Indian Heart Journal 73 (2021) 555–560

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Original Article

Comparison of multiple risk scores in assessing medium-to long-term clinical outcomes in unstable angina / non-ST-elevation myocardial infarction patients undergoing multi vessel percutaneous coronary intervention: An observational, registry-based study in India

Gailin Sebastian [a, *], Vivek Pillai [a], Ashraf Manzil [a], Ramakrishna Damodara [a], Ish Kalra [a], Zameel Abdul [a], Oommen Mathew [b]

[a] Department of Cardiology, Government Medical College, Kannur, Kerala, India
[b] Population Research Center, University of Kerala, Thiruvananthapuram, Kerala, India

ARTICLE INFO

Article history:
Received 31 January 2021
Accepted 2 August 2021
Available online 5 August 2021

Keywords:
Non-ST-Elevation myocardial infarction
Multivessel coronary artery disease
Percutaneous coronary intervention
Risk scores
SYNTAX

ABSTRACT

Objective: Post-revascularization mortality in multivessel coronary artery disease (MVCAD) has been explored via several risk scores. Here, we assessed and compared various risk scores in predicting medium to long-term clinical outcomes in unstable angina/non-ST-elevation myocardial infarction (UA/NSTEMI) patients with MVCAD undergoing percutaneous coronary intervention (PCI).

Methods: We analyzed a cohort of a tertiary care center registry enrolling patients in South India, Kerala, with MVCAD (N = 200) who had undergone PCI between 2010 and 2018. The outcomes evaluated were all-cause mortality and major adverse cardiac events (MACE). The risk scores assessed included SYNTAX score (SS), residual SYNTAX score (rSS), SYNTAX revascularization index (SRI), age, creatinine, and ejection fraction (ACEF) score, clinical SYNTAX score (cSS), and SYNTAX score II (SSII).

Results: Of the analyzed risk scores, SSII had the best predictive capability with the area under the curve (AUC) of 0.79 in c-statistics, followed by ACEF score and cSS with AUCs of 0.74 and 0.65, respectively for all-cause mortality ($p < 0.01$). Kaplan–Meier survival curves and multivariate analysis by Cox regression showed SSII with cut-offs of >35.15 and > 29.55 to be the only score associated with higher mortality and MACE, respectively.

Conclusions: In UA/NSTEMI patients with relatively less complex MVCAD treated by PCI, the SSII, ACEF and cSS risk scores could predict the outcomes better. The SSII showed the best predictive performance for all-cause mortality and MACE. Scores based on baseline and residual atherosclerotic burden (SS, rSS, and SRI) performed poorly in predicting the mortality and MACE.

1. Introduction

Multivessel coronary artery disease (MVCAD), defined as significant disease involving two or more epicardial coronary arteries is a strong predictor of medium-to long-term mortality. The proportion of myocardium at risk is higher, with the resultant increase in events in CAD.[1,2] Percutaneous coronary intervention (PCI) is more commonly undertaken as a treatment modality in MVCAD.[3,4] Myocardial revascularization improves survival in patients with MVCAD. Critical factors determining adequacy of revascularization include vessel size, angiographic and functional severity of the lesion and viability of the myocardial territory.[5] Clinical features, extent and complexity of baseline CAD and the post-PCI residual disease have been shown to influence mortality independently and are thus considered in the risk stratification of MVCAD patients.[2,6–9]

Different risk scores have been developed to determine the best revascularization option and the amount of disease to be treated. The SYNTAX score (SS) is an angiography-based tool to assess the total myocardium at risk and the complexity of CAD, thereby

* Corresponding author.
E-mail addresses: gailinbs74@gmail.com (G. Sebastian), docvivpillai@yahoo.com (V. Pillai), ashsmfz@yahoo.com (A. Manzil), drcdram@yahoo.com (R. Damodara), kalra_ish@yahoo.com (I. Kalra), mail2zameel@gmail.com (Z. Abdul), oommenpm@gmail.com (O. Mathew).

https://doi.org/10.1016/j.ihj.2021.08.001

quantifying the atherosclerotic burden.[2,6,10] Residual SYNTAX score (rSS) is the SS calculated after PCI to quantify the burden of residual CAD.[7,11] SYNTAX revascularization index (SRI) is derived from rSS and SS to better quantify the proportion of disease treated by PCI.[9] Risk scores that incorporate clinical factors like age, creatinine, and ejection fraction (ACEF) score, clinical SYNTAX Score (cSS), and SYNTAX Score II (SSII) have also been developed and validated.[8,12]

Complete revascularization (CR), in which all ischemic myocardial territories are treated, was beneficial in long-term clinical trials, which showed a positive relationship between the proportion of CAD treated and the reduction in cardiovascular events. Incomplete revascularization (IR), on the other hand reduces periprocedural complications especially in high-risk patients. But IR showed a higher risk of future adverse cardiovascular events.[13] Thus before PCI, clinical features, the complexity of CAD and whether to go for CR or reasonable IR need to be considered. This is especially important in the unstable angina/non-ST-elevation myocardial infarction (UA/NSTEMI) setting, where the SS is known to miscalculate the actual long-term risk.[14]

To date, data on the accuracy of different risk models on independent prediction of medium-to long-term prognosis is scarce in the UA/NSTEMI population. Hence, the present study aimed to assess and compare the six risk scores that used clinical characteristics, baseline atherosclerotic burden, and post-PCI residual disease to predict all-cause mortality and major adverse cardiac events (MACE) in UA/NSTEMI patients undergoing multivessel PCI.

2. Methods

2.1. Study design and population

This was an observational, registry-based study conducted in the tertiary care cardiac center in Government Medical College, Kannur, Kerala in South India. Data of 200 consecutive patients who had undergone multivessel PCI between 2010 and 2018 were taken. Patients with a diagnosis of UA/NSTEMI with >70 % angiographic stenosis in two or more major coronary arteries and angiographically assessed to be suitable for revascularization by PCI were included in the study. Those with a history of ST-segment elevation myocardial infarction (STEMI), prior coronary artery bypass grafting (CABG) or PCI, those with complex left main disease and single-vessel disease were excluded from the study.

Data consisting of patients' history, cardiovascular risk factors, left ventricular function, angiographic features and the six risk scores were made from the registry using dedicated software. Follow-up protocol consisted of outpatient visits at thirty days, six months and then yearly after PCI. Over the phone consultations were made with those who could not attend the outpatient department.

Written informed consent was obtained from all the patients. The study was conducted following the principles of the Declaration of Helsinki and the International Conference on Harmonization and approved by the local ethics committee.

2.2. Outcomes

The outcomes evaluated were all-cause mortality and MACE which included all-cause death and hospital admissions for acute cardiovascular events, repeat revascularization, and heart failure.

2.3. Clinical assessment

Peripheral artery disease (PAD) was diagnosed with a history of intermittent claudication or revascularization surgery and ultrasonological or angiographic evidence of the disease.[15] Chronic obstructive pulmonary disease (COPD) was diagnosed with consistent clinical features and a history of chronic use of bronchodilators and steroids.[16] Creatinine clearance (CrCl) was calculated with the Cockcroft–Gault equation.[17] All the patients were re-assessed during follow up visits at the pre-specified intervals and the evaluation was limited to clinical assessment, biochemical investigations and measurement of left ventricular ejection fraction (LVEF). Pre-procedural and follow-up LVEF were measured by transthoracic echocardiography using biplane Simpson method.

2.4. Coronary angiography and risk scores

SS for each angiogram was performed by two interventional cardiologists blinded to the study using an online calculator. rSS was defined as the SS calculated after PCI.[11] SRI was calculated as $100 \times (1 - [\text{rSS/baseline SS}])$.[18] The modified ACEF score was based on the ACEF score and calculated as age/ejection fraction+1 point for every 10 mL/min decrease in CrCl below 60 mL/min/1.73 m^2 with a maximum of six points.[19] The cSS was calculated as SS × modified ACEF score.[20] SSII was computed using two angiographic (SS and left main CAD) and six clinical variables: age, gender, PAD, COPD, CrCl, and LVEF.[8,21]

2.5. Statistical analysis

Categorical variables were expressed as numbers and percentages and continuous variables as mean ± standard deviation (SD). Mortality predictions based on the risk scores were assessed using Cox logistic regression analysis, with each score as an independent linear predictor. Kaplan–Meier survival analysis was performed to compare the mortality and MACE with two sets of each score with a cut-off between them. The log-rank test was conducted to determine the significance of the difference between the two values. The risk scores' predictive performance and discriminative ability were evaluated with c-statistics and Kaplan–Meier analyses.[22] All statistical analyses were performed using SPSS for Windows, Version 23.0 (IBM Corp., USA).

3. Results

Among the 565 patients enrolled in the registry, 278 had MVCAD. Of these, 200 were included in the analysis.

3.1. Demographic and baseline characteristics

Most of the subjects were males (77 % [n = 154]). The mean age of patients was 57.9 years (range: 33–81). Pre-existing diseases such as systemic arterial hypertension, diabetes mellitus, dyslipidemia and smoking history were present in 34.0 %, 44.5 %, 15.5 %, and 13.5 % of patients, respectively. Left ventricular systolic function was normal in 63.8 % of patients, with 3.5 % having severe systolic dysfunction. Mean CrCl was 67.26 mL/min/1.73 m^2 (SD: 20.9; range: 22.6–146). The mean number of stents used was 2.66 (SD: 0.68; range: 1–5). Staged procedure was performed in 16.5 % (n = 33) patients. The mean follow-up period was 51.3 months (SD: 26.3; range: 12–118). During follow-up, 20 (10 %) subjects died, and 41 (20.5 %) had major clinical events of which 7 (3.5 %) had repeat revascularization and 13 (6.5 %) had ACS which were conservatively managed. Mean SS, rSS, and SSII scores were 16.7 (SD: 5.4), 4.9 (SD: 4.4), and 29.8 (SD: 9.5), respectively. Baseline characteristics are shown in Table 1.

3.2. Risk scores and outcomes

The discriminative performance of the risk scores is shown in Table 2. The SSII had the best predictive accuracy for all-cause mortality with a c-statistics area under the curve (AUC) of 0.79 (95 % confidence interval [CI]: 0.70–0.89). The ACEF score also performed well (AUC: 0.74; 95 % CI: 0.64–0.86). The predictive performance of both SS and rSS was significantly low compared to SSII and ACEF score. SSII with cut-offs of ≥35.15 and ≥ 29.55 was significantly associated with higher mortality and MACE, respectively. Patients having SSII of ≥35.15 had a median time to mortality of 79 months (95 % CI: 56.23–101.77). ACEF score and cSS performed similarly. rSS with a cut-off of >5.5 did not discriminate between mortality and MACE. SRI >79.65 was associated with worse mortality though statistically insignificant (Table 3, Fig. 1). Multivariate analysis by Cox regression showed SSII with cut-offs >35.15 and > 29.55 to be the only score associated with higher mortality and MACE, respectively (Table 3).

4. Discussion

The most important finding of the present study was that in UA/NSTEMI patients with MVCAD undergoing PCI, scores based on clinical and angiographic features predicted outcomes better than those based on angiography alone. The scores assessing residual disease and completeness of revascularization performed poorly.

The SS was developed as an angiographic stratification tool to establish evidence-based guidelines to determine the best revascularization strategy in patients with complex multivessel and left main disease.[10] In the landmark SYNTAX trial, a higher score of >34 differentiated clinical outcomes between CABG and PCI.[23] The SS was then evaluated in multiple trials and was incorporated into medical guidelines.[24,25] Inter and intra-observer variability, consideration of lesions in small vessels (1.5 mm) which are less likely to be functionally important and patient categorization into tertiles are among the several inherent limitations with SS.[26] Most importantly, it was shown not to serve the purpose of determining the prognosis in those with low scores.[27] In our study, SS performed poorly in predicting hard endpoints. It must be noted that our study population had an overall low syntax score suggesting less anatomic complexity.

Long-term mortality predictions were impacted by anatomic and clinical characteristics, as shown previously. A meta-analysis comparing SS with cSS to validate their predictive abilities on adverse clinical outcomes showed that cSS was associated with better predictive ability for all-cause mortality with relative risk: 1.04 (95 % CI: 1.03–1.05).[28] The Evaluation of the Xience versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial[29] to validate SSII showed that the predicted four-year mortality as per SSII was at an equilibrium between PCI and CABG for up to intermediate anatomic complexity.

In the present study, SSII showed the best predictive capability for mortality with an AUC of 0.79, followed by ACEF (AUC: 0.74) and cSS (AUC: 0.65). Furthermore, SSII had the best overall accuracy for risk stratification, followed by cSS and ACEF. SSII with cut-offs ≥35.15 and ≥ 29.55 was significantly associated with higher mortality and MACE, respectively in MVCAD. The superior performance was obtained without any additional computational complexity. It is noteworthy that both cSS and SSII are made with ACEF score as the backbone. SSII is obtained by adding three clinical (gender, PVD, COPD) and one angiographic (left main) variable to the cSS.[8] These findings suggest that both cSS and SSII are useful tools in routine clinical decision making, helping in the individualized and more precise assessment of post-ACS patients undergoing PCI.[20,21] SSII has been validated in different trials; however, limited data exists comparing different risk scores in UA/NSTEMI patients.[24–26,30–32] The present study could compare and evaluate the SSII in UA/NSTEMI patients undergoing multivessel PCI.

CR is often not achieved in MVCAD due to clinical or technical reasons despite innovations and procedural advances in PCI. IR and its prognostic implications are still unclear and inconsistent among studies because standardized definitions were not used. rSS <8 and SRI >70 % were proposed as the best cut-offs predicting a reduction in mortality.[7,9] A notable finding in this study was that the residual disease burden and percentage of treated disease calculated using rSS and SRI were not predictive of outcomes. rSS, with a cut-off of

Table 1
Patient baseline characteristics (N = 200).

Age (years), mean (range)	57.9 (33–81)
Male, %	77.0
Systemic hypertension, %	34.0
Diabetes mellitus, %	44.5
Dyslipidemia, %	15.5
History of smoking/tobacco use, %	13.5
Family h/o coronary artery disease, %	12.5
Chronic kidney disease, %	6.5
Cerebrovascular accident, %	1.5
Peripheral arterial disease, %	8
Creatinine clearance (ml/min/1.73m^2), mean (SD, range)	67.26 (20.93, 22.6–146)
LVEF (%), mean (SD, range)	53.8 (18.5, 28–66)
Number of stents used per patient, mean (SD, range)	2.6 (0.68, 1–5)
Staged procedure, %	16.5
Period of follow up (months), mean (SD, range)	51.3 (26.3, 12.0–118.0)
SS, mean (SD, range)	16.7 (5.4, 6.0–32.0)
rSS, mean (SD, range)	4.9 (4.4, 0.0–22.5)
SRI, mean (SD, range)	71.6 (23.9, 10.5–100.0)
ACEF Score, mean (SD, range)	1.1 (0.3, 0.6–2.4)
cSS, mean (SD, range)	18.6 (8.8, 4.8–53.1)
SSII, mean (SD, range)	29.8 (9.5, 11.6–59.0)

LVEF: left ventricular ejection fraction; SD: standard deviation; SS: SYNTAX Score; rSS: residual SYNTAX Score; SRI: SYNTAX revascularization index; ACEF: age, creatinine, and ejection fraction; cSS: clinical SYNTAX Score; SSII: SYNTAX Score II.

Table 2
C-statistics with *p* values for comparison of the predictive performance of risk scores.

Scores	C-statistics	95 % CI	*p*-value					
			SS	rSS	ACEF	cSS	SRI	SSII
SS	0.541	0.42–0.66	–	<0.01	0.117	<0.01	0.369	0.001
rSS	0.557	0.43–0.68	<0.01	–	0.656	<0.01	<0.01	0.472
SRI	0.639	0.53–0.75	0.369	<0.01	0.067	0.706	–	0.128
ACEF	0.746	0.64–0.86	0.117	0.656	–	<0.01	0.067	<0.01
cSS	0.657	0.53–0.79	<0.01	<0.01	<0.01	–	0.706	<0.01
SSII	0.795	0.70–0.89	0.001	0.472	<0.01	<0.01	0.128	–

CI: confidence interval; SS: SYNTAX Score; rSS: residual SYNTAX Score; SRI: SYNTAX revascularization index; ACEF: age, creatinine, and ejection fraction; cSS: clinical SYNTAX Score; SSII: SYNTAX Score II.

Table 3
Cox logistic regression for all-cause mortality - Multivariate analysis.

	Cut-off	Odds (95 % CI)	*p*-value
SYNTAX Score	≥12.5	1.21 (0.26–5.67)	0.808
Residual SYNTAX Score	≤5.50	2.03 (0.51–8.13)	0.318
SYNTAX Revascularization Index	≥79.65	1.01 (0.28–3.59)	0.993
ACEF Score	≥1.05	2.93 (0.54–15.87)	0.212
Clinical SYNTAX Score	≥15.27	3.04 (0.71–13.01)	0.134
SYNTAX score II	≥35.15	5.72 (1.81–18.08)	0.003

CI, confidence interval.

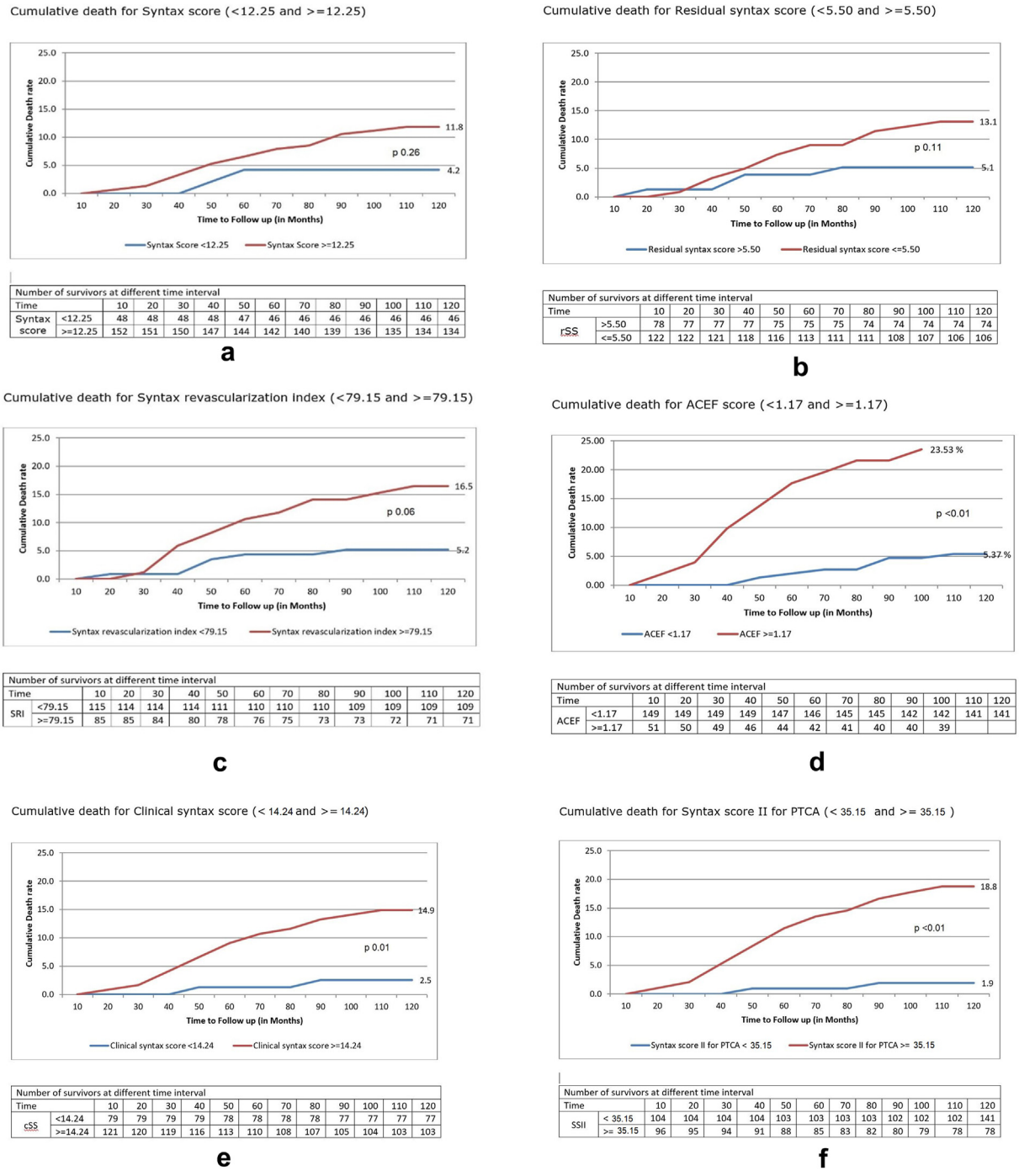

Fig. 1. Kaplan-Meier survival function for all-cause mortality based on different scores.
Legend: Kaplan-Meier survival function for all-cause mortality based on different scores. The discriminative ability is assessed by two sets of values for each score separated by a cut off. P values are derived from log rank test.

5.5, failed to discriminate mortality and MACE. Ironically, SRI >79.65 was associated with increased mortality, though this was not statistically significant. It must be noted that SRI alone does not give an idea about the absolute amount of untreated disease. The low baseline SS of our study population combined with low post PCI rSS (4.9) meant that the high mean SRI (71.6) achieved could have been offset by other clinical factors, thus contributing to this finding. Results are mixed with these scores in previous studies. In some trials, these scores were independent predictors of mortality.[2,7,18] But in recent trials, IR showed no effect on mortality but had a variable impact on reinfarction.[28,33,34] These results also open up the possibility of further improving the predictive capability of SSII with functional evaluation of borderline lesions through fractional flow reserve measurement. Addressing those functionally significant lesions would lead to more meaningful CR.[27] Therefore, long-term follow-up studies in MVCAD combining risk assessment with baseline clinical and angiographic data and additional functional evaluation of borderline lesions are needed to validate the above findings.

4.1. Limitations

As generally observed in any retrospective studies, the current study too was limited by being an observational registry-based retrospective analysis from a single center with limited number of patients. Detailed data on the CABG group was unavailable, so the validation of SSII for CABG was not possible. We have tried to overcome the potential limitations through robust statistical methods including multivariate logistic regression analysis to exclude significant confounders. To validate the score and to assess the additional advantage of functional evaluation, a randomized prospective study would be needed in the future.[29]

5. Conclusion

To conclude, in UA/NSTEMI patients with MVCAD and relatively low baseline SS treated by PCI, the SSII based on baseline clinical and angiographic characteristics showed better risk assessment than purely anatomic score such as SS or scores assessing post-PCI residual diseases such as rSS and SRI. The SSII was the most accurate predictor of medium-to long-term clinical events and mortality, followed by ACEF score and cSS. The routine application of SSII would further improve the decision-making process for revascularization in post-ACS MVCAD patients.

Role of the funding source

The study was funded by the Department of Cardiology, Government Medical College, Kannur, Kerala, India. The sponsor had a role in study design, including collecting, analyzing, and interpreting data.

Submission declaration

The work described has not been published previously and is not considered for publication elsewhere. The manuscript draft is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or any other language, including electronically without the written consent of the copyright holder.

Declaration of competing interest

The authors declare no conflict of interest in the study.

Acknowledgment

The authors would like to acknowledge MD. Najeeb Ashraf from SciVoc Healthcare Consulting Pvt. Ltd. For their language editing and proofreading contribution.

What is Already Known?

The SYNTAX based risk scores have been compared and validated in complex multivessel CAD. SSII is known to have better predictive capability of mortality compared to SS in multivessel CAD.

What this Study Adds?

- Comparison of six risk scores in UA/NSTEMI patients with less complex MVCAD undergoing PCI.
- SYNTAX Score II, ACEF Score, and clinical SYNTAX Score showed best mortality prediction.
- SYNTAX Score, Residual Syntax Score, and SYNTAX Revascularization Index Score performed worst.
- SYNTAX Score II helps in more accurate individualized assessment of patient risk.

References

1. Leaman DM, Brower RW, Meester GT, et al. Coronary artery atherosclerosis: severity of the disease, severity of angina pectoris and compromised left ventricular function. *Circulation*. 1981;63:285–299.
2. Mohr FW, Morice MC, Kappetein AP, et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. *Lancet*. 2013;381:629–638.
3. Kolh P, Windecker S, Alfonso F, et al. ESC/EACTS guidelines on myocardial revascularization: the task force on myocardial revascularization of the European society of Cardiology (ESC) and the European association for cardiothoracic surgery (EACTS). Developed with the special contribution of the European association of percutaneous cardiovascular interventions (EAPCI). *Eur Heart J*. 2014;35:2541–2619, 2014.
4. Levine GN, Bates ER, Blankenship JC, et al. ACC/AHA/SCAI focused update on primary percutaneous coronary intervention for patients with ST-elevation myocardial infarction: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention and the 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology/American heart association task force on clinical practice guidelines and the society for cardiovascular angiography and interventions. *Circulation*. 2015;133:1135–1147, 2016.
5. Zimarino M, Curzen N, Cicchitti V, et al. The adequacy of myocardial revascularization in patients with multivessel coronary artery disease. *Int J Cardiol*. 2013;168:1748–1757.
6. Morice MC, Serruys PW, Kappetein AP, et al. Five-year outcomes in patients with left main disease treated with either percutaneous coronary intervention or coronary artery bypass grafting in the synergy between percutaneous coronary intervention with taxus and cardiac surgery trial. *Circulation*. 2014;129:2388–2394.
7. Farooq V, Serruys PW, Bourantas CV, et al. Quantification of incomplete revascularization and its association with five-year mortality in the synergy between percutaneous coronary intervention with taxus and cardiac surgery (SYNTAX) trial validation of the residual SYNTAX score. *Circulation*. 2013;128:141–151.
8. Farooq V, van Klaveren D, Steyerberg EW, et al. Anatomical and clinical characteristics to guide decision making between coronary artery bypass surgery and percutaneous coronary intervention for individual patients: development and validation of SYNTAX score II. *Lancet*. 2013;381:639–650.
9. Généreux P, Campos CM, Farooq V, et al. Validation of the SYNTAX revascularization index to quantify reasonable level of incomplete revascularization after percutaneous coronary intervention. *Am J Cardiol*. 2015;116:174–186.
10. Sianos G, Morel MA, Kappetein AP, et al. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. *EuroIntervention*. 2005;1:219–227.
11. Généreux P, Palmerini T, Caixeta A, et al. Quantification and impact of untreated coronary artery disease after percutaneous coronary intervention: the residual SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) score. *J Am Coll Cardiol*. 2012;59:2165–2174.
12. Farooq V, Vergouwe Y, Räber L, et al. Combined anatomical and clinical factors for the long-term risk stratification of patients undergoing percutaneous coronary intervention: the Logistic Clinical SYNTAX score. *Eur Heart J*. 2012;33:3098–3104.
13. Zimarino M, Curzen N, Cicchitti V, et al. The adequacy of myocardial revascularization in patients with multivessel coronary artery disease. *Int J Cardiol*. 2013;168:1748–1757.
14. Serruys PW, Farooq V, Vranckx P, et al. A global risk approach to identify patients with left main or 3-vessel disease who could safely and efficaciously be treated with percutaneous coronary intervention: the SYNTAX Trial at 3 years. *JACC Cardiovasc Interv*. 2012;5:606–617.
15. Serruys PW, Ong ATL, Morice M-C, et al. Arterial Revascularisation Therapies Study Part II - sirolimus-eluting stents for the treatment of patients with multivessel de novo coronary artery lesions. *EuroIntervention*. 2005;1:147–156.
16. Nashef SA, Roques F, Sharples LD, et al. EuroSCORE II. *Eur J Cardio Thorac Surg*. 2012;41:734–744.
17. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron*. 1976;16:31–41.
18. Généreux P, Campos CM, Yadav M, et al. Reasonable incomplete revascularisation after percutaneous coronary intervention: the SYNTAX Revascularisation Index. *EuroIntervention*. 2015;11:634–642.
19. Ranucci M, Castelvecchio S, Menicanti L, et al. Risk of assessing mortality risk in elective cardiac operations: age, creatinine, ejection fraction, and the law of parsimony. *Circulation*. 2009;119:3053–3061.

20. Garg S, Sarno G, Garcia-Garcia HM, et al. A new tool for the risk stratification of patients with complex coronary artery disease: the Clinical SYNTAX Score. *Circ Cardiovasc Interv*. 2010;3:317–326.
21. Campos CM, Stanetic BM, Farooq V, et al. SYNTAX II study group. Risk stratification in 3-vessel coronary artery disease: applying the SYNTAX score II in the heart team discussion of the SYNTAX II trial. *Cathet Cardiovasc Interv*. 2015;86: E229–E238.
22. Harrell Jr FE, Califf RM, Pryor DB, et al. Evaluating the yield of medical tests. *J Am Med Assoc*. 1982;247:2543–2546.
23. Serruys PW, Morice MC, Kappetein AP, et al. SYNTAX Investigators. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med*. 2009;360:961–972.
24. Windecker S, Kolh P, Alfonso F, et al. ESC/EACTS guidelines on myocardial revascularization. *EuroIntervention*. 2014;10:1024–1094, 2015.
25. Fihn SD, Gardin JM, Abrams J, et al, American College of Cardiology Foundation. ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: executive summary: a report of the American College of Cardiology foundation/American heart association task force on practice guidelines, and the American College of physicians, American association for thoracic surgery, preventive cardiovascular nurses association, society for cardiovascular angiography and interventions, and society of thoracic surgeons. *Circulation*. 2012;126:3097–3137, 2012.
26. Stone GW, Sabik JF, Serruys PW, et al. Everolimus-eluting stents or bypass surgery for left main coronary artery disease. *N Engl J Med*. 2016;375: 2223–2235.
27. Kobayashi Y, Lønborg J, Jong A. On behalf of the DANAMI-3-PRIMULTI, FAME, and FAMOUS-NSTEMI Study Investigators. Prognostic value of the residual SYNTAX score after functionally complete revascularization in. *ACS. J Am Coll Cardiol*. 2018;72:1321–1329.
28. Chen J, Tang B, Lin Y, et al. Validation of the ability of SYNTAX and clinical SYNTAX scores to predict adverse cardiovascular events after stent implantation: a systematic review and meta-analysis. *Angiology*. 2016;67:820–828.
29. Campos CM, van Klaveren D, Farooq V, et al. Long-term forecasting and comparison of mortality in the evaluation of the xience everolimus ElutingStent vs. Coronary artery bypass surgery for effectiveness of left main revascularization (EXCEL) trial: prospective validation of the SYNTAX score II. *Eur Heart J*. 2015;36:1231–1241.
30. Campos CM, Garcia-Garcia HM, Klaveren DV, et al. Validity of SYNTAX score II for risk stratification of percutaneous coronary interventions: a patient-level pooled analysis of 5,433 patients enrolled in contemporary coronary stent trials. *Int J Cardiol*. 2015;187:111–115.
31. Sotomi Y, Cavalcante R, van Klaveren D, et al. Individual long-term mortality prediction following either coronary stenting or bypass surgery in patients with multivessel and/or unprotected left main disease: an external validation of the SYNTAX score II model in the 1,480 patients of the BEST and PRECOMBAT randomized controlled trials. *JACC Cardiovasc Interv*. 2016;9: 1564–1572.
32. Xu B, Généreux P, Yang Y, et al. Validation and comparison of the long-term prognostic capability of the SYNTAX score-II among 1,528 consecutive patients who underwent left main percutaneous coronary intervention. *JACC Cardiovasc Interv*. 2014;7:1128–1137.
33. Chang M, Ahn JM, Kim N, et al. Complete versus incomplete revascularization in patients with multivessel coronary artery disease treated with drug-eluting stents. *Am Heart J*. 2016;179:157–165.
34. Su CS, Shen CH, Chang KH, et al. Clinical outcomes of patients with multivessel coronary artery disease treated with robot-assisted coronary artery bypass graft surgery versus one-stage percutaneous coronary intervention using drug-eluting stents. *Medicine (Baltim)*. 2019;98, e17202.