Comparison of syntax score and syntax score II to predict peri-procedural myocardial injury during percutaneous coronary intervention

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Abstract

Background

Peri-procedural myocardial infarction (PPI) is an increase in cardiac enzymes during percutaneous coronary intervention. The development of this condition is associated with a poor prognosis. In this study, we aimed to evaluate the development of PPI in patients undergoing elective percutaneous coronary intervention and the factors that predict patients who developed PPI.

Method:

A total of 160 consecutive patients who underwent percutaneous coronary intervention were enrolled in the study. Patients were divided into two groups as PPI developing and not developing PPI. The clinical characteristics, laboratory and angiographic features of groups were compared. The SS and SS II was calculated by using the online calculator.

Results

PPI was developed in 44 (27.5%) patients during PCI procedure. SS, SSII, glomerular filtration rate (GFR), age were identified as independent predictors of PPI. A higher rate of PPI was observed in those with SS II over 35. When compared of the ROC curves showed that area under curve of SS II was larger than that of SS (AUC 0.855 vs. 0.741, p = 0.039)

Conclusion

In the study; age GFR, SS and SSII were observed to be independent predictors of PPI. SSII may be a more useful tool than SS for prediction PPI during elective percutaneous coronary intervention.

Introduction

Peri-procedural myocardial injury (PPI) is a common situation during percutaneous coronary intervention (PCI) [1, 2]. PPI can be caused by plaque shift, side branch occlusion, microvascular injury due to distal embolization during PCI procedure[3]. Studies have shown that even small elevations in cardiac biochemical markers are associated with poor clinical outcomes[4]. Therefore, studies have been conducted on various markers for prediction of PPI, which may develop prior to the procedure.

Syntax score (SS) is an anatomic and morphologic scoring system that quantitatively characterizes coronary vasculature according to the complexity of obstructive coronary lesions. [5, 6]. The syntax score which is used to describe the severity of coronary artery disease (CAD) predicts post-PCI events[7]. The syntax score II is a newer scoring system used to show the survey of patients directed to coronary artery
bypass gref (CABG) or PCI [6]. Although the association between the complexity-severity of CAD and PPI has been shown[8]. The relationship between SS II and SS in patients with PPI hasn’t been studied yet.

We aimed to investigate the association between PPI and SS, SS II, in patients with stable CAD who underwent PCI.

**Method**

In this study, a total of 160 patients with stable CAD who had objective ischemia symptoms and thus, underwent PCI procedure between January 2017 and June 2017, and who were eligible for the study conditions were included. Patients who underwent stent implantation in the lesions over 30 mm with or without side branches, and those undergone stent implantation providing a side branch of at least 2 mm in diameter in the case of the the lesions under 30 mm and the patients who underwent bifurcation procedure were included in this study[9]. Patients who previously underwent stent implantation or CABG, those having unstable angina pectoris, acute coronary syndrome, and which complicated during the procedure due to the development of dissection or no reflow were exluded from the study.

**Angiographic and Laboratuary parameters analysis**

The angiography was performed in all patients with a transfemoral approach. 7 Fr catheters were used with the Seldinger method. Patients to undergo PCI procedures were given klopidogrel (600mg), 100 mg ASA and 70 IU/Kg unfractionated heparin. SS II and SS were calculated using a calculator (http://www.syntaxscore.com) (Figure1). Two cardiologists who were blinded to the study evaluated and calculated SS II and SS. In angiograms with conflicting results, both cardiologists evaluated these angiograms a consensus was provided. Any large coronary vessel with a diameter narrowing by 50 percent or more was considered as important stenosis.

**Laboratuary analysis**

Blood samples collected at admissions were used for evaluations. The Cockroft-Gault formula was used to calculate the glomerular filtration rate (GFR).

Modified Simpson method was used for left ventricular ejection fraction (EF). All patients gave written or verbal consents. This study protocol was confirmed by the local ethics committee in conformity with the Declaration and Good Clinical Practice guidelines.

Cardiac biomarkers were obtained from venous blood samples that were collected before, at 8-24h and at 24 h after the procedure. Troponin-I were measured with immunoassays (Abbot Park, IL 60064,USA). PPI was defined by elevation of cTnl values >5×99 th percentile upper normal in patients with normal values (≤ 99th percentile upper normal). In addition, symptoms of myocardial ischaemia or new ischemic electrocardiographic changes or showing a new regional wall motion disnormality are required.

**Statistycal analysis**
The data analysis was applied using SPSS software (version 20.0, SPSS Inc., Chicago, Illinois) and MedCalc Software (12.7.8, Mariakerke, Belgium). Categorical variables compared with the χ² or Fisher’s exact test was summarized as percentages. Continuous variables were stated as mean ± Standard deviation. The Kolmogorov–Smirnov test was used to assess distribution of continuous variables. To predict PPI, age, left main coronary artery, peripheral arterial disease (PAH), chronic obstructive pulmonary disease (COPD), GFR, EF, SS, and SSII were analysed. The parameters with p< 0.05 were included in the multiple logistic analysis. The cut-off values of SS II and SS for prediction of periprosedural injury were determined by using receiver-operating characteristic (ROC) analysis. Bland Altman test was used for comparison of ROC curves analysis.

Results

In 44 (27.5%) patients developed PPI during PCI procedure. Angiographic characteristics, clinical features of groups are shown in Table 1. Age, presence of LMCA disease, GFR, EF, COPD, PAH, SS and SS II were different in two groups. 102 patients had SSII < 35 and 58 had SSII ≥ 35. There were differences between two groups in age, heart rate, presence of LMCA disease, GFR, EF, PAH, double vessel PCI and PPI (Table 2).
|                              | NO PPI (n = 116) | PPI (n = 44) | p     |
|------------------------------|------------------|--------------|-------|
| Age (years)                  | 61.5 ± 10.5      | 72.6 ± 9.15  | <0.001|
| Sex (male)(% )               | 34(29.3)         | 10(22.7)     | 0.405 |
| Diabetes Mellitus (n, %)     | 44(37.9)         | 12(27.3)     | 0.207 |
| Hypertension (n ,% )         | 65(56)           | 31(70.5)     | 0.096 |
| Hyperlipidemia (n, %)        | 34(29.3)         | 14(31.8)     | 0.757 |
| Smoking (n, % )              | 56(48.3)         | 21(47.7)     | 0.951 |
| SBP (mmHg)                   | 128.1 ± 26.9     | 130.6 ± 36.3 | 0.765 |
| DBP (mmHg)                   | 74.7 ± 18.0      | 75.0 ± 23.2  | 0.699 |
| Heart Rate(p/min)            | 70.5 ± 10.2      | 68.2 ± 11.1  | 0.256 |
| Bifurcation lesions          | 30(25.8)         | 17(38.6)     | 0.113 |
| Glucose (mg/dL)              | 129 ± 53         | 123 ± 57     | 0.464 |
| LDL-C (mg/dL)                | 123.3 ± 35.6     | 131.8 ± 33.1 | 0.174 |
| HDL- C (mg/dL)               | 41.6 ± 9.6       | 39.0 ± 7.9   | 0.113 |
| TG (mg/dL)                   | 186.5 ± 32.2     | 176.2 ± 35.6 | 0.083 |
| LMCA (n ,% )                 | 8(6.9)           | 10(22.7)     | 0.005 |
| GFR (mL/min/1.73 m2)         | 102.0 ± 21.5     | 84.8 ± 24.8  | <0.001|
| EF (%)                       | 54.6 ± 6.1       | 48.7 ± 8.1   | <0.001|
| COPD                         | 13(11.2)         | 12(27.3)     | 0.012 |
| PAD                          | 10(8.6)          | 18(40.9)     | <0.001|
| Double-vessel PCI            | 18(15.5)         | 12(27.3)     | 0.089 |
| Syntax score                 | 19.5 ± 7.4       | 27.0 ± 8.8   | <0.001|
| Syntax score II              | 29.7 ± 7.8       | 44.8 ± 9.6   | <0.001|
| LAD                          | 43(37.1)         | 10(22.7)     | 0.227 |
| CX                           | 41(35.3)         | 19(43.2)     |       |

LMCA: Left Main Coronary Artery, LAD: Left ascending artery, CX: Circumflexial artery, RCA: Right coronary artery, PAD: peripheral artery disease, CAPD: Chronic Obstructive Pulmonary Disease, EF: Ejection Fraction
|                     | NO PPI  | PPI     | p       |
|---------------------|---------|---------|---------|
|                     | (n = 116) | (n = 44) |         |
| RCA                 | 32(27.6)  | 15(34.1) |         |

**LMCA: Left Main Coronary Artery, LAD: Left ascending artery, CX: Circumflexial artery, RCA: Right coronary artery, PAD: peripheral artery disease, CAPD: Chronic Obstructive Pulmonary Disease, EF: Ejection Fraction**

| Table 2                                                                 |
|-------------------------------------------------------------------------|
| The baseline clinical and laboratory characteristics of the patients   |
| according to SS II subgroups                                           |
|                                                                         |
| | SS II < 35 | SS II > 35 | p       |
| | (n = 102)  | (n = 58)    |         |
| Age (years)                | 60.4 ± 10.1 | 71.8 ± 9.5 | < 0.001 |
| Sex, female (n, %)         | 24(23.5)    | 20(34.5) | 0.136 |
| Diabetes Mellitus (n, %)   | 33(32.4)    | 23(39.7) | 0.352 |
| Hypertension (n, %)        | 53(52)      | 43(74.1) | 0.006 |
| Hyperlipidemia (n, %)      | 28(27.5)    | 20(34.5) | 0.351 |
| Smoking (n, %)             | 52(51)      | 25(43.1) | 0.338 |
| Heart Rate (p/min)         | 70.3 ± 10.8 | 65.0 ± 9.9 | 0.002 |
| Glucose (mg/dL)            | 121 ± 49    | 139 ± 60 | 0.056 |
| LDL-C (mg/dL)              | 125.0 ± 35.5 | 126.8 ± 34.5 | 0.758 |
| HDL-C (mg/dL)              | 41.7 ± 9.7  | 39.4 ± 8.2 | 0.142 |
| TG (mg/dL)                 | 184.2 ± 32.0 | 182.6 ± 35.6 | 0.762 |
| LMCA disease               | 3(2.9)      | 15(25.9) | < 0.001 |
| GFR (mL/min/1.73 m2)       | 108.3 ± 18.9 | 77.9 ± 18.3 | < 0.001 |
| Ejection Fraction (%)      | 55.8 ± 5.2  | 48.0 ± 7.5 | < 0.001 |
| COPD (n, %)                | 12(11.8)    | 13(22.4) | 0.075 |
| PAD (n, %)                 | 6(5.9)      | 22(37.9) | < 0.001 |
| Double-vessel PCI (n, %)   | 8(7.8)      | 22(37.9) | < 0.001 |
| Peri-prosedural injury (n,%)| 11(10.8) | 33(59.6) | < 0.001 |

LDL-C low-density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol, TG: triglyceride, GFR: glomerular filtration rate, LMCA: left main coronary artery, PAD: peripheral arterial disease, COPD: chronic obstructive pulmonary disease, EF: ejection fraction.
In the univariate analysis Age, COPD, LMCA disease, PAD, GFR, EF, SS, SSII found to be significant for PPI. In multivariate analysis: Age ([OR] = 1.071, 95% [CI]: 1.006–1.140, P = 0.031), GFR ([OR] = 1.056 [CI]: 1.015–1.095, P = 0.007), SS ([OR] = 1.075 [CI]: 1.003–1.153, P = 0.042), and SS II ([OR] = 1.176 [CI]: 1.082–1.278, P < 0.001) were found independent predictors for PPI (Table 3).

|                          | Univariate analysis | Multivariate analysis |
|--------------------------|---------------------|-----------------------|
|                          | OR, 95%CI           | P value               | OR          | 95% CI      | P value   |
| Age                      | 1.117 (1.070–1.166) | < 0.001               | 1.071       | 1.006–1.140 | 0.031     |
| COPD                     | 0.337 (0.140–0.811) | 0.012                 |             |             |           |
| LMCA                     | 0.252 (0.092–0.689) | 0.005                 |             |             |           |
| PAD                      | 0.136 (0.056–0.330) | < 0.001               |             |             |           |
| GFR                      | 0.966 (0.950–0.983) | < 0.001               | 1.054       | 1.015–1.095 | 0.007     |
| EF                       | 0.893 (0.848–0.941) | < 0.001               |             |             |           |
| Syntax score             | 1.105 (1.056–1.156) | < 0.001               | 1.075       | 1.003–1.153 | 0.042     |
| Syntax Score II          | 1.123 (1.079–1.168) | < 0.001               | 1.176       | 1.082–1.278 | < 0.001   |

GFR: glomerular filtration rate, LMCA: left main coronary artery, PAD: peripheral arterial disease, COPD: chronic obstructive pulmonary disease, EF: ejection fraction,

ROC curve was carried out in order to determine the best cut off value for SSII and SS in prediction of PPI. The optimal threshold point of SS in the prediction of PPI was > 22, with 68.1% specificity and 79.5% sensitivity (AUC: 0.741, 95% CI: 0.650–0.833, P < 0.001). The optimal threshold point of SS II in the prediction of PPI was > 35, with 75.0% specificity and 79.5% sensitivity (AUC: 0.8551, 95% CI: 0.795–0.916, P < 0.001). Comparing the ROC curves showed that SSII is a better PPI predictor than SS (0.855 vs 0.741, p = 0.039) (Fig. 2).

**Discussion**

In the study, we aimed to assess the effects of SS and SSII on the development of PPI in patients who undergo PCI procedure. In our work, the SSII was shown to be superior to the SS in predicting the development of PPI in patients with stable coronary artery disease who underwent elective PCI procedure.

PPI development after PCI is a very common situation and has prognostic significance[10]. Many studies have shown that even small elevations in enzyme levels following PCI procedure increase risk of death and associated with a worse prognosis[11]. Therefore, determination of the parameters that predicting the development of PPI after PCI may be important in order to prevent development of PPI prior to the procedure, to improve the treatment methods, or in premedication.
Studies analyzing myocardial involvement such as MR and IVUS have shown that distal embolization or side branch narrowing during the PCI procedure are two important factors in the development of PPI. In addition, scorings carried out during angiography have indicated that plaque burden, bifurcation anatomy, and complex lesions predict PPI development.

SS is a risk score designed to be helpful in directing physicians to prefer CABG or PCI in patients with triple-vessel disease. In a previous study, SS was shown as a parameter predicting PPI compared to various risk scores. Supporting to the previous study, in our study we found that SS was significantly higher in PPI group.

Studies have shown that PPI development was more common after PCI procedure in patients with chronic renal failure and that low GFR was an independent predictor of PPI development. Similarly, in our study GFR was to be an independent predictor of PPI development.

Association between multiple vascular disease and COPD has been shown in studies. In a study, have been shown that the patients with COPD who underwent PCI procedure had a higher incidence of myocardial injury. Supporting this, in the present study higher incidence of COPD was observed among the patients who developed PPI. However, according to multivariate analysis, COPD was not an independent predictor.

SS II anatomical is a score developed by adding different parameters to SS, including age, sex, creatinine clearance, peripheral vascular disease, COPD, left ventricular EF, and LMCA disease. In a study by Yesin et al. SSII was shown to be superior to SS in predicting of no reflow pathophysiology of which includes common factors with PPI. In our study, we showed that the association between PPI development and SSII was higher than SS. Parameters such as age, COPD and low GFR are known to be associated with microvascular circulation disorder. Because of SS II to include these additional parameters may be partially explain why SSII is PPI.

In conclusion, our study showed that SSII is better than of SS in the predicting of the risk for PPI development. SSII may be considered to be a more useful tool than SS in order to improve the existing treatment that aim improving clinical outcomes for patients with PCI and to evaluate the new strategies to reduce PPI. However, we believe that it may be beneficial to evaluate this result with further larger studies.

Study limitations:

This study was a single-center study with a small number of patients. In addition, short- and long-term follow-ups of the patients who developed PPI were not performed. As another limitation, patients with unstable angina pectoris and those underwent grafting after CABG were not included in the study.

Declarations
Acknowledgement

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Figures
Figure 1

The left coronary artery system of patient. Syntax Score = 22 and Syntax Score II = 41.8 (The Patient's age: 79; Creatinine clearance: 90; LVEF (%): 45 Gender: Female; Left Main Lesion: No; Chronic Obstructive Pulmonary Disease: Yes; Peripheral artery Disease: No
Figure 2

The comparison of the area under the curves (AUC) of ROC curve analyses for syntax score and syntax score II