ORIGINAL ARTICLE

Comparison of Anatomical and Clinical Scores in Predicting Outcomes in Primary Percutaneous Coronary Intervention

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Abstract

Background: Different scores based on anatomical and/or clinical features have been developed for risk stratification of patients undergoing percutaneous coronary intervention (PCI). Studies comparing the ability of these different models in predicting major adverse cardiac and cerebrovascular events (MACCE) in patients submitted to primary PCI are limited.

Objectives: The aim of this study was to compare the ability of the scores SYNTAX (SS), Clinical SYNTAX (CSS), ACEF, and modified ACEF ($ACEF_{Mod}$) to predict MACCE in patients with ST-elevation myocardial infarction (STEMI) submitted to primary PCI.

Methods: We analyzed 311 consecutive patients with STEMI submitted to primary PCI between April/2011 and December/2015. The area under the ROC curve was calculated to evaluate the ability of these scores in predicting MACCE. P-values were considered significant at < 0.05.

Results: Mean age of the patients was 60.2 ± 12.0 years, 35.4% were females, and 22.5% had diabetes. MACCE occurred in 23.8% of the patients. The area under the ROC curve was 0.586 (p = 0.028) for ACEF, 0.616 (p = 0.003) for SS, 0.623 (p = 0.002) for $ACEF_{Mod}$, and 0.658 (p < 0.001) for CSS. In multivariate analysis, only high SS (p = 0.011) and CSS (p = 0.002) were independent predictors of MACCE.

Conclusions: High SS and CSS were independent predictors of MACCE. In our cohort of STEMI patients undergoing primary PCI, pure anatomical SS calculated at the baseline coronary angiography was a useful tool to predict MACCE. (Int J Cardiovasc Sci. 2018;31(1)26-32)

Keywords: Myocardial Infarction; Percutaneous Coronary Intervention; Coronary Artery Disease; Probability.

Introduction

Different scores based on anatomical and/or clinical features have been developed for risk stratification of patients undergoing percutaneous coronary intervention (PCI). However, studies comparing the ability of these different models to predict cardiac events in patients submitted to primary PCI are limited.

The SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) score (SS)[1] was developed as part of the SYNTAX[2] trial with the objective of characterizing and objectively quantifying the severity and extent of coronary artery disease.[3] SS is broadly used to stratify the outcomes of elective PCI in left main and multivessel coronary intervention when compared with coronary artery bypass grafting (CABG). Recent studies have utilized this tool to stratify outcomes after primary PCI but are limited by short duration of follow-up or small numbers of patients.[4-12]

Age, creatinine and ejection fraction (ACEF)[13] score appears to be equivalent to more complex scores in predicting mortality in patients undergoing elective CABG. This score has also been applied in patients submitted to PCI to stratify risk of mortality and myocardial infarction (MI).[11,14-16] Modified ACEF score (ACEF$_{Mod}$) considers creatinine clearance (CrCl) as a semicontinuous variable, representing a better estimate of the underlying renal function compared with serum creatinine. This modification improves the predictive accuracy of ACEF in patients undergoing PCI.[17]

Combining clinical and anatomical variables in the same score provides a better performance in risk stratification.[3] The Clinical SYNTAX score (CSS) incorporates ACEF$_{Mod}$ to SS and is able to predict major adverse cardiac and cerebrovascular events (MACCE) in patients with complex coronary artery disease.[15] However, limited number of studies have evaluated the role of this score in patients undergoing PCI.[11,12,15]

Risk stratification is a relevant issue in patients undergoing PCI after MI.[16] The aim of this study was to compare SS, CSS, ACEF, and ACEF$_{Mod}$ in predicting MACCE in patients with ST-elevation MI (STEMI) undergoing primary PCI.

Methods

This cohort study included consecutive patients with STEMI undergoing primary PCI between April/2011 and December/2015 in a tertiary university hospital in southern Brazil. STEMI was defined as a typical chest pain at rest associated with ST-segment elevation of at least 1 mm in two contiguous leads in the frontal plane or 2 mm in the horizontal plane, or typical pain at rest in patients with a new, or presumably new, left bundle-branch block. Exclusion criteria were previous CABG (excluded in the SYNTAX trial[2]), absence of admission laboratory testing or echocardiogram, and lack of 30-day follow-up. The study was approved by the institution's Research and Ethics Committee and informed consent was obtained from all patients.

All patients were pretreated with a loading dose of acetylsalicylic acid (300 mg) and clopidogrel (600 mg). Unfractioned heparin was used during the procedure (70-100 IU/kg). Use of IIb/IIIa glycoprotein, aspirative thrombectomy, and PCI technical strategies (*i.e.*, predilation, direct stent placement, postdilation) were performed according to the operator's choice. Coronary flow before and after the procedure was assessed and described according to the Thrombolysis in Myocardial Infarction (TIMI) criteria.[18] Anticoagulants were suspended after the end of the procedure, and double antiplatelet therapy was recommended for 12 months after the event.

SS was derived from the sum of individual scores for each separate lesion (defined as > 50% stenosis in vessels > 1.5 mm). Full details on the SS calculation are reported elsewhere.[1] ACEF was computed as follows: (age/left ventricle ejection fraction) + 1 if serum creatinine value was > 2 mg/dL.[13] In ACEF$_{Mod}$, 1 point was added for every 10 mL/min reduction in CrCl < 60 mL/min/1.73 m^2 (up to a maximum of 6 points).[15] Therefore, a CrCl between 50 to 59 mL/min/1.73 m^2, 40 to 49 mL/min/1.73 m^2, and 30 to 39 mL/min/1.73 m^2 would receive 1, 2, and 3 points, respectively. CSS was calculated retrospectively for each patient using the following formula: CSS = SS x ACEF$_{Mod}$.[15] We determined cutoff values for the scores above to define them as low or high risk. These cutoff values were obtained by multiplying sensitivity and specificity of each value within the receiver operator characteristic (ROC) curve of the different scores; the value with the highest product (sensitivity X specificity) was established as the cutoff point.

Blood samples were collected by venipuncture before the procedure, as part of routine patient care. CrCl was estimated according to the Modification of Diet in Renal Disease (MDRD) equation. Left ventricular ejection fraction (LVEF) was determined before patient discharge using transthoracic echocardiography and applying either Simpson (in the presence of segmental dysfunction) or Teicholz method.

Clinical follow-up was performed with either outpatient visit or telephone contact. MACCEs were defined as death from all cause, new MI, stroke, Canadian Cardiovascular Society (CCS) class III/IV angina, or rehospitalization for congestive heart failure 30 days after the primary PCI. New MI was defined as recurrent chest pain with ST-segment elevation or new Q waves and increase in serum biomarkers after their initial decrease. Stroke was defined as a new, sudden-onset focal neurological deficit of presumably cerebrovascular cause, irreversible (or resulting in death), and not caused by other readily identifiable causes.

Statistical analysis

Continuous variables are expressed as mean (± standard deviation) or median (interquartile range).

Categorical variables are represented by relative and absolute frequencies. ROC curves were used to evaluate the discriminatory power of the different scores. Comparison of ROC curves was performed by DeLong test using the software R, version 3.1.2. Patients groups were compared using independent samples Student's t test (for normally distributed variable) or Mann-Whitney U test (for other variables) for continuous variables and χ^2 test or Fisher's exact tests for categorical variables. Multivariate analysis was performed by multiple logistic regression. P-values were considered significant at < 0.05. Data were analyzed using *Statistical* Package for the Social Sciences (SPSS), version 18.0.

Results

We included 311 (78.3%) of the 397 patients who underwent primary PCI for STEMI in the analyzed period. Mean age was 60.2 ± 12.0 years, 35.4% were women, and 22.5% had diabetes. LVEF was $< 40\%$ in 18.3%, and estimated CrCl was < 60 mL/min/1.73 m² in 21.9% of the patients. Complete demographic data are described in Table 1.

Complete procedure-related data are shown in Table 2. The incidence of MACCE at 30 days was 23.8%, as detailed in Table 3.

ROC curves are presented in Figure 1. All curves were statistically significant, and the CSS curve had the largest area under the curve (AUC): CSS > ACEF$_{Mod}$ > SS > ACEF. However, when the AUCs were compared two-by-two with DeLong test, there was no statistically significant differences, except in the comparison of ACEF *versus* CSS (p = 0.02) (Figure 2).

Univariate analysis of MACCE according to high or low risk score values (cutoff point determination previously described in the Methods section) showed that high-risk CCS, SS, ACEF, and ACEF$_{Mod}$ were significantly associated with higher MACCE rates (p < 0.001, p < 0.001, p < 0.002, and p < 0.040, respectively). Other clinical variables associated with MACCE in univariate analysis were age > 65 years (p = 0.007), female sex (p = 0.041), Killip 3 or 4 (p < 0.001), and postprocedural TIMI 0-2 (p = 0.006). When adjusted by these variables, only SS and CSS remained independent predictors of MACCE (Table 4).

Discussion

We assessed in the present study the ability of SS, CSS, ACEF, and ACEF$_{Mod}$ in predicting MACCE in STEMI

Table 1 – Demographic data

Variable	n = 311
Age (years)	60.2 ± 12.0
Female sex	110 (35.4)
Hypertension	196 (63.0)
Diabetes	70 (22.5)
Current smoking	161 (51.8)
Previous MI	27 (8.7)
Previous stroke	20 (6.4)
Killip 3 or 4	35 (11.3)
Creatinine > 2 mg/dL	12 (3.9)
Previous ASA use	70 (22.5)
LVEF (%)	50.9 ± 13.1
SYNTAX score	15.5 (10.0-21.5)
Clinical SYNTAX score	19.0 (10.0-35.7)
ACEF score	1.19 (0.94-1.55)
Modified ACEF score	1.21 (0.95-1.88)

Abbreviations: MI: myocardial infarction; ASA: acetylsalicylic acid; LVEF: left ventricular ejection fraction. Data are presented as number (%), mean (± standard deviation) or median (interquartile range).

patients undergoing primary PCI. Our data showed that CSS had the largest AUC; however, when compared two-by-two, the AUC for CSS was only statistically larger than that for ACEF. When we divided the scores between low and high risk, high-risk SS and CSS emerged as independent MACCE predictors; high-risk ACEF and ACEF$_{Mod}$ were predictors of MACCE in univariate analysis, but this association was lost after adjustment for clinical variables.

The prognostic value of the ACEF score in patients who underwent PCI after acute MI was assessed by Lee et al.,[16] who analyzed 12,000 patients in this setting. The ACEF was significantly higher in nonsurvivors (1.95 ± 0.82 *versus* 1.28 ± 0.50, p < 0.001) and was an independent predictor of 1-year mortality (HR, p < 0.001). Capodanno et al.[17] have demonstrated that including CrCl (calculated either by MDRD or Cockcroft-Gault) in ACEF yields superior calibration compared with the original serum creatinine-based equation, and improves the predictive accuracy of ACEF in patients undergoing

Table 2 – Procedural data	
Variable	n = 311
Pain-to-door time (hours)	4 (3.00-6.75)
Door-to-balloon time (minutes)	68 (55.0-90.0)
Cardiac arrest	24 (7.7)
Total AV block	20 (6.4)
IABP	10 (3.2)
Radial access	178 (57.2)
Anterior MI	140 (45.0)
Culprit vessel	
LAD artery	131 (42.1)
Right coronary artery	112 (36.0)
Circumflex artery	38 (12.2)
Other vessels	30 (9.7)
Three-vessel disease	63 (20.3)
Thrombus aspiration	115 (37.0)
DES	12 (3.9)
Postprocedural TIMI 3	277 (89.1)
Abciximab use	134 (43.1)
Contrast volume (mL)	180 (150-250)
Implanted stents	1.29 ± 0.68
Treated lesions	1.19 ± 0.52

Abbreviations: AV: atrioventricular; IABP: intraaortic balloon pump; MI: myocardial infarction; LAD: left anterior descending; DES: drug-eluting stent; TIMI: Thrombolysis in Myocardial Infarction. Data are presented as number (%), mean (± standard deviation) or median (interquartile range).

Table 3 – In-hospital and 30-day MACCE	
MACCE	**n (%)**
In-hospital death	31 (9.3)
In-hospital reinfarction	9 (2.7)
Stent thrombosis	6 (1.8)
In-hospital stroke	4 (1.2)
30-day death	35 (10.5)
30-day CCS 3-4 angina	17 (5.1)
30-day rehospitalization for CHF	14 (4.2)
30-day reinfarction	13 (3.9)
30-day stroke	5 (1.5)
30-day MACCE	74 (23.8)

Abbreviations: MACCE: major adverse cardiac and cerebrovascular events; CCS: Canadian Cardiovascular Society; CHF: congestive heart failure. Data are presented as number (%).

PCI. In our analysis, despite having a larger area under the ROC curve compared with ACEF and SS, ACEF$_{Mod}$ was not an independent predictor MACCE.

The use of SS, originally developed in patients with stable coronary disease, has also been evaluated in acute coronary syndromes for outcome prediction.[4-12] In a study including 807 patients with STEMI, Garg et al.[5] identified SS as an independent predictor of mortality, MACCE, and stent thrombosis up to a 1-year follow-up. However, it is important to highlight that the study was not performed aiming to define cutoff points for the analyzed scores to predict MACCE, but only to define the relationship of SS with MACCE
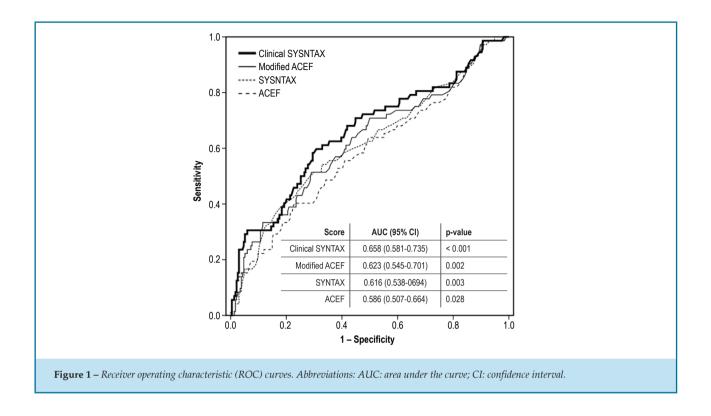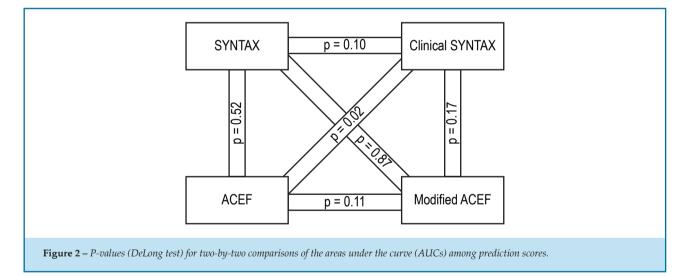
occurrence. The same author showed an improvement in the ability of the SS to predict MACCE and mortality in patients undergoing PCI by combining SS and ACEF$_{Mod}$, (CSS).[15] This improvement was also observed in the present study.

The use of CSS in patients with STEMI was evaluated in two studies,[11,12] which showed an improved outcome prediction accuracy compared with SS. Cetinkal et al.[11] recently evaluated 433 patients in this setting with the objective of validating CSS as a predictor of prognosis, and also evaluated SS and ACEF. The primary endpoint was a composite of all-cause mortality, MI, and cerebrovascular events, with a follow-up of 15 months. CSS > 26 was identified as an independent predictor of events. The AUC was 0.66 (p < 0.001), 0.59 (p = 0.01), and 0.64 (p < 0.001) for CSS, SS, and ACEF, respectively. However, all cases were performed by femoral access and there was an extremely low mortality in patients with low/moderate CSS (one death over 285 patients in a 15-month follow-up), which jeopardizes the external validity of the study.

Girasis et al.[12] analyzed 848 patients undergoing PCI with drug-eluting stents (only 25.3% were patients with STEMI) and demonstrated that both SS and CSS were able to stratify risk of very long-term adverse clinical outcomes. The AUC for the incidence of MACCE was 0.61 (95% CI: 0.56-0.65) and 0.62 (95% CI: 0.57-0.67),

Figure 1 – *Receiver operating characteristic (ROC) curves. Abbreviations: AUC: area under the curve; CI: confidence interval.*

Score	AUC (95% CI)	p-value
Clinical SYNTAX	0.658 (0.581-0.735)	< 0.001
Modified ACEF	0.623 (0.545-0.701)	0.002
SYNTAX	0.616 (0.538-0694)	0.003
ACEF	0.586 (0.507-0.664)	0.028

Figure 2 – *P-values (DeLong test) for two-by-two comparisons of the areas under the curve (AUCs) among prediction scores.*

respectively. Nevertheless, it is important to highlight the small proportion of patients with STEMI and the lower anatomical complexity compared with our patients [median SS 10.0 (6-16) *versus* 15.5 (10.0-21.5) in the present study]. Also of note, use of drug-eluting stent in all STEMI patients is a distant reality in developing countries.

There are some limitations in our study. First, the retrospective design may have influenced the quality and consistency of the collected data. Second, the relatively small number of patients may have reduced the power of the study to detect some associations. Third, the fact that the study was conducted at a single center may also be considered a limitation.

Table 4 – Multivariate analysis of the incidence of MACCE according to high or low score values

Scores	n	MACCE n (%)	p-value	Adjusted OR (95% CI)	Adjusted p-value
SYNTAX ≥ 18.25	Yes: 116	39 (33.6)	0.002	2.11 (1.19-3.74) *	0.011*
	No: 190	33 (17.4)			
Clinical SYNTAX ≥ 26.0	Yes: 115	43 (37.4)	< 0.001	2.49 (1.39-4.44) †	0.002†
	No: 162	29 (15.2)			
ACEF ≥ 1.235	Yes: 138	41 (29.7)	0.040	1.35 (0.77-2.37) †	0.297†
	No: 173	33 (19.1)			
Modified ACEF ≥ 1.505	Yes: 107	38 (35.5)	0.001	1.35 (0.77-2.37) †	0.079†
	No: 204	36 (17.6)			

*Abbreviations: OR: odds ratio; CI: confidence interval. *Adjusted for age > 65 years, female sex, Killip 3 or 4, and postprocedural TIMI 0-2. † Adjusted for female sex, Killip 3 or 4, and postprocedural TIMI 0-2.*

Conclusion

SS and CSS were independent MACCE predictors in this study. In our cohort of primary PCI in patients with STEMI, pure anatomical SS calculated at baseline coronary angiography was a useful tool in predicting short-term MACCE.

Author contributions

Conception and design of the research: Pivatto Junior F, Bergoli LCC, Wainstein MV. Acquisition of data: Pivatto Junior F, Araujo GN, Valle FH, Bergoli LCC, Machado GP, Fuhr B, Cassol EP, Krepsky AMR. Analysis and interpretation of the data: Pivatto Junior F, Wainstein RV, Wainstein MV. Statistical analysis: Pivatto Junior F. Writing of the manuscript: Pivatto Junior F. Critical revision of the manuscript for intellectual content: Pivatto Junior F, Araujo GN, Valle FH, Bergoli LCC, Machado GP, Fuhr B, Cassol EP, Krepsky AMR, Wainstein RV, Wainstein MV. Supervision / as the major investigador: Pivatto Junior F.

References

1. Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A, Dawkins K, et al. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. EuroIntervention. 2005;1(2):219-27. PMID: 19758907.

2. Serruys PW, Morice MC, Kappetein AP, Colombo A, Holmes DR, Mack MJ, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med. 2009;360(10):961-72. doi: 10.1056/NEJMoa0804626. Erratum in: N Engl J Med. 2013;368(6):584.

3. Yadav M, Palmerini T, Caixeta A, Madhavan MV, Sanidas E, Kirtane AJ, et al. Prediction of coronary risk by SYNTAX and derived scores: synergy between percutaneous coronary intervention with taxus and cardiac surgery. J Am Coll Cardiol. 2013;62(14):1219-30. doi: 10.1016/j.jacc.2013.06.047.

4. Magro M, Nauta S, Simsek C, Onuma Y, Garg S, van der Heide E, et al. Value of the SYNTAX score in patients treated by primary percutaneous coronary intervention for acute ST-elevation myocardial infarction: The MI SYNTAX score study. Am Heart J. 2011;161(4):771-81. doi: 10.1016/j.ahj.2011.01.004.

5. Garg S, Sarno G, Serruys PW, Rodriguez AE, Bolognese L, Anselmi M, et al; STRATEGY and MULTISTRATEGY Investigators. Prediction of 1-year clinical outcomes using the SYNTAX score in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention: a substudy of the STRATEGY (Single High-Dose Bolus Tirofiban and Sirolimus-Eluting Stent Versus Abciximab and Bare-Metal Stent in Acute Myocardial Infarction) and MULTISTRATEGY (Multicenter Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction Study) trials. JACC Cardiovasc Interv. 2011;4(1):66-75. doi: 10.1016/j.jcin.2010.09.017.

6. Kul S, Akgul O, Uyarel H, Ergelen M, Kucukdagli OT, Tasal A, et al. High SYNTAX score predicts worse in-hospital clinical outcomes in patients undergoing primary angioplasty for acute myocardial infarction. Coron Artery Dis. 2012;23(8):542-8. doi: 10.1097/MCA.0b013e3283599486.

7. Yang CH, Hsieh MJ, Chen CC, Chang SH, Wang CY, Lee CH, et al. SYNTAX score: an independent predictor of long-term cardiac mortality in patients with acute ST-elevation myocardial infarction. Coron Artery Dis. 2012;23(7):445-9. doi: 10.1097/MCA.0b013e3283587835.

8. Yang CH, Hsieh MJ, Chen CC, Wang CY, Chang SH, Lee CH, et al. The prognostic significance of SYNTAX score after early percutaneous transluminal coronary angioplasty for acute ST elevation myocardial infarction. Heart Lung Circ. 2013;22(5):341-5. doi: 10.1016/j.hlc.2012.12.003.

9. Brown AJ, McCormick LM, Gajendragadkar PR, Hoole SP, West NE. Initial SYNTAX score predicts major adverse cardiac events after primary percutaneous coronary intervention. Angiology. 2014;65(5):408-12. doi: 10.1177/0003319713483542.

10. Ayça B, Akın F, Celik O, Cetin S, Sahin I, Gülşen K, et al. Does SYNTAX score predict in-hospital outcomes in patients with ST elevation myocardial infarction undergoing primary percutaneous coronary intervention? Kardiol Pol. 2014;72(9):806-13. doi: 10.5603/KP.a2014.0064.

11. Cetinkal G, Dogan SM, Kocas C, Abaci O, Arslan S, Balaban Kocas B et al. The value of the Clinical SYNTAX Score in predicting long-term prognosis in patients with ST-segment elevation myocardial infarction who have undergone primary percutaneous coronary intervention. Coron Artery Dis. 2017;27(2):135-42. doi: 10.1097/MCA.0000000000000332.

12. Girasis C, Garg S, Räber L, Sarno G, Morel MA, Garcia-Garcia HM, et al. SYNTAX score and Clinical SYNTAX score as predictors of very long-term clinical outcomes in patients undergoing percutaneous coronary interventions: a substudy of SIRolimus-eluting stent compared with pacliTAXel-eluting stent for coronary revascularization (SIRTAX) trial. Eur Heart J. 2011;32(24):3115-27. doi: 10.1093/eurheartj/ehr369.

13. Ranucci M, Castelvecchio S, Menicanti L, Frigiola A, Pelissero G. Risk of assessing mortality risk in elective cardiac operations: age, creatinine, ejection fraction, and the law of parsimony. Circulation. 2009;119(24):3053-61. doi: 10.1161/CIRCULATIONAHA.108.842393.

14. Wykrzykowska JJ, Garg S, Onuma Y, de Vries T, Goedhart D, Morel MA, et al. Value of age, creatinine, and ejection fraction (ACEF score) in assessing risk in patients undergoing percutaneous coronary interventions in the 'All-Comers' LEADERS trial. Circ Cardiovasc Interv. 2011;4(1):47-56. doi: 10.1161/CIRCINTERVENTIONS.110.958389.

15. Garg S, Sarno G, Garcia-Garcia HM, Girasis C, Wykrzykowska J, Dawkins KD, et al; ARTS-II Investigators. A new tool for the risk stratification of patients with complex coronary artery disease: the Clinical SYNTAX Score. Circ Cardiovasc Interv. 2010;3(4):317-26. doi: 10.1161/CIRCINTERVENTIONS.109.914051.

16. Lee JH, Bae MH, Yang DH, Park HS, Cho Y, Jeong MH, et al; Korea Acute Myocardial Infarction Registry Investigators. Prognostic value of the age, creatinine, and ejection fraction score for 1-year mortality in 30-day survivors who underwent percutaneous coronary intervention after acute myocardial infarction. Am J Cardiol. 2015;115(9):1167-73. doi: 10.1016/j.amjcard.2015.02.001.

17. Capodanno D, Marcantoni C, Ministeri M, Dipasqua F, Zanoli L, Rastelli S, et al. Incorporating glomerular filtration rate or creatinine clearance by the modification of diet in renal disease equation or the Cockcroft-Gault equations to improve the global accuracy of the Age, Creatinine, Ejection Fraction [ACEF] score in patients undergoing percutaneous coronary intervention. Int J Cardiol. 2013;168(1):396-402. doi: 10.1016/j.ijcard.2012.09.026.

18. Sheehan FH, Braunwald E, Canner P, Dodge HT, Gore J, Van Natta P, et al. The effect of intravenous thrombolytic therapy on left ventricular function: a report on tissue-type plasminogen activator and streptokinase from the Thrombolysis in Myocardial Infarction (TIMI phase 1) trial. Circulation. 1987;75(4):817-29. PMID: 3103950.