepted:** 29.01.2018
Corresponding Author: Adil Bayramoglu, Ordu University, School of Medicine, Department of Cardiology, Ordu, Turkey
E-mail: adilbayramoglu@gmail.com

Patients with ST elevation myocardial infarction, non-st-elevated myocardial infarction, unstable angina pectoris, Ejection fraction ≤ 50%,patients with moderate-to-severe valve disease, patients with non-drug-eluting stents, patients with chronic renal failure, patients with chronic liver failure, patients with CRP, high sedation and coronary angiography with stent restenosis plus newly developed critical stenosis were excluded.

Coronary angiography and angioplasty were performed by femoral approach using 6F (French) catheters. All angiographic measurements were made in diastole. Restenosis after coronary arteriovenous intervention was defined as> 50% stenosis, which is intimal proliferation in the control angiography (9).

Blood samples taken immediately and NT-pro BNP measured before coronary intervention. The quantitative measurement of NT-pro BNP was performed in full flush with a fluorescence immunoassay kit (FIA 8000, Quantitative Immunoassay Analyzer, California). Note that the whole blood sample is homogeneous; the sample taken with the special pipette was studied after it was added on disposable test cards. Again biochemical parameters were studied in the biochemistry laboratory prior to coronary intervention.

Statistical Analysis

The data analysis was conducted using SPSS (version 20.0, SPSS Inc., Chicago, IL, USA) and Med Calc statistical software (trial version 12.7.8, Mariakerke, Belgium). Continuous variables data are expressed as the mean ± standard deviation. Categorical variables were compared using Chi-square or Fisher's exact tests and summarized as percentages. To predict IRS age, diabetes mellitus (DM), hypertension (HT), hyperlipidemia (HL), smoking and NT-pro BNP were included in the multiple logistic analysis. Receiver operating characteristic (ROC) curves were used to predict the future incidence of IRS.

RESULTS

The demographic, laboratory, and angiographic characteristics of the 80 subjects included in the study are given in Table 1.

ISR was detected in 24 of 80 patients with coronary re-angiography. Age, DM history, pretreatment NT-pro BNP levels were statistically different between the groups. In addition, in the evaluation of the responsible artery, it was observed that the development of restenosis was higher in the LAD artery (p <0.001). In the multivariate regression analysis; Age (OR = 1.067; 95% CI 1.002-1136, P = 0.042) and NT-pro BNP (OR = 1.023, 95% CI 1.008-1.038.p = 0.002) have been shown that they were independent predictors of IRS (Table 2). The optimal threshold NT-pro BNP value for predicting IRS was >111, with a 56.5% sensitivity and 92% specificity (area under the curve [AUC]: 0.749, 95% CI: 0.639-0.840, P <0.001) Figure 1.

Table 1. Clinical Characteristics and Angiographic Findings in Two Groups

		IRS positive group (n=24)	IRS negative group (n=56)	p
Age (years)		65.0±10.7	57.6±10.3	0.005
Sex (%, male)		17(70.8)	29(50.1)	0.114
Diabetes Mellitus (n, %)		11(45.8)	13(23.2)	0.043
Hypertension (n, %)		15(62.5)	42(75)	0.258
Hyperlipidemia (n, %)		10(41.7)	20(35.7)	0.606
Smoking (n, %)		6(25)	18(32.1)	0.502
Heart Rate(p/min)		71±16	69±19	0.201
Ejection Fraction %		56.5±6.1	55.1±7.8	0.680
Stent length(mm)		26.3±15.2	25.7±8.4	0.254
Stent diameter (mm)		2.9±0.3	3.0±0.4	0.115
B-blocker (n, %)		17(70.8)	44(78)	0.771
CCB (n, %)		2(8.3)	5(8.9)	0.199
Statin (n, %)		20(83)	50(89)	0.656
Aspirin (n, %)		24(100)	55(98)	0.956
Low Density Lipoprotein		123±35	113±26	0.229
High Density Lipoprotein		44±6.7	46±9.5	0.306
Triglyseride		187±117	201±122	0.643
NT-Pro BNP		79.3(5-469)	34.2(5-121)	0.001
Glucose		137±81	119±48	0.229
IRA	LMCA	-	-	<0.001
	LAD	12(50)	28(50)	
	CX	7(29)	13(23)	
	RCA	15(26)	5(21)	

CCB: Calcium Channel Blocker, CX: Circumflex Artery, , IRA: Infarct Related Artery, LMCA: Left Main Coronary Artery , LAD: Left Ascending Artery, RCA: Right Coronary Artery, NT-Pro BNP:N terminal Brain Natriuretic peptide

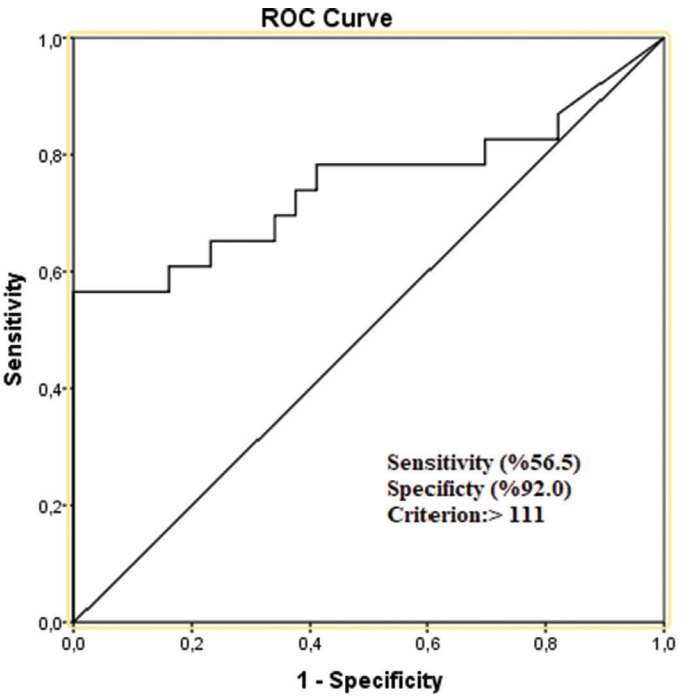

Figure 1. ROC curve graphics to detect the best cut-off value for the NT-pro BNP in predicting the In-stent restenosis

Table 2. Univariate and Multivariate Analysis for IRS

	Univariate analysis		Multivariate analysis		
	OR 95%CI	P value	OR	95% CI	P value
Age	1.071	0.005	1.067	1.002–1136	0.042
Smoking	1.421	0.502			
Diabetes Mellitus	0.357	0.043			
Hypertension	1.800	0.258			
Hyperlipidemia	0.778	0.606			
NT-Pro BNP	1.020	0.001	1.023	1.008-1.038	0.002

DISCUSSION

In this study it has been shown that NT-pro BNP and age are effective and independent parameters in predicting the presence of IRS in previously revascularized stable coronary patients.

Recently, the relationship between the level of natriuretic peptides and cardiovascular diseases has interested to clinicians. NT-proBNP, a marker of myocardial stress, has taken place in international guidelines as an indicator of both prognostic and therapeutic outcomes in heart failure (10). Natriuretic peptides are known to release circulation in coronary artery disease (11). It has also been shown that NT-pro BNP levels increase rapidly but temporarily after exercise testing in stable coronary artery disease, which is related to the size of the ischemic area (11). In addition, Heeschen et al found that ischemia is an important marker of NT-proBNP release (12). Although ischemia can not be shown to directly increase NT-proBNP, the data show that transient ischemia increases NT-proBNP synthesis from cardiomyocytes, either directly or by increasing wall stress (12).

Sir Jung-Ju et al showed that involving patients with stable angina and acute coronary syndrome with normal systolic function, the relationship between NT-pro BNP values before and after coronary angiography in patients with revascularization was investigated and NT-proBNP has been shown to be an independent predictor of low specificity for re-invasive revascularization (13). Seo Na Hong et al showed that NT-pro BNP it was found that NT-pro BNP could predict ISR in patients with preserved systolic functions. In this study, NT-pro BNP levels were significantly higher in ISR-detected patients before control coronary angiography. Seo Na Hong et al also included patients with acute coronary syndrome to their study (8). In our study, only patients with stable coronary artery disease that were previously revascularized were included and it was observed that NT-pro BNP values an independent predictor of IRS. Furthermore, in our study with only stable coronary artery disease patients, ROC curve analysis showed an IRS of 56.5% sensitivity and 92% specificity (AUC 0.749). Similar to the study done by Seo Na Hong et al., It was found that the development of IRS in the patients with stable coronary artery which had previously been interfered with LAD artery was higher than the other vessels. In previous studies, age has been shown to be a risk factor for the IRS (14). Similarly, in our work, old age has been shown to be an independent factor in the development of IRS.

In conclusion, we concluded that NT-pro BNP measurement in stable coronary artery patients undergoing coronary angiography may be a useful parameter in predicting restenosis. However, we believe that further clinical trials will be useful for this.

Acknowledgements

Declaration of interests: The authors declare that they have no competing interests.

REFERENCES

1. Bonow RO, Bacharach SL, Green MV, Kent KM, Rosing DR, Lipson LC, el al. Impaired left ventricular diastolic filling in patients with coronary arterydisease : Assessment with radionuclide angiography. Circulation 1981;64(2):315-23.
2. Libby P, Ridker PM, Hansson GK. Leducq Transatlantic Network on Atherothrombosis. Inflammation in atherosclerosis: From pathophysiology to practice. J Am Coll Cardiol 2009;54(23):2129-38.
3. Yavuz F, Ozer O, Ercan S, Yuce M, Davutoglu V, Alici H, et al. Relationship between coronary in-stent restenosis and plasma urotensin II level. Minerva Cardioangiol 2014;62(3):297-303.
4. Barlis P, Horrigan MC, Chan RK, Ajani AE, Proimos G, Schumer W, et al. What is the best contemporary treatment for ın-stent restenosis? Cardiovascular Revasc Med 2005;6(4)179-81.
5. Batyraliev T, Avşar Ö. Stent İçi Restenoz ve İlaçlarla Kaplı Stentler. Türk Girişimsel Kardiyoloji Dergisi 2007;11:163-9.
6. Oremus M, Raina PS, Santaguida P, Balion CM, McQueen MJ, McKelvie R, et al. A Systemic review of BNP as A predictor of prognosis In persons with coronary artery disease. Clin Biochem 2008;41(4-5)260-5.
7. Sabatina MS, Morrow DA, de Lemos JA, Omland T, Desai MY, Tanasijevic M et al. Acute Changes In Circulating Natriuretic Peptide Levels In Relation to Myocardial Ischemia. J Am Coll Cardiol 2004;44(10):1988-95.
8. Hong SN, Ahn Y, Yoon NS, Lee KH, Kim YS, Hwang SH, et al. Usefulness of serum N-terminal pro-brain natriuretic peptide to predict ın-stent restenosis in patient with preserved left ventricular function and normal troponin I evels. Am J Cardiol 2007;99(8):1051-4.
9. Lee S, Yoon CH, Oh IY, Suh JW, Cho YS, Cho GY, et al. Angiographic patterns of restenosis with 2nd generation drug-eluting stent:comparative analysis from a 10-year single-center experience. Int Heart J 2015;56(1):6-12.
10. Wei P, Wang HB, Fu Q, Bai J, Zhu Q. Levels of BNP and stress blood glucose in acute coronary syndrome patients and their relationships with the severity of coronary artery lesion. Cell Biochem Biophys 2014 ;68(3):535-9.
11. Marumoto K, Hamada M, Hiwada K. Increased Secretion of Atrial and Brain Natriuretic Peptides During Acute Myocardial Ischaemia Induced by Dynamic Exercise In Patient With Angina Pectoris. Clin Sci (Lond) 1995;88(5):551-6.
12. Heeschen C, Hamm CW, Mitrovic V, Lantelme NH, White HD. N-Terminal pro-B-type natriuretic peptide levels for dynamic risk stratification of patients with acute coronary syndromes. Circulation 2004;110(20):3206-12.
13. Sir JJ, Chung WY, Hwang SJ, Kang HJ, Cho YS, Koo BK, et al. N-Terminal Pro-B-type natriuretic peptide as a predictor of repeat coronary revascularization. Int J Cardiol 2008;126(3):322-32.
14. Taniwaki M, Stefanini GG, Silber S, Richardt G, Vranckx P, Serruys PW, et al. 4-year clinical outcomes and predictors of repeat revascularization in patients treated with new-generation drug-eluting stents: a report from the RESOLUTE all-comers trial (a randomized comparisonof a zotarolimus-eluting stent with an everolimus-eluting stent for percutaneous coronary ıntervention). J Am Coll Cardiol 2014;63(16):1617-25.