Research Article

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Predictive value of SYNTAX score on in-hospital outcomes after Percutaneous Coronary Intervention (PCI)

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Background: The SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) score has emerged as an anatomical-based tool that quantitatively determines the coronary vasculature due to 9 criteria such as number, location, complexity, and functional impact of angiographically obstructive lesions. Because of the fact that the same study of this scoring system has not been performed in Iran, we aimed to do this study to predict the value of SYNTAX score on in-hospital outcomes after Percutaneous Coronary Intervention (PCI) in patients referred to Heshmat Hospital, Rasht, Iran.

Methods: The present cross-sectional study conducted at Heshmat Heart Center, Rasht, Iran. Patients admitted for elective or primary PCI of coronary arteries due to the acute coronary syndrome, ST segment elevation myocardial infarction and chest pain. Each patient's medical data such as clinical characteristics, procedures and adverse events collected from data bank and medical records. The SYNTAX score was calculated using SYNTAX score version 2.58 (SYNTAX SCORE I, www.syntaxscore.com). All in-hospital outcomes were entered in SPSS software version 23 and analysis was done.

Results: In this study 431 patients underwent PCI. The average age of the samples was 57.10 ± 10.67 years (range 23-85 years). However, the average SYNTAX score in the samples was 15.93 ± 5.53 points. The mean SYNTAX score is significantly higher in positive cases of CVA after PCI (p=0.001), hypotension (p=0.001), arrhythmia (p=0.001), in-hospital death (p=0.002), unsuccessful PCI (p=0.001), CIN (p=0.001) and total adverse event incidence (p=0.001) but not with vascular disorders (p=0.769). ROC curve for predicting outcomes of PCI in the patients based on SYNTAX score, showed the total cutoff point of it was 19.5 and under curve area was calculated 0.79 (CI=0.716-0.865, p<0.0001).

Conclusion: It seems that SYNTAX score utilization for samples with anatomic complexity, can predict the in-hospital outcomes in our setting.

Keywords: SYNTAX score, hospital, Percutaneous coronary intervention

Introduction

The SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) score has emerged as an anatomical-based tool that quantitatively determines the coronary vasculature due to 9 criteria such as: Number, location, complexity, and functional impact of angiographically obstructive lesions. The coronary arteries are classified based on the ARTS (Arterial Revascularization Therapies Study) investigators' modification of the American Heart Association classification of coronary tree segments [1,2]. The SYNTAX score (SS) established as part of the SYNTAX trial, which objectively characterizes and quantifies the extension and severity of coronary artery disease (CAD) [3]. Evaluation of the SS within the SYNTAX trial and external datasets indicated the SS ability in predicting adverse ischemic events in patients undergoing percutaneous coronary intervention (PCI) within indicated [4-6]. The SS usage is generalized to miscellaneous clinical settings [3-15]. Percutaneous coronary intervention (PCI) is an ineffective therapeutic technique for people who suffer from coronary artery disease (CAD). Although these techniques' peri-procedural complications declined over time and become one of the most extensively applied treatments in cardiology, still it has high risks in patients with complex coronary lesions. The complex lesion subsets in Interventional cardiology include vessel bifurcation, the presence of thrombus, the involvement of the left main trunk, and the increasing number of difficult lesions that are now treated [16-18]. Therefore, it is essential to determine the risk of complications in patients undergoing PCI for complex lesions [19]. The risk scoring system will help cardiologists to predict in-hospital outcomes and make an informed clinical decision. Identification

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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and evaluation of the clinical risk factors facilitates comparison of therapeutic approaches efficacy.

According to the importance of predicting cardiac outcomes for cardiologists and the above considerations, also lack of the same study of this scoring system in Iran we decided to perform this study to predict the value of SYNTAX score on in-hospital outcomes after Percutaneous Coronary Intervention (PCI) in patients referred to Heshmat Hospital, Rasht, Iran.

Methods

This cross-sectional study performed in Heshmat heart center. In this research, we evaluated the SYNTAX score regarding in-hospital outcomes of patients undergoing PCI. Patients admitted for PCI of coronary arteries between April 2012 and April 2013, either selectively or primarily due to acute coronary syndrome, ST segment elevation myocardial infarction and chest pain were included. We performed all interventions based on the indications in the latest guidelines following standard techniques, and before the procedure, all patients provided written informed consent. The exclusion criteria contain patients underwent balloon angioplasty and/or stenting in coronary arteries with Drug-Eluting Stent (DES) or Bare Metal Stents (BMS), patients with a history of previous coronary artery bypass grafting (CABG). Also, patients unwilling to consent or follow-up after PCI was excluded.

Each patient medical data such as clinical characteristics, procedures and adverse events collected from data bank and medical records. The SYNTAX score was calculated by an Interventional cardiologist using dedicated software (www.SYNTAXscore.com). Afterwards, patients were divided into two groups according to the SYNTAX score (Group I: SYNTAX score ≤ 22, Group II: SYNTAX>22) [20] regarding the development of in-hospital adverse events. Adverse events were CVA, hypotension, arrhythmia, death, unsuccessful PCI, Contrast-Induced Nephropathy (CIN) and vascular event. The demographic and past medical history of patients, such as gender, age, history of hypertension, hyperlipidemia, diabetes mellitus, smoking, Coronary Artery Disease, Congestive Heart Failure, Chronic Kidney Disease, Cerebrovascular Accident and familial history. We considered that all deaths were due to cardiac disease unless another reason had been established. Diagnosis of acute myocardial infarction confirmed by myocardial symptoms, electrocardiography along with evidence of increased levels of myocardial necrosis markers in order to determine the chronic kidney disease, the level of patient's creatinine clearance before the procedure was measured and the cutoff value for creatinine clearance considered less than 60 ml/min.

SYNTAX score calculation

The total SYNTAX score was derived from the summation of the individual scores for each separate lesion (defined as ≥ 50% stenosis in vessel ≥ 1.5 mm). Full details on SYNTAX score calculation are reported elsewhere [3]. All angiographic variables relevant to SS were analyzed by 2 of 3 independent experienced cardiologists who were blind to the data process and angiograms (obtained before the procedure) clinical outcomes.

Statistical analysis

All in-hospital outcomes were entered in SPSS software version 23. All qualitative variables were expressed as absolute frequencies and percentages and continuous variables were presented as the mean ± standard deviation. Grouped data of SYNTAX score were analyzed using the chi-squared test or Fisher's exact P-values of less than 0.05 were regarded as statistically significant. The receiver operating characteristic (ROC) curve was used to assess the SYNTAX scores' ability to discriminate patients with outcomes and also the cutoff point was determined for it.

Relation of in-hospital outcome as a dependent variable with independent variables including age, sex, hypertension, hyperlipidemia, diabetes, smoking, CAD, CHF, CKD, CVA and positive family history were evaluated with single logistic regression analysis. In fact, predictive value of SYNTAX score was evaluated with multiple and single regression analyses.

Ethical considerations

Our study was in compliance with the declaration of Helsinki. Also the study protocol was approved by the ethics committee of the Faculty of Medicine, Guilan University of Medical Sciences. All patients were informed about the technique and informed consents form was signed by them.

Results

In this study 431 patients underwent PCI. The mean age of the subjects was 57.10 ± 10.67 years (range 23-85 years). 292 patients were male (67.7%) and 139 patients were female (32.3%). Other demographic data are listed in **Table 1**.

The SYNTAX score ranged from 3 to 55 points. According to the original assortment for SYNTAX score, in this study we had 49 patients (11.4%) with high SS and 382 patients with had high SS (more than 22) which showed a predominance of patients with low SYNTAX.

The mean and the median SYNTAX score in total number of our population, respectively was 15.93 ± 5.53 and 15 points. Patients were divided into two groups: Group I: 49 patients with SS less than 22 and Group II: 382 patients with SS 22 and more. The mean of SS in Group I was 26.59 ± 7.12 and in Group II was 4.56 ± 3.41. Primary percutaneous coronary intervention (pPCI) was done in 52 patients: 41 patients (78.8%) in Group I and 11 patients (21.2%) in Group II. Outcomes of patients are listed in **Table 2**.

There was no significant association between mean of SYNTAX score and sex (p=0.949), age (p=0.478), hypertension (p=0.727), hyperlipidemia (p=0.579), diabetes mellitus (p=0.715), smoking (p=0.675), CAD (p=0.489), CHF (p=0.560), CKD (p=0.696) and (p=0.886). However, there was remarkable association between the mean of SYNTAX score and familiar history (FH) (p=0.029). The distribution of adverse in-hospital events can be seen in **Figure 1**. The mean of SYNTAX score is significantly elevated in positive cases of hypotension (p=0.0113), arrhythmia (p<0.001), in-hospital deaths (p<0.001), unsuccessful PCI (p<0.001), and total outcome incidence (p<0.001). Total adverse events were seen in 24 patients (48.98%) in high score group and in 20 patients (5.24%) in low score of hypotension which was meaningfully different (p<0.001).

ROC curve for predicting outcomes of PCI in the patients based on SYNTAX score can be seen in **Figure 2**. Area under the curve is calculated 0.786 (CI=0.716-0.865, p<0.001) which is presenting the significance of AUC for predicting in-hospital events due to PCI. The best cutoff point with high sensitivity (59.1%) and specificity (90.2%) was 19.5 for SYNTAX score. Higher cut off point lead to lowering the sensitivity and elevating the specificity (**Figure 3**). For instance, to achieving 95% specificity, the cutoff point will be 24.5.

Table 1

Baseline clinical and demographic data of patients hospitalized for PCI.

Characteristics		Group I	Group II	p value
Gender	Male (n %)	259 (67.8%)	33 (67.3%)	0.949
Age (years)		56.93 ± 10.47	58.38 ± 12.14	0.478
Hypertension		177 (46.3%)	24 (48.9%)	0.727
Hyperlipidemia		164 (42.9%)	19 (38.7%)	0.579
Diabetes Mellitus		115 (30.1%)	16 (32.6%)	0.715
Smoking		80 (20.9%)	9 (18.3%)	0.675
Coronary Artery Disease		35 (9.1%)	6 (12.2%)	0.489
Congestive Heart Failure		141 (36.9%)	16 (32.6%)	0.56
Chronic Kidney Disease		3 (0.7%)	0 (%0.0)	0.696
Cerebrovascular Accident		1 (0.2%)	0 (%0.0)	0.886
Familial History		60 (16%)	2 (4%)	0.029

Table 2

Incidence of adverse events in patients underwent PCI.

Variables (outcomes)	Group I	Group II	p value
CVA	0 (%0)	1 (%2. 04)	0.184
Hypotension	0 (%0)	2 (%4.05)	0.013
Arrhythmia	6 (%1.5)	8 (%16)	<0.001
Death	1 (%0.25)	4 (%8)	<0.001
Unsuccessful PCI	3 (%7.5)	14 (% 28)	<0.001
CIN	2 (%0.50)	2 (%4.0)	0.065
Vascular event	6 (% 1.57)	2 (%4.08)	0.228
ReMI	0 (%0)	0 (%0)	-*
Total	20 (% 5.24)	24 (%48.98)	<0.001

CVA= Cerebrovascular Accident; PCI= Percutaneous Coronary Intervention; CIN= Contrast-Induced Nephropathy; ReMI= Re-Myocarial infarction.

*Regarding fixed numbered entered as outcome, analysis with SPSS software had not been done.

Table 3

Single logistic regression analysis.

Variables	CI	Odds Ratio	p-value
Age	1.019- 1.085	1.052	0.02
Syntax Score	1.112- 1.247	1.78	<0.001
Gender	0.640- 2.350	0.731	0.538
Hypertension	0.416- 1.452	0.778	0.43
Hyperlipidemia	0.570- 2.024	1.074	0.826
Diabetes Mellitus	0.428-1.601	0.828	0.574
Smoking	0.366- 1.565	0.757	0.453
Coronary Artery Disease	0.358- 3.120	1.057	0.92
Congestive Heart Failure	0.474- 1.709	0.9	0.748
Chronic Kidney Disease	0.200- 2.515	0.223	0.225
CVA	0.000-0	0	1
Familial History	0.737- 8.199	2.458	0.143

CVA=Cerebrovascular Accident

Moreover, we showed that there is a significant association between total outcome and each specific outcome e.g. mortality–unsuccessful PCI-Primary PCI–arrythmia and hypotension with high SYNTAX score group comparing to low SYNTAX score group.

Relation of in-hospital outcomes (dependent variables) and independent variables including age, sex, hypertension, hyperlipidemia, smoking, CAD, CHF, CKD, CVA and positive familial history was evaluated by single logistic regression (**Table 3**). It was shown that age (OR=1.052, CI=1.019-1.085, p<0.02) and SYNTAX score (OR=1.78, CI=1.112-1.247, p<0.001) had significant association; however other variables had no association with the independent variables; in–hospital outcomes. Also, in multiple logistic regression analysis, which both Age and SYNTAX score were entered concurrently, (p<0.1), it was showed that Age (OR=1.052, CI=1.019-1.085, p<0.02) and SYNTAX score (OR=1.78, CI=1.112-1.247, p<0.001) had remarkable association with in-hospital outcomes.

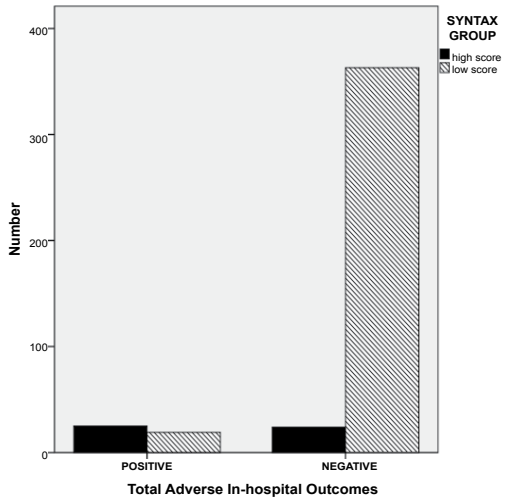

Figure 1. Total in-hospital outcomes based on SYNTAX score categories.

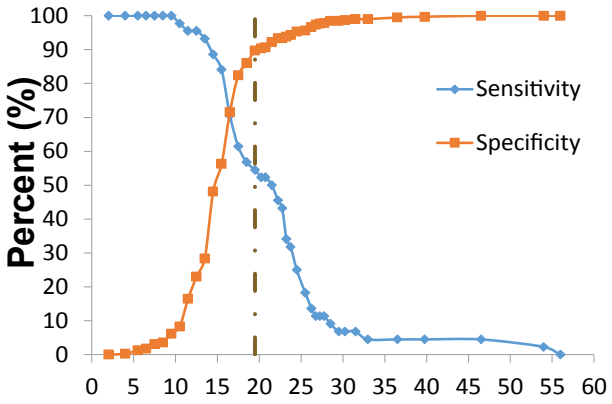

Figure 2. SYNTAX score ROC curve used to predict outcomes. AUC= 0.79; *AUC= area under the curve; ROC= receiver operating characteristic.*

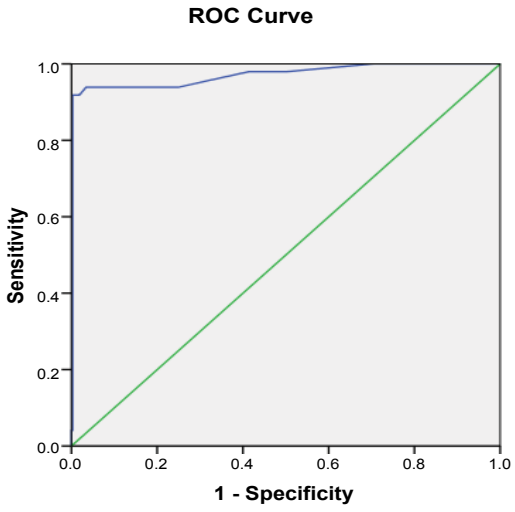

Figure 3. SYNTAX score ROC curve used to predict outcomes with specificity of 0.95%.

Discussion

In this study we attempted to evaluate a simple PCI scoring system, according to angiographic lesions, for predicting the risk of in-hospital outcome in patients underwent PCI. A total of 431 patients that enrolled in the Heart Center were participated in testing the system. This scoring system related well with the rates of in-hospital outcome. Total in-hospital outcomes were seen more in high SYNTAX score group rather than low SYNTAX score group.

The angiographic SYNTAX score algorithm is according to adding each lesions complexity point (more than 50% of vessels cross-sectional area loss, as identified on coronary angiography [3]. Although the SYNTAX score's significant role in choosing the proper myocardial revascularization method in multi-arterial CAD patients' is not deniable, however, its efficiency in patients with one- or two-vessel disease is unclear [21]. Our study results revealed that the in-hospital outcomes after PCI in the high SYNTAX group were significantly more than a low SYNTAX score group, which was aligned with Serruys et al. study, in which the high score group undergoing PCI showed higher major adverse cardiac events (MACE), also the rates of cardiac and cerebrovascular adverse event compared with the group undergoing CABG surgery (23.4% vs. 10.9%; P = 0.001). Additionally, in percutaneously treated group more tendencies in elevating the rate of combined death outcomes, acute myocardial infarction, and stroke were observed (11.9% vs. 7.6%; P = 0.08) [22]. Ayca et al. reported that SYNTAX score (SS) has the ability to predict in-hospital outcomes in ST elevation myocardial infarction (STEMI) patients who undergo primary percutaneous coronary intervention (pPCI). Their study included 538 STEMI patients, which similar to ours grouping, they were divided into low SS (<22) and high SS (>22) groups. The patients' SS were computed from an SS of all patients was calculated from a primary angiogram. Then in the following week, based on patients' echocardiography the Left ventricular systolic functions were assessed during hospital stays the reinfarction and mortality rates were obtained directly from the center's health information management. Within the hospitalization period the high SS group in comparison to low SS group showed more no-reflow (41% and 25.1%, p < 0.001, respectively), less ejection fraction (38.2 ± 7.5% and 44.6 ± 8.8%, p<0.001, respectively), and higher rates of re-infarction (9.5% and 7.3%, p=0.037, respectively) and mortality (0.9% and 0.2%, p=0.021, respectively) [23]. In a study by Endo et al. the angiographic lesion complexity score and in-hospital outcomes after percutaneous coronary intervention were assessed. Their research sample included 2218 patients underwent PCI for at least one complex lesion. Findings revealed that the patients with higher-risk score were older (p<0.001) and had a present or previous heart failure (p=0.02 and p=0.01, respectively). The group with a higher-risk score had remarkably greater in-hospital event rates for death, heart failure, and cardiogenic shock (from 0 to 4 risk score; 1.7%, 4.5%, 6.3%, 7.1%, 40%, p<0.001) respectively. Also results showed that this group had bleeding with a hemoglobin drop of more than 3.0g/dL (3.1%, 11.0%, 13.1%, 10.3%, 28.6%, p<0.001), and postoperative myocardial infarction (1.5%, 3.1%, 3.8%, 3.8%, 10%, p=0.004), respectively were seen. The relevance with adverse health outcomes remained even after adjustment for known clinical predictors (odds ratio 1.72, p<0.001) [20]. Moreover, in other researches also the SYNTAX score was analyzed in different populations. In a subanalysis study of the Limus Eluted from a Durable Versus ERodable Stent Coating (LEADERS) by Windecker et al. mean SYNTAX score of 13.3 (± 8.7) was reported. In this study with a sample of 1,397 undergoing PCI patients, results showed a lower MACE-free survival rate in the tertile with higher SYNTAX

scores (low=92.2%; intermediate=91.1%; and high=84.6%; p=0.001) [24]. Also in this tertile higher rate of mortality (low=1.5%; intermediate=2.1%; and high=5.6%; p=0.002) and target-vessel revascularization were observed (low=6.3%; intermediate=7.8%; and high=11.3%; p=0.001) [25]. The same results were established in three year assessment of patients in the Arterial Revascularization Therapies Study Part II, Sirolimus-eluting stents for the treatment of patients with multi-vessel de novo coronary artery lesions (ARTS II) -also in order to characterize the independent predictors of major adverse cardiac events, a multivariate analysis was carried out. The analysis presented the SYNTAX score as one of the strongest predictors (odds ratio [OR] 1.43, 95% confidence interval [95% CI] 1.08–1.90; p=0.014), and diabetes mellitus was (OR 1.76, 95% CI 1.13–2.74; p=0.012) [22]. Chakravarty et al. studied the effect of co-morbidities on the ability of SYNTAX score to predict long-term outcomes of unprotected left main coronary artery revascularization. The median SYNTAX score in PCI and CABG group were 26 and 28, respectively (p=0.5). The result in the PCI group indicated that a higher quartile was associated with worse survival (62.1% of the SYNTAX score of ≥ 36 vs. 82.4% the SYNTAX score of <36, p=0.03), all-cause mortality, myocardial infarction, cerebrovascular events, and target vessel revascularization-free (MACCE) survival (47.7%, SYNTAX score ≥ 20 vs. 76.6%, SYNTAX score<20, p=0.02) [19]. In research by JQ et al. the SYNTAX scores role in predicting long-term incidences of major adverse cardiac and cerebrovascular events (MACCE) in 203 patients undergoing PCI for the 3-vessel disease were assessed. Generally, the SYNTAX score ranged from 6 to 66. The SS mean ± standard deviation and median were 27.9 ± 12.6 and 26 respectively. In a one-year study, the SYNTAX score remarkably predicted the risk of MACE (HR 1.07/U increase, 95% CI 1.04 to 1.11, p<0.001). Also, analysis of the MACE rate revealed a significant increment of the MACE in patients with the highest SYNTAX score tertile (17.9%) in comparison to those with the lowest SYNTAX score tertile (1.4%, p<0.001) or intermediate SYNTAX score tertile (6.2%, p=0.041) [6]. Khan et al. studied the prognostic impact of the residual SYNTAX score on in-hospital outcomes in patients undergoing primary percutaneous coronary intervention. The mean of the SYNTAX score (SS) was 4.7 (± 7.2). The findings showed an association between a high SS with the primary outcome (p<0.0001), in-hospital death (p=0.0026), peri-procedural death (p<0.0001), CHF (p<0.0004) and acute kidney injury (p<0.0019). Furthermore, the high SS presented as an independent predictor of the primary outcome (OR of 3.82) [7].

Barbosa et al. assessed the SYNTAX score impact on risk stratification after percutaneous coronary intervention in 243 non-selected patients. The mean SYNTAX score was 11.6 ± 6.2 points. In their clinical follow-up of 7.2 ± 4.9 months, the incidence of MACE compared between three tertiles. The results showed that the MACE incidence was higher in tertile III compared to tertiles I and II (2.5% vs. 6.4% vs. 14.1%; p=0.0075) [21]. This was similar to our study tertile categories. In our study in the ROC curve for predicting outcomes of PCI in the patients based on SYNTAX score, the total cutoff point was 19.5 (sensitivity=59.1%, Specificity=90.2%) with an area under the curve of 0.79 (CI=0.716-0.865, p<0.0001). Overall Ayca et al. indicated SS as an independent predictor of no-reflow (OR 1.081, 95% CI 1.032-1.133, p=0.001). Also ROC analysis identified SS>19.75 as the best cutoff value, predicting no-reflow (sensitivity of 66%, specificity of 54%, ROC area under the curve: 0.650, 95% CI 0.59-0.70, p<0.001) and they concluded that SS is a useful tool with the ability of predicting in-hospital outcomes of patients with STEMI undergoing pPCI [23-25]. JQ et al. presented the SYNTAX score as a significantly accurate predictor of the rate of MACCE with an area under the receiver operator curve of 0.77 (95% CI 0.65 to 0.90, p<0.001). The SYNTAX score of 29.5 was identified as the optimal cutoff to predict MACE with a sensitivity of 82.4% and specificity of 65.6% [6]. Barbosa et al demonstrated that the ROC curve with an area under the curve of 0.667 (p=0.012), indicating a moderate capacity to predict the MACE development [21]. Their results were similarly near to our results and predicting the capacity of SYNTAX score was moderate in both studies.

In single and multivariate analysis, age had a statistically significant association with SYNTAX score, which based on the significant association of age and SYNTAX score with in-hospital outcome after PCI; we showed a significant association of age-adjusted SYNTAX score with the outcome.

Conclusion

The SYNTAX score was independently related to in-hospital outcomes in patients underwent PCI. It is a good predictor of mortality and other outcomes, with high sensitivity and specificity, and can be used to identify them by using non-expensive and time-saving methods. The SYNTAX score utilization for patients with anatomic complexity treated with PCI in practice, can predict outcomes in our setting. Although our study revealed important information on the application of the SYNTAX score in PCI practice, it faced the main limitation which was the small study sample size. It is recommended that each center constitute angiographic profile for referring patients and characterize the clinical outcomes profile in their patient population in Iran. So more data will be collected in a larger population with multicenter patterns and evaluating the SYNTAX score usage with higher efficacy. Also, other projects for the future could be inter-observer variability study and evaluation of the association of long term outcomes with of SYNTAX score, which could show the importance of this scoring system.

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Conflict of Interest

All authors declare no any conflict of interests.

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