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High-Sensitivity Cardiac Troponin T is Associated with SYNTAX Score and Diabetes Mellitus in Patients with Stable Coronary Artery Disease

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Abstract

High-sensitivity cardiac troponin T (hs-cTnT) and the Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score are emerging as important prognostic markers in stable coronary artery disease (CAD). We aimed to investigate the relationship between hs-cTnT and extent and complexity of CAD assessed with STNTAX score. Measurements were obtained from 411 patients with stable CAD (Mean age = 61.7 ± 9.9 years, male/female = 247/164). The patients were divided into two groups according to the median hs-TnT value (hs-cTnT$_{low}$ group < 9.65 pg/ml and hs-cTnT$_{high}$ group ≥ 9.65 pg/ml). SYNTAX score values were higher in hs-cTnT$_{high}$ group compared with hs-cTnT$_{low}$ group ($p < 0.05$). Hs-cTnT was independently associated with SYNTAX score (β = 0.661, p<0.001) and diabetes (β = 0.107, p = 0.031) in multiple linear regression analysis. The cutoff value of hs-cTnT obtained by the ROC curve analysis was 9.62 ng/L for the prediction of higher SYNTAX score. In multivariate logistic regression analysis, hs-cTnT, age, diabetes, creatinine and hs-CRP were an independent predictor for higher SYNTAX score. Despite very low circulating concentrations, changes in hs-cTnT concentrations are associated with extent and complexity of CAD and presence of diabetes in patients with stable CAD.

Keywords: High-sensitivity troponin T; SYNTAX; Coronary artery disease; Diabetes

Introduction

New generation of high sensitivity cardiac troponin (hs-cTn) assays has recently been developed, which allows for the detection of even minor myocardial necrosis with high precision [1]. The most of the patients with stable coronary artery disease (CAD) have cardiac troponin T concentrations that are undetectable with conventional assays [2]. The increased diagnostic and prognostic accuracy of the hs-cTnT assay versus the conventional cTnT assay has recently been reported in stable CAD [3]. Recent studies have shown that the hs-cTnT allow risk stratification of patients with stable congestive heart failure [4] and acute coronary syndromes [5]. Moreover, hs-cTnT level at levels below the limit of detection of conventional assays is related with increased mortality in stable CAD [2,3].

The Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score quantifies extent and complexity of angiographic disease [6]. SYNTAX score is being used to make revascularization decisions and predict long-term mortality and morbidity in patients with coronary artery disease [7-9]. Moreover, SYNTAX score has the power to predict adverse cardiac events such as no-reflow in patients with ST elevation myocardial infarction treated with primary percutaneous intervention [10].

The patients with stable CAD have hs-cTnT concentrations at levels below the limit of detection of conventional assays, but little is known regarding the association of hs-cTnT levels with extent and complexity of CAD in patients with stable CAD [11]. In addition, the role of hs-cTnT in determining ways of revascularization in patients with stable CAD is unclear. In this study, we aimed to assess the relationship between hs-cTnT level and extent and complexity of CAD assessed by SYNTAX score in patients with stable CAD.

Methods

Study population

Between December 2012 and April 2013, 411 consecutive patients (247 males and 164 females; mean age: 61.7 + 9.9 years) with angiographically proven CAD admitted to our cardiology clinic for angiography were included in the study. The patients were divided into 2 groups according to the median hs-cTnT value (hs-cTnT$_{low}$ group < 9.5 pg/ml and hs-cTnT$_{high}$ ≥ 9.5 pg/ml). Coronary angiography was performed for the investigation of ischemic heart disease based on clinical indications (198 patients had typical ischemic chest discomfort, 143 patients had positive treadmill test, 13 patients had positive dobutamine stress echo and 57 patients had positive myocardial perfusion scintigraphy). The patients with coronary lesions with a diameter stenosis of ≥ 50% in ≥ 1.5mm vessels were included in the study. All patients were clinically stable (without typical chest pain that occurs at rest within last 48 hours, alteration of previous ischemic symptoms, new ST-segment elevation or depression, new development of Q wave, T-wave tenting or inversion or serial increases in serum biochemical markers of cardiac necrosis). Exclusion criteria were the presence of neoplastic disease, heart failure, recent major surgical procedure, or liver or kidney disease. Patients with previous myocardial infarction, previous coronary angioplasty or bypass surgery, normal coronary angiogram, valvular, myocardial, or pericardial disease were also excluded. The study was conducted according to the recommendations set forth by the Declaration of Helsinki on Biomedical Research Involving Human Subjects. The institutional ethics committee approved the study protocol and each participant provided written informed consent.

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After detailed medical history and complete physical examination, each participant was questioned for major cardiovascular risk factors such as age, sex, diabetes mellitus, smoking status, and hypertension. In addition, body mass index was calculated and systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded.

Transthoracic echocardiography was performed for each patient (Vivid 7 GE Medical System, Horten, Norway). Ejection fraction (EF) was calculated using Simpson's method [5].

Blood samples

Fasting venous blood samples were obtained from all patients to determine their plasma levels of fasting blood glucose, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglyceride, creatinine, high sensitive C reactive protein (hs-CRP) and hemoglobin. Creatine kinase-myocardial band form (CK-MB) was measured with an assay that uses 2 monoclonal antibodies (CKMB STAT) on an Elecsys 2010 analyzer (Roche Diagnostics) by electrochemiluminescence immunoassay. Serum concentrations of hs-cTnT on admission were measured using an Elecsys 2010 analyzer (cobas e 411; Elecsys, Roche Diagnostics, made in Germany). The limit of blank (LoB) was 3 ng/L, and values under the limit were routinely classified as 2.99 ng/L. The upper reference limit (99th percentile) was 14 ng/L, and the lowest concentration with a coefficient of variance (CV) ≤ 10% was 13 ng/L.

Coronary angiography and SYNTAX score

All patients underwent coronary angiography with the Judkins technique [12]. Coronary angiography was performed with standard femoral approach with a 6-F diagnostic catheter. Coronary lesions leading to ≥ 50% diameter stenosis in ≥ 1.5 mm vessels were scored separately and added together to provide the cumulative SYNTAX score which was prospectively calculated using the SYNTAX score algorithm on the baseline diagnostic angiogram [6]. Two experienced interventional cardiologists analyzed the SYNTAX score; the opinion of a third analyst was obtained and the final judgment was made by consensus in cases of a disagreement. The final score was calculated from the individual lesion scores by analysts who were blinded to procedural data and clinical outcome.

The median SYNTAX score was 10.3 and above the median SYNTAX score was accepted as higher SYNTAX score.

Statistical analysis

All analyses were conducted using SPSS 17.0 (SPSS for Windows 17.0, Chicago, Illinois). Continuous variables were expressed as mean ± standard deviation and categorical variables were expressed as percentages. Analysis of normality was performed with the Kolmogorov-Smirnov test. SYNTAX score, hsCRP and triglyceride values were normalized by logarithmic transformation and expressed as median (25 and 75% interquartiles). The logarithmic transformation of SYNTAX score, hsCRP and triglyceride values was used for statistical analysis. Comparison of categorical variables between the groups was performed using the chi-square test. Comparisons of continuous variables between the 2 groups were performed using the independent samples t test. The correlation between hs-cTnT and angiographic, clinical and laboratory parameters was assessed by the Pearson correlation test. Multiple linear regression analysis was performed to identify the independent relations of hs-cTnT by including the parameters, which were correlated with hs-cTnT on bivariate analysis. The cutoff value of hs-cTnT obtained by the ROC curve analysis for the prediction of higher SYNTAX score. Multivariate, stepwise backward conditional logistic regression analysis was used to determine the independent predictors of high SYTAX score (10.3). All significant parameters in the bivariate analysis were selected in the multivariate model. To avoid over fitting and collinearity in assessing the multivariate model, independent variables have been tested for intercorrelation. Collinearity between variables was excluded before modelling. Finally, age, hypertension, diabetes, EF, SBP, DBP, hs-cTnT, creatinine, hs-CRP, and LDL-C were selected in the multivariate model. A 2-tailed $P < 0.05$ was considered as statistically significant.

Results

Baseline characteristics

Baseline, clinical, laboratories, echocardiographic and angiographic characteristics of groups were showed in Table-1. In comparison of two groups there was significant difference between the groups at age, hypertension and diabetes ($p < 0.05$, for all). LDL-C, fasting glucose, hs-CRP and creatinine levels were higher in hs-cTnT$_{high}$ group compared with hs-cTnT$_{low}$ group ($p < 0.05$, for all). There was no significant difference at CK-MB levels ($p > 0.05$).

SYNTAX score values were higher in hs-cTnT$_{high}$ group compared with hs-cTnT$_{low}$ group ($p < 0.05$). On the other hand, there was no significant difference at EF values ($p > 0.05$).

Bivariate and multivariate relationships of high sensitive cardiac troponin T

Bivariate and multivariate relationships of hs-cTnT were demonstrated in Table-2. Hs-cTnT level was associated with age ($r = 0.339$, $p < 0.001$), hypertension ($r = 0.170$, $p = 0.001$), diabetes ($r = 0.492$, $p < 0.001$), SYNTAX score ($r = 0.692$, $p < 0.001$), EF value ($r = -0.126$, $p = 0.011$), creatinine level ($r = 0.416$, $p < 0.001$), hs-CRP level ($r = 0.293$, $p < 0.001$), fasting glucose ($r = 0.184$, $p < 0.001$) and oral anti-diabetic drug use ($r = 0.441$, $p < 0.001$). Relationship between hs-cTnT and SYNTAX score was demonstrated in Figure-1.

Multiple linear regression analysis showed that hs-cTnT level was independently associated with SYNTAX score ($\beta = 0.661$, $p < 0.001$) and diabetes ($\beta = 0.107$, $p = 0.031$).

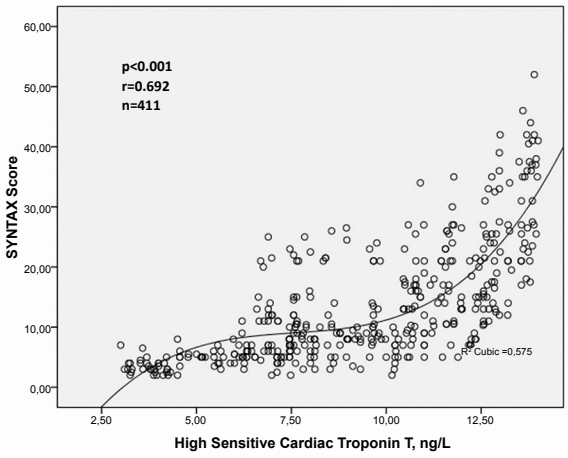

Figure 1: Scatter graphic showing strong correlation between high sensitive cardiac troponin T and SYNTAX score in all of the patients with stable coronary artery disease.

ROC curve analysis

The cutoff value of hs-cTnT obtained by the ROC curve analysis was 9.62 ng/L for the prediction of higher SYNTAX score (sensitivity: 78.5%, specificity: 77.7%, Figure-2). The area under the curve (AUC) was 0.860 (95%CI 0.825-0.894, p < 0.001).

Bivariate and multivariate relationships of high SYNTAX score

Bivariate and multivariate relationships of high SYNTAX score were demonstrated in Table-3. High SYNTAX score was associated with age (r = 0.426, p < 0.001), hypertension (r = 0.220, p = 0.001), diabetes (r = 0.604, p < 0.001), SBP (r = 0.140, p = 0.004), DBP (r = 0.112, p = 0.023), hs-cTnT (r = 0.692, p < 0.001), EF value (r =-0.177, p < 0.001), creatinine level (r = 0.423, p < 0.001), hs-CRP level (r = 0.485, p < 0.001), fasting glucose (r = 0.166, p = 0.001), LDL-C (r = 0.114, p < 0.022), statin use (r = 0.215, p < 0.001), angiotensin converting enzyme inhibitor (r = 0.099, p = 0.044) and oral anti-diabetic drug use (r = 0.442, p < 0.001).

Multivariate logistic regression analysis showed that age (odds ratio = 1.06, p = 0.001), diabetes (β = 0.155, p= 0.001), hs-cTnT (odds ratio = 1.64, p < 0.001), creatinine (odds ratio = 1.89, p = 0.001) and hs-CRP (odds ratio = 2.45, p = 0.001) were independent predictors of higher SYNTAX score.

Discussion

This is the first study that investigated the relationship between hs-cTnT and extent and complexity of CAD in patients with stable CAD. The main finding of this study is that; (1) SYNTAX score and diabetes were independently associated with hs-cTnT; (2) The cutoff value of hs-cTnT obtained by the ROC curve analysis was 9.62 ng/L for the prediction of higher SYNTAX score; (3) hs-cTnT, age, diabetes, creatinine and hs-CRP were an independent predictor for higher SYNTAX score.

Recent studies have demonstrated that hs-cTnT assays increase the accuracy of diagnosis in the early period of acute myocardial infarction and hs-cTnT allows for the detection of even minor myocardial necrosis with high precision [1,13]. The elevated levels of hs-cTnT in patients with stable or unstable angina presenting with undetectable

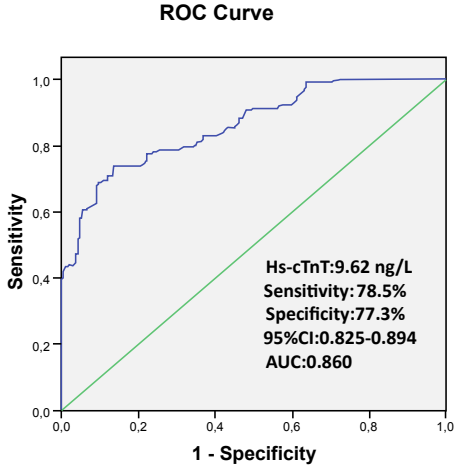

Figure 2: Receiver–operator characteristic (ROC) curve analysis for high sensitive cardiac troponin T

Variables	hs-cTnT$_{low}$ group (n:205)	hs-cTnT$_{high}$ group (n:206)	P
Baseline characteristics			
Age, years	59.1 ± 9.6	64.3 ± 9.5	**<0.001**
Gender (Male)	120 (58.3%)	127 (62.0%)	0.253
Body mass index, kg/m^2	27.5 ± 3.7	27.6 ± 3.6	0.864
Systolic blood pressure, mmHg	124.5 ± 17.2	127.4 ± 16.2	0.082
Diastolic blood pressure, mmHg	76.3 ± 10.0	77.8 ± 9.8	0.137
Heart Rate, beat/minute	76.9 ± 10.0	75.2 ± 9.2	0.082
Hypertension, n (%)	85 (41.3%)	110 (53.7%)	**0.008**
Diabetes mellitus, n (%)	32 (15.5%)	122 (59.5%)	**<0.001**
Hyperlipidemia, n (%)	132 (64.1%)	117 (57.1%)	0.088
Smoking, n (%)	73 (35.4%)	62 (35.2%)	0.155
Laboratory findings			
Total Cholesterol, mg/dl	191.4 ± 43.8	182.0 ± 44.2	**0.033**
Triglyceride, mg/dl median (25th-75th)	138 (113-227.5)	147 (97.5-210)	0.353
HDL-C, mg/dl	42.8 ± 18.8	40.3 ± 9.5	0.078
LDL-C, mg/dl	128.3 ± 38.7	117.2 ± 38.5	**0.016**
Fasting glucose, mg/dl	119.2 ± 57.5	142.7 ± 74.9	**<0.001**
CK-MB, ng/mL	2.6 ± 1.2	2.9 ± 1.3	0.321
HsCRP, mg/dl median (25th-75th)	0.82 (0.54-1.12)	1.10 (0.73-1.60)	**<0.001**
Creatinine, mg/dl	0.81 ± 0.20	0.98 ± 0.26	**<0.001**
Hemoglobin, mg/dL	13.9 ± 3.4	14.1 ± 3.6	0.334
Ejection Fraction, %	64.4 ± 4.6	63.6 ± 4.5	0.104
SYNTAX Score median (25th-75th)	6.0 (4.5-10)	17 (10.8-25.5)	**<0.001**
Previous medications, n (%)			
ACE-I	35 (17.0%)	46 (22.4%)	0.103
Angiotensin receptor blocker	51 (24.8%)	54 (26.3%)	0.399
Statin	86 (41.7%)	84 (40.9%)	0.543
Beta blocker	16 (7.7%)	15 (7.3%)	0.632
Aspirin	59 (28.6%)	65 (31.7%)	0.356
Oral anti-diabetic	15 (7.3%)	105 (51.2%)	<0.001

Hs-cTnT; high-sensitivety cardiac troponin T, **HDL-C**; high density lipoprotein cholesterol, **LDL-C**; low density lipoprotein cholesterol, **HsCRP**; high sensitive C reactive protein, **SYNTAX;** the Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery, **ACE-I;** angiotensin converting enzyme inhibitor.

Data are n (%) for categorical variables, means ± SD for continuous variables, or median (25 and 75% interquartiles) for non–normally distributed variables.

Table 1: Baseline, clinical, laboratory, echocardiographic and angiographic characteristics of groups

conventional cardiac troponin T are significantly associated with decreased survival [3]. Omland et al reported that cardiac troponin T concentrations as measured with a highly sensitive assay were significantly associated with the incidence of heart failure as well as cardiovascular death in patients with stable CAD [2].

Present study showed that hs-cTnT levels were independently associated with extent and complexity of CAD assessed with SYNTAX score in patients with stable CAD. Although the majority of patients with stable CAD have cardiac troponin T concentrations that are undetectable with conventional assays, the relationship between hs-cTnT and SYNTAX score was not investigated in previous studies. However, in patients with stable CAD, the relationship between hs-cTnT and coronary atherosclerosis was investigated in limited number of studies [3,11,13]. Laufer et al. [11] reported that coronary atherosclerosis assessed with multi-slice computed tomography in symptomatic patients without acute coronary syndrome was associated with quantifiable circulating levels of hs-cTnT, even in mild

Variables	R	p value	Standardized ß regression coefficients	p value
Age, years	0.339	<0.001	0.053	0.184
Hypertension	0.170	0.001	0.003	0.927
Diabetes	0.492	<0.001	0.107	**0.031**
SYNTAX score	0.692	<0.001	0.661	**<0.001**
Ejection fraction, %	-0.126	0.011	0.003	0.943
Creatinine, mg/dl	0.416	<0.001	-0.056	0.228
Hs-CRP, mg/dl	0.293	<0.001	-0.066	0.116
Glucose, mg/dl	0.184	<0.001	-0.043	0.276
Oral anti-diabetic use	0.441	<0.001	-0.045	0.263

SYNTAX; the Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery, **HsCRP**; high sensitive C reactive protein.

The natural log transformation of SYNTAX score and hsCRP was used in bivariate analysis and in the linear regression model.

Table 2: Bivariate and multivariate associations of high sensitive troponin T

Variables	r	p	OR	CI 95% Lower-upper	p
Age, years	0.426	<0.001	1.06	1. 03-1.21	0.001
Hypertension	0.220	0.001			
Diabetes	0.604	<0.001	1.55	1.39-3.14	**0.001**
Ejection fraction, %	-0.177	<0.001			
SBP, mmHg	0.140	0.004			
DBP, mmHg	0.112	0.023			
Hs-cTnT	0.692	<0.001	1.64	1.42-2.13	**<0.001**
Creatinine, mg/dl	0.423	<0.001	1.89	1.32-3.84	0.001
Hs-CRP, mg/dl	0.485	<0.001	2.45	1.45-4.11	0.001
LDL-C, mg/dl	0.114	0.022			
Glucose, mg/dl	0.166	0.001			
Statin use	0.215	<0.001			
ACEI use	0.099	0.044			
Oral anti-diabetic use	0.442	<0.001			

SYNTAX; the Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery, **SBP;** systolic blood pressure, **DBP;** diastolic blood pressure, **Hs-cTnT;** high-sensitivety cardiac troponin T, **HsCRP**; high sensitive C reactive protein, **LDL-C**; low density lipoprotein cholesterol, **ACE-I;** angiotensin converting enzyme inhibitor.

OR: Odds ratio

The natural log transformation of SYNTAX score and hsCRP was used in bivariate analysis and in the multivariate logistic regression model.

Table 3: Bivariate and multivariate associations of high SYNTAX score.

CAD. In that study, the degree of stenosis of atherosclerotic lesions was classified as none (no luminal stenosis), mild (1 or more lesions with diameter stenosis of 20% to 50%), moderate (1 or more lesions with diameter stenosis of 50% to 70%) and severe lesions (1 or more lesions with diameter stenosis of ≥ 70%). But, SYNTAX score, which reflects the extent and complexity of CAD, was not used and coronary angiography was not applied in the study of Laufer et al. Previous one study reported that patients with non-calcified and with remodeled plaque showed higher hsTnT levels than those with normal vessels or with only calcified plaque [14]. This result supports that hs-cTnT levels would increase with complexity of coronary atherosclerosis as higher SYNTAX score.

Ndrepepa et al. [3] investigated to identify factors that were associated with increased levels of high-sensitivity troponin T in patients with stable (mostly) or unstable angina undergoing revascularization. They found that patients with upper tertile of hs-cTnT have higher incidence of multivessel disease compared patients with low tertile [3]. They also reported that the elevated level of hs-cTnT in patients with stable or unstable angina was significantly associated with reduced survival. In the study, Ndrepepa et al. did not use SYNTAX score. In our study, we used SYNTAX score for assessing the extent and complexity of CAD and found that hs-cTnT was an independent predictor of higher SYNTAX score. The cutoff value of hs-cTnT obtained by the ROC curve analysis was 9.62 ng/L for the prediction of higher SYNTAX score (sensitivity: 78.5%, specificity: 77.7%). Thus, our results suggest that hs-cTnT can be used to determine the need for revascularization in patients with stable CAD.

The pathophysiological mechanisms underlying the association between hs-cTnT with extent and complexity of CAD are still unclear. Traditionally, it was thought that release of cTn is equivalent to myocardial necrosis. However, in previous studies, even mild stable CAD was associated with quantifiable circulating levels of hs-cTnT in patients without acute coronary syndrome [2,3,11]. Recently, Sabatine et al. [15] showed that transient stress test–induced ischemia is associated with increase of cTnI as detected with an ultrasensitive cTnI assay. The level of cTnI increase was proportionally related to the extent of ischemia as assessed by nuclear perfusion imaging. Hickman et al. [16] reported that cardiac troponin may be released by ischemia alone, without necrosis. In that review [16], authors have suggested that the presence of membranous blebs in cardiac myocytes is enabling troponin to be released from cardiac cells due to ischemia alone, without necrosis. Moreover, some animal studies have suggested that short episodes of ischemia may result in the release of cTnT, without demonstration of cell death [17]. Because the more complex and severe lesions may increase proportion of ischemia, this could explain the higher levels of circulating troponin in these patients. However, in present study, the association between quantitative ischemia measurement and hs-cTnT level was not investigated. On the other hand, an alternative mechanism was suggested by the data of Rittersma et al. [18] who demonstrated that in 50% of the cases, organized older thrombi were visible at the site of the culprit lesion in acute myocardial infarction patients admitted for thrombectomy. This suggests that thrombus formation at the site of atherosclerotic lesions is not a rare event and is not necessarily linked to clinically manifest plaque rupture and vessel occlusion. Dislodgement of these thrombi in small coronary vessels could be a potential cause for micro-injury [11]. Therefore, thrombus formation not causing acute coronary syndrome at the site of more complex atherosclerotic lesions detected with higher SYNTAX score may be responsible for higher hs-cTnT release.

High sensitive cardiac troponin T level was independently associated with presence of diabetes in present study. Elevations of hs-cTnT are encountered frequently in population of diabetic patients [19]. Moreover, hs-cTnT levels in patients with diabetes appeared to be stable over time and associated with conventional CV risk factors [19]. Diabetes may predispose to elevations in the cardiac troponin level via a number of different mechanisms: increased ventricular mass, predisposition to silent ischemia, microvascular obstruction, more complex and severe coronary lesions and toxic effects of metabolites at abnormal concentrations [20,21]. Diabetes may create an additional bridge for the association between SYNTAX score and hs-cTnT in patients with stable CAD. Relationship between diabetes and SYNTAX score was showed in previous studies [11].

In present study, hs-cTnT was associated with age, hypertension, creatinine level, EF and hs-CRP level as well as diabetes and SYNTAX score in bivariate analysis. Previous studies reported the association between hs-cTnT with these parameters [22-25]. However, in our study, these relationships were not independent in multivariate regression analysis. Present studies reported that the risk factors such

as age, EF and renal dysfunction were associated with SYNTAX score [11]. Therefore, the strong relationship between hs-cTnT and SYNTAX score may be suppressed the relationship between hs-cTnT with these risk factors in multivariate analysis.

Clinical implication

Ndrepepa et al. [3] showed that hs-cTnT can reliably stratify the risk of mortality in patients with stable (mostly) or unstable angina. In or study, we demonstrated that hs-cTnT in patients with stable CAD was an independent predictor of higher SYNTAX score, which reflects the extent and complexity of CAD. The cutoff value of hs-cTnT obtained by the ROC curve analysis was 9.62 ng/L for the prediction of higher SYNTAX score (sensitivity: 78.5%, specificity: 77.7%). Thus, our results suggest that the assessment of hs-cTnT, in addition to clinical evaluation, can be a supplementary factor in determining the need for revascularization in patients with stable CAD. All stable CAD patients with higher hs-cTnT should be encouraged to undergo the coronary angiography.

Study limitation

Because of stress test was not performed to nearly half of patients in present study, quantitative ischemia measurement was not investigated. Therefore, in our study, it is difficult to investigate the relationship between ischemia and hs-cTnT.

Conclusion

Despite very low circulating concentrations, changes in hs-cTnT concentrations are associated with extent and complexity of CAD and diabetes in patients with stable CAD. In addition to clinical evaluation, the assessment of hs-cTnT level in patients with stable CAD can be a supplementary factor in determining ways of revascularization.

Acknowledgments

Conflicts of Interests: The authors report no conflicts of interest.

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