ORIGINAL ARTICLE

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Does SYNTAX score II predict poor myocardial perfusion in ST-segment elevation myocardial infarction?

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Abstract

Background: *SYNTAX score II (SS-II) has been demonstrated to predict long-term outcomes in unprotected left main or multiple vessels in patients with coronary artery disease. However, its prognostic value for patients with ST-segment elevation myocardial infarction (STEMI) remains unknown. The poor myocardial perfusion (myocardial blush grade [MBG] 0/1) after primary percutaneous coronary intervention (pPCI) has a negative prognostic value in patients with STEMI. We aimed to assess SS-II and its possible relationships with MBG 0/1 in patients with STEMI treated with pPCI.*

Methods: *The study included 477 patients with STEMI who underwent pPCI between October 2010 and May 2014. SYNTAX Score II and MBG were determined in all patients. Myocardial blush grade were divided into MBG 0/1 (poor myocardial perfusion) and MBG 2/3 (normal myocardial perfusion). Patients were divided into three tertiles: $SS\text{-}II_{low}$ (≤ 20), $SS\text{-}II_{intermediate}$ (20–26) and $SS\text{-}II_{high}$ (≥ 26).*

Results: *Compared with the $SS\text{-}II_{intermediate}$ and $SS\text{-}II_{low}$ tertiles, the $SS\text{-}II_{high}$ tertile had more MBG 0/1 (46.1%, 32.1% and 21.8%, p < 0.001, respectively). On multivariate logistic regression analysis, SS-II was an independent predictor of MBG 0/1 (hazard ratio 1.084, 95% confidence interval 1.050–1.119, p < 0.001). Receiver operating characteristic analysis identified SS-II > 24 as the best cut-off value predicting MBG 0/1 (sensitivity of 66%, specificity of 54%).*

Conclusions: *High SS-II is an independent predictor of MBG 0/1 in patients with STEMI undergoing pPCI.* (Cardiol J 2016; 23, 3: 317–323)

Key words: SYNTAX score II, myocardial perfusion, myocardial blush grade, ST-segment elevation myocardial infarction, primary percutaneous coronary intervention

Introduction

ST-segment elevation myocardial infarction (STEMI) is a major public health problem and a leading cause of death all over the world. The primary goal in the treatment of STEMI is to open infarct-related artery as soon as possible [1]. The best way to achieve this goal is rapid determination and reperfusion of the infarct-related artery by means of primary percutaneous coronary intervention (pPCI). Despite providing epicardial coronary blood flow, patients may suffer impaired myocardial reperfusion and have poor prognosis [2, 3]. Myocardial blush grade (MBG) is a simple visual angiographic assessment of myocardial perfusion in the infarct area, first described by van't Hof et al. [4]. The occurrence of MBG 0/1 is associated with a larger infarct size, lower left ventricular ejection fraction (LVEF), increased mortality, and congestive heart failure [5–8]. Therefore, MBG is often used as an endpoint in clinical trial. Recently, the SYNTAX score II (SS-II), as a combination of clinical factors and SYNTAX score, can predict long-term mortality and morbidity in patients with complex coronary artery disease [9–12]. However, its prognostic value in STEMI remains unknown.

We hypothesized that SS-II may predict the MBG 0/1 in patients with STEMI treated with pPCI. We also evaluated the predictive performance of the SS-II to predict MBG 0/1 in patients with STEMI undergoing pPCI.

Methods

Patient population

We analyzed the clinical and angiographic data of 497 consecutive patients diagnosed with acute STEMI within 12 h from the symptom onset in the period between October 2010 and May 2014. Patients undergoing conservative therapy (n = 6), thrombolysis (n = 3), or prior coronary artery bypass grafting (n = 3), poor imaging quality (n = 8) were excluded from the study. Moreover, patients with stroke in 3 months, active bleeding, recent trauma, or major surgery in 1 month, and contraindications to dual antiplatelet therapy to 12 months were not included in the study. STEMI was defined according to the following criteria: chest pain lasting longer than 20 min and associated with ST-segment elevation 1 mm in at least 2 limb electrocardiographic leads or 2 mm in at least 2 contiguous precordial leads, or the presence of new developed left bundle branch block pattern [1]. The diagnosis was confirmed by the elevation in troponin levels. The study protocol was approved by the hospital's institutional Review Board.

Stent and post-procedural management

All patients took aspirin (300 mg) and clopidogrel (300–600 mg, according to weight) loading dose before diagnostic coronary angiogram. Before pPCI, an intravenous bolus injection of heparin (100 IU/kg) was administered to achieve a target activated clotting time to 250–300 s except for the cases of tirofiban administration, whose loading dose was 50 IU/kg. If the infarct related artery had intracoronary large thrombus burden (thrombus score ≥ 3) [13] after predilatation was carried out, a thrombectomy catheter was used. Post-dilatation after stent implantation was prescribed at the operator's discretion. All patients were recommended 100 mg of aspirin and 75 mg of clopidogrel per day for at least 1 year. Continuation of antiplatlet and other cardiac medications were prescribed at the physician's discretion.

Determination of SS-II and MBG

The SS-II has been previously described in detail [11]. Briefly, SS-II includes 2 anatomical variables (SYNTAX score and left main coronary artery disease) and 6 clinical variables (age, creatinine clearance (CrCl), LVEF, sex, chronic obstructive pulmonary disease, and peripheral vascular disease). Because patients with STEMI were excluded from the initial SYNTAX score algorithm [14], therefore, we followed a definition that occluded infarct related artery scored as an occluded artery of < 3-month duration, which was used in the studies in STEMI patients [15, 16]. According to the baseline diagnostic angiograms, each coronary lesion producing ≥ 50% diameter stenosis in vessels ≥ 1.5 mm was scored separately, which was calculated using the algorithm available on the web site [17]. SYNTAX score (including left main coronary artery) was assessed by 2 independent and interventional cardiologists blinded to the clinical data, who had experience in calculating the SYNTAX score of > 100 patients before assisting in our study. The k value for interobserver variability that was used to estimate the SYNTAX scores was 0.75, while the k value for the intraobserver variability was 0.85. If there occurred any disagreement regarding the SYNTAX scores, the average of the values from the 2 readers was used as the final value.

Myocardial perfusion was assessed by MBG using the best projection for each coronary artery. Duration of cine filming was required to exceed 3 cardiac cycles in the washout phase to assess the

washout of myocardial blush. The effectiveness of myocardial reperfusion was assessed angiographically after PCI by MBG as the following [18]: MBG 0 — failure of dye to enter the microvasculature: minimal or no ground glass appearance ("blush") of the myocardium; MBG 1 — dye slowly enters but fails to exit the microvasculature: ground glass appearance that fails to clear from the microvasculature, and dye staining is present > 30 s later; MBG 2 — delayed entry and exit of dye from the microvasculature and dye is strongly persistent after 3 cardiac cycles of the washout phase and either does not or only minimally diminishes in intensity during wash out; MBG 3 — normal entry and exit of dye from the microvasculature. Blush of the myocardium that is either gone or only mildly persistent at the end of the washout phase. On the basis of post-intervention, the patients were divided into MBG 0/1 group (poor myocardial perfusion) and MBG 2/3 (normal myocardial perfusion) group as previous studies described [7, 18].

Statistical analysis

Continuous data were expressed as mean ± standard deviation and were compared using the ANOVA or Kruskal-Wallis test as appropriate. Categorical variables were expressed as percentages and compared by the χ^2 test or Fisher's exact test as appropriate. Multivariate logistic regression analysis was performed to ascertain variables independently associated with MBG 0/1 after pPCI. Variables with a p value of < 0.10 in an univariate analysis were included in the model: age, smoking, sex, the length of stent in culprit lesion, stent diameter, Killip classification, thrombectomy, tirofiban, LVEF, onset to balloon, thrombosis, hypertension, diabetes mellitus and SS-II (per 1 point increase). Receiver operating characteristic (ROC) curve was used to determine the cut-off point for the SS-II in the prediction of MBG 0/1. For all analyses, a 2-sided p < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS software (version 17, SPSS Inc., Chicago, IL).

Results

Patients and baseline characteristics

From October 2010 and May 2014, a total of 477 patients with a mean age of 60.5 ± 10.6 years were enrolled in the study. For our analysis, the overall SS-II in the studied population did not demonstrate a normal distribution, ranging from 8 to 73, with a median of 24. The SS-II tertiles were SS-II$_{low}$ ≤ 20 (n = 158), 20 < SS-II$_{intermediate}$ < 26

(n = 151), SS-II$_{high}$ ≥ 26 (n = 168). Baseline clinical characteristics of the studied population across the 3 tertiles were summarized in Table 1. Patients in the SS-II$_{high}$ tertile were less likely to be prescribed aspirin and clopidogrel at discharge, although there was no difference in angiotensin converting enzyme inhibitor, beta-blocker and statin. Other clinical characteristic such as diabetes mellitus, previous myocardial infarction, hyperlipidemia, chronic obstructive pulmonary disease, family history of coronary artery disease were similar among SS-II tertiles.

Angiographically, patients in the SS-II$_{high}$ tertile were more likely to have 3-vessel diseases, unprotected left main disease, small vascular disease, diffuse disease, calcification disease and MBG 0/1 after PCI, compared with lower 2 tertiles. Intra-aortic balloon pump, thrombosis disease, bifurcation disease, chronic total occlusion disease, turtous disease, anterior infarction, no-flow before pPCI, pre- and post-dilatation, tirofiban and thrombectomy did not differ among SS-II tertiles. The diameter and length of stents were significantly shorter in SS-II$_{high}$ tertile than those in the other 2 tertiles (p < 0.001 and p = 0.01, respectively). Angiographic and procedural characteristics across the 3 tertiles were summarized in Table 2.

Considering MBG 0/1 after pPCI, while frequency of MBG 0/1 in the SS-II$_{high}$ tertile was 53.0%, whereas the frequency of MBG 0/1 in the SS-II$_{intermediate}$ tertile and SS-II$_{low}$ tertile was 41.1% and 26.6% separately (p = 0.033 and p < 0.001, respectively). Patients in the SS-II$_{high}$ tertile had higher MBG 0/1 rates. On multiple regression, the SS-II was shown to be an independent predictor for MBG 0/1 (hazard ratio [HR] 1.084, 95% confidence interval [CI] 1.050–1.119, p < 0.001). Sex (HR 0.368, 95% CI 0.212–0.640, p < 0.001), diabetes mellitus (HR 1.774, 95% CI 1.024–3.074, p = 0.041), thrombectomy (HR 0.525, 95% CI 0.319–0.865, p = 0.011), the length of stent in culprit lesion (HR 1.041, 95% CI 1.007–1.077, p = 0.019) and stent diameter (HR 0.381, 95% CI 0.268–0.541, p < 0.001) were other independent predictors for MBG 0/1 on multivariate logistic regression analysis (Table 3). In addition, ROC analysis identified SS-II > 24 as the best cut-off value predicting MBG 0/1 (sensitivity of 66%, specificity of 54%, area under curve: 0.646, 95% CI 0.597–0.696, p < 0.001; Fig. 1).

Discussion

In this study, we found that SS-II was independently associated with the development of MBG

Table 1. Baseline clinical characteristics according to SYNTAX score II (SS-II) tertiles for primary percutaneous coronary intervention.

Variable	SS-II$_{low}$, ≤ 20 (n = 158)	SS-II$_{intermediate}$, 20–26 (n = 151)	SS-II$_{high}$, ≥ 26 (n = 168)	P
Age [years]	52.0 ± 9.0	60.9 ± 8.4	68.2 ± 7.4	< 0.001*
Female	8/158 (5.1%)	28/151 (18.5%)	102/168 (60.7%)	< 0.001*
Weight [kg]	71.4 ± 7.0	69.4 ± 7.6	62.5 ± 7.6	< 0.001*
Smoking	60/158 (38.0%)	47/151(31.1%)	31/168 (18.5%)	< 0.001*
Diabetes mellitus	21/158 (13.3%)	24/151 (15.9%)	33/168 (19.6%)	0.296
Hypertension	54/158 (34.2%)	72/151 (47.7%)	81/168 (48.2%)	0.017*
Previous MI	5/158 (3.2%)	14/151 (9.3%)	11/168 (6.5%)	0.086
Hyperlipidemia	4/158 (2.5%)	2/151 (1.3%)	5/168 (3%)	0.644
Cerebrovascular disease	10/158 (6.3%)	24/151 (15.9%)	28/168 (16.7%)	0.009*
PVD	0/158 (0%)	5/151 (3.3%)	2/168 (1.2%)	0.035*
COPD	5/158 (3.2%)	4/151 (2.6%)	8/168 (4.8%)	0.565
Family history of CAD	12/158 (7.6%)	8/151 (5.3%)	8/168 (4.8%)	0.519
Left ventricular ejection fraction;	58.6 ± 8.1	54.4 ± 10.4	52.0 ± 11.2	< 0.001*
Killip classification 3–4	3/158 (1.9%)	6/151 (4.0%)	14/168 (8.3%)	0.022*
Creatinine [mL]	67.4 ± 11.9	68.1 ± 16.8	71.7 ± 20.3	0.046*
Clearance of creatine	116.3 ± 25.2	100.1 ± 24.4	73.9 ± 21.2	< 0.001*
Aspirin	157/158 (99.4%)	141/151 (93.4%)	150/168 (89.3%)	0.001*
Clopidogrel	154/158 (97.5%)	142/151 (94.0%)	151/168 (89.3%)	0.018*
ACEI	58/158 (36.7%)	61/151 (40.4%)	54/168 (35.2%)	0.307
Beta-blocker	98/158 (62.0%)	92/151 (60.9%)	100/168 (59.5%)	0.898
Statin	140/158 (88.6%)	133/151 (88.1%)	138/168 (82.1%)	0.171

*p < 0.05; data are expressed in numbers (percentages), mean ± standard deviation, percentages are rounded; MI — myocardial infarction; PVD — peripheral vascular disease; COPD — chronic obstructive pulmonary disease; CAD — coronary artery disease; ACEI — angiotensin--converting enzyme inhibitor

0/1 in the setting of STEMI. SS-II > 24 had a 66% sensitivity and 54% specificity for predicting MBG 0/1 in patients undergoing pPCI.

Many studies show that MBG 0/1 is a significant independent predictive marker of mortality, microvascular circulation, and myocardial perfusion in patients undergoing pPCI after STEMI [19, 20]. The previous studies reported MBG 0/1 after pPCI was 51.1–66% [18, 21], however we found the frequency of MBG 0/1 was 40.5%. In our study, most patients were treated with simple technique process in complicated lesions in order to rescue more cardiomyocytes as soon as possible. Complicated techniques such as mini-crush stenting, culotte stenting, V-stenting, or T-stenting were not used in bifurcation lesion. Diffused disease was treated by using short-stent strategy.

We also found that SS-II was an independent predictor of MBG 0/1. Patients in SS-II$_{high}$ tertile have a more complex anatomy of coronary artery, such as left main lesion, 3-vessels disease, diffuse disease, calcification disease, and small vascular disease, and increased medical co-morbidities, such as peripheral vascular disease, cerebrovascular disease, decreased CrCl, older and fewer smokers. Several mechanisms may explain the association between SS-II and MBG 0/1. First, diffuse disease often signifies an impaired microcirculatory resistance index [22]. Second, collateral circulation to the microvascular bed will be insufficient if the donor artery is also diseased. Third, oxidative stress is increased in acute coronary syndrome with the severity of coronary artery disease, whereas oxidant stress reduces the vasodilatatory effects of nitric oxide, adenosine, and prostacyclin [23–25]. Interestingly, there were fewer smokers in the patient group with MBG 0/1. This may be related to the smokers' paradox, which means smoking does confer a biologically mediated benefit on survival [26, 27]. Smoking causes prolonged activation of the sympathetic nervous system and acute release of epinephrine, these effects could in theory contribute to a mechanism such as myocardial preconditioning. Therefore, to improve microvascular cir-

Table 2. Angiographic and procedural characteristic according to SYNTAX score II (SS-II) tertiles for percutaneous coronary intervention (PCI).

Variable	SS-II$_{low}$, ≤ 20 (n = 158)	SS-II$_{intermediate}$, 20–26 (n = 151)	SS-II$_{high}$, ≥ 26 (n = 168)	P
Number of diseased vessels:				< 0.001*
1-vessel disease	99 (62.7%)	74 (49.0%)	79 (47%)	
2-vessel disease	50 (31.6%)	54 (35.8%)	44 (21.2%)	
3-vessel disease	9 (5.7%)	23 (15.2%)	45 (26.8%)	
Unprotected left main lesion	1/158 (0.6%)	1/151 (0.7%)	4 (2.4%)	< 0.001*
Small vascular lesion	3/158 (1.9%)	5/151 (3.3%)	15/168 (8.9%)	0.007*
Chronic total occlusion	3/158 (1.9%)	6/151 (4.0%)	12/168 (7.1%)	0.067
Diffuse lesion	6/158 (3.8%)	14/151 (9.3%)	26/168 (15.5%)	0.002*
Calcification lesion	2/158 (1.3%)	5/151 (3.3%)	17/168 (10.1%)	0.001*
Bifurcation lesion	21/158 (13.3%)	26/151 (17.2%)	27/168 (16.1%)	0.616
Thrombose lesion	115/158 (72.8%)	109/151 (72.2%)	118/168 (70.2%)	0.867
Turtous lesion	0/158 (0%)	2/151 (1.3%)	2/168 (1.2%)	0.472
Intra-aortic balloon pump	0/158 (0%)	0/151 (0%)	3/168 (1.8%)	0.110
Thrombectomy	49/158 (31%)	38/151 (25.2%)	38/168 (22.6%)	0.213
Tirofiban therapy	48/158 (30.4%)	46/151 (30.5%)	54/168 (32.1%)	0.927
Balloon predilatation	106/158 (67.1%)	107/151 (70.9%)	114/168 (67.9%)	0.753
Balloon postdilatation	40/158 (25.3%)	27/151 (17.9%)	31/168 (18.5%)	0.191
No-flow before PCI	134/158 (84.8%)	137/151 (90.7%)	156/168 (92.9%)	0.051
No-flow after PCI	12/158 (7.6%)	19/151 (12.6%)	35/168 (20.8%)	0.002*
Myocardial blush grade 0/1	42/158 (26.6%)	62/151 (41.1%)	89/168 (53.0%)	< 0.001*
Total length of stent	25 ± 9.9	23 ± 11.3	20 ± 12.9	0.01*
Stent diameter	2.8 ± 0.9	2.6 ± 1.1	2.3 ± 1.3	< 0.001*
Anterior infarction	64/158 (40.5%)	69/151 (45.7%)	67/168 (39.9%)	0.522

*p < 0.05; values are n/N (%) or mean ± standard deviation

Table 3. Predictors of the myocardial blush grade 0/1.

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P	OR (95% CI)	P
Age	0.989 (0.957–1.022)	0.514	0.993 (0.965–1.022)	
Sex	0.351 (0.188–0.655)	0.001	0.368 (0.212–0.640)	< 0.001*
The length of stent	1.039 (1.004–1.076)	0.029	1.041 (1.007–1.077)	0.013*
Hypertension	1.236 (0.810–1.886)	0.325	1.230 (0.808–1.873)	
Diabetes mellitus	1.694 (0.967–2.968)	0.066	1.774 (1.024–3.074)	0.041*
Stent diameter	0.387 (0.270–0.554)	< 0.001	0.381 (0.268–0.541)	< 0.001*
Left ventricular ejection fraction	1.006 (0.981–1.031)	0.628	1.005 (0.981–1.031)	
Smoking	0.744 (0.461–1.200)	0.226	0.765 (0.477–1.227)	
Killip classification 3/4	1.736 (0.620–4.863)	0.294	1.692 (0.609–4.706)	
Onset to balloon	1.308 (0.810–2.114)	0.272	1.000 (0.999–1.001)	
Thrombectomy	0.525 (0.314–0.877)	0.014	0.525 (0.319–0.865)	0.009*
Tirofiban	0.437 (0.763–1.872)	0.437	1.201 (0.769–1.877)	
Thrombosis lesion	0.879 (0.548–1.411)	0.595	0.907 (0.567–1.450)	
SYNTAX score II	1.093 (1.034–1.156)	0.002	1.084 (1.050–1.119)	< 0.001*

*p < 0.05; OR — odds ratio; CI — confidence interval
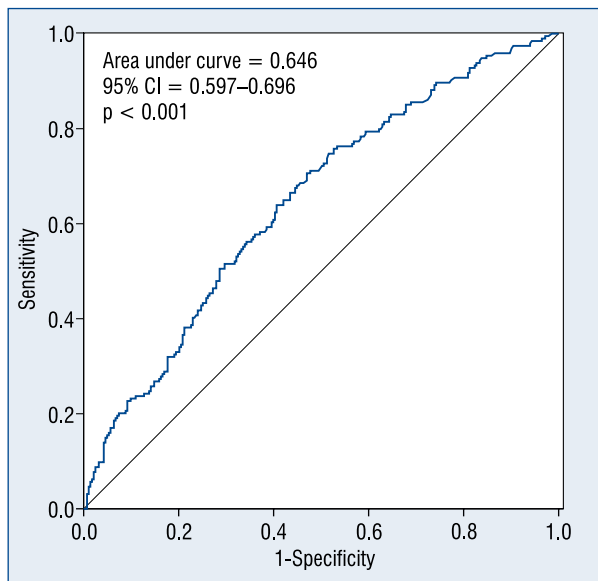
Figure 1. Receiver operating characteristic curve analysis for SYNTAX score II in predicting myocardial blush grade; CI — confidence interval.

culation, pharmacologic agents such as nicorandil and nitroprusside and thrombus aspiration should be used in high SS-II tertile in STEMI.

To the best of our knowledge, the relationship between SS-II and MBG has not previously been investigated. Our results demonstrate for the first time the predictive value of SS-II and MBG 0/1 in the setting of STEMI treated with pPCI. We found that high SS-II was significant and correlated with MBG 0/1. In this study, with the help of SS-II, we can obtain the predictive information about MBG after primary PCI. These results are in agreement with studies showing that the SS-II has a risk-predictive value in patients undergoing elective PCI [11, 28].

Limitations of the study

Our study has some limitations. First, this was a retrospective study based on a relatively small number of patients and the study population was from a single center. Second, the method of measurement of SYNTAX score, which is one of the SS-II parameters, presented a limitation. Third, because there was a male dominance in patients in our study, the results may not be applicable in groups with female dominance.

Conclusions

SYNTAX score II, combined of clinical factors and SYNTAX score, is an independent predictor

of the MBG 0/1 in patients with STEMI treated with pPCI. In addition, high SS-II may be helpful in identifying high-risk patients and determine appropriate treatment strategies. SYNTAX score II can be calculated before primary PCI, thereby facilitating risk prediction for STEMI patients, even prior to revascularization.

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Conflict of interest: None declared

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