

## ORIGINAL STUDIES

# Impact of the residual SYNTAX score on clinical outcomes after percutaneous coronary intervention for patients with chronic renal insufficiency

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## Abstract

**Objectives:** This study demonstrated the prognostic value of the residual SYNTAX score (rSS) for patients with chronic renal insufficiency (CRI).

**Background:** The rSS has been proposed as a useful tool for quantifying and stratifying the degree and complexity of residual stenosis and predicting long-term clinical outcomes following percutaneous coronary intervention (PCI). However, it has never been validated for patients with CRI.

**Methods:** A total of 2,468 consecutive patients with an estimated glomerular filtration rate <90 ml/min/1.73 m<sup>2</sup> who underwent PCI were retrospectively enrolled. Patients with rSS >0 were defined as having incomplete revascularization and were stratified into the reasonable incomplete revascularization (RICR; 0 < rSS ≤ 8) group or the incomplete revascularization (ICR; rSS >8) group. Their outcomes were compared to those of the complete revascularization (CR) group.

**Results:** During follow-up (median, 3 years; range, 1.5–5 years), the ICR group had the highest incidence of all-cause death, cardiac death, myocardial infarction (MI), unplanned revascularization, stroke, and major adverse cardiovascular and cerebrovascular events (MACCE). Despite having higher rates of unplanned revascularization and MACCE, RICR group had comparable all-cause mortality, cardiac mortality, MI, and stroke with CR group. A multivariable Cox analysis indicated that rSS was an independent predictor of cardiac death, MI, unplanned revascularization, stroke, and MACCE. Furthermore, compared with baseline SYNTAX score, rSS had stronger prognostic accuracy when predicting the risk of unplanned revascularization, stroke, and MACCE at the 3-year follow-up.

**Conclusions:** The rSS is a powerful indicator of clinical outcomes and may help determine reasonable levels of revascularization for patients with CRI following PCI.

## KEYWORDS

cardiac death, coronary artery disease, myocardial infarction, revascularization

## 1 | INTRODUCTION

Chronic kidney disease (CKD) is a common high-risk comorbidity that increases cardiovascular mortality and morbidity rates.<sup>1</sup> Furthermore, CKD has been confirmed to be associated with lower procedural success rates, more complications, and worse clinical outcomes, including restenosis or stent thrombosis following percutaneous coronary intervention (PCI).<sup>1,2</sup>

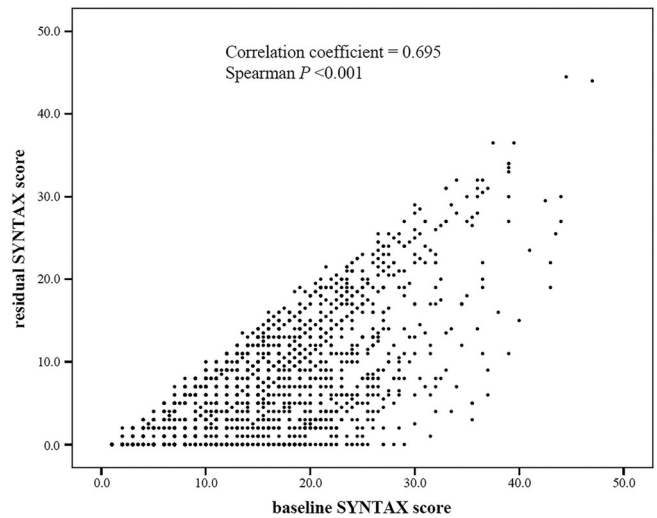
Percutaneous coronary intervention has become an important option for treating patients with coronary artery disease (CAD), and achieving complete revascularization (CR) is a desired goal of PCI. Previous studies suggested that CR was more advantageous than incomplete revascularization (ICR) and that residual disease was associated with adverse clinical outcomes after PCI.<sup>3-6</sup> However, for patients with more complex lesions, CR is not always achieved. Recent studies have shown that patients with an acceptable burden of obstructive CAD after revascularization have outcomes similar to those of subjects who achieved CR.<sup>7-9</sup> Therefore, the concept of reasonable incomplete revascularization (RICR) has been proposed.<sup>7-9</sup>

The residual SYNTAX score (rSS), which was recently proposed as an objective, quantitative measure of the degree and complexity of residual stenosis after PCI, has been validated as an independent predictor of worse clinical outcomes after PCI in different population cohorts.<sup>5,10-19</sup> However, no previous study assessed the utility of rSS for patients with chronic renal insufficiency (CRI). The purpose of this study was to assess the prognostic value of rSS for patients with CRI at the 3-year (median) follow-up.

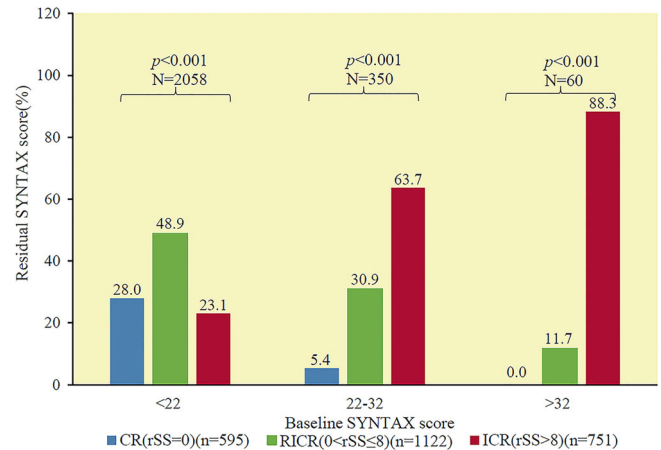
## 2 | METHODS

### 2.1 | Study population and angiographic analysis

From January 2014 to September 2017, 14,174 consecutive cases underwent PCI at Cangzhou Central Hospital, Hebei Medical University. Among them, 2,529 consecutive cases with an estimated glomerular filtration rate (eGFR) <90 ml/min/1.73 m<sup>2</sup> were retrospectively enrolled. The eGFR was calculated using the following simplified modification of

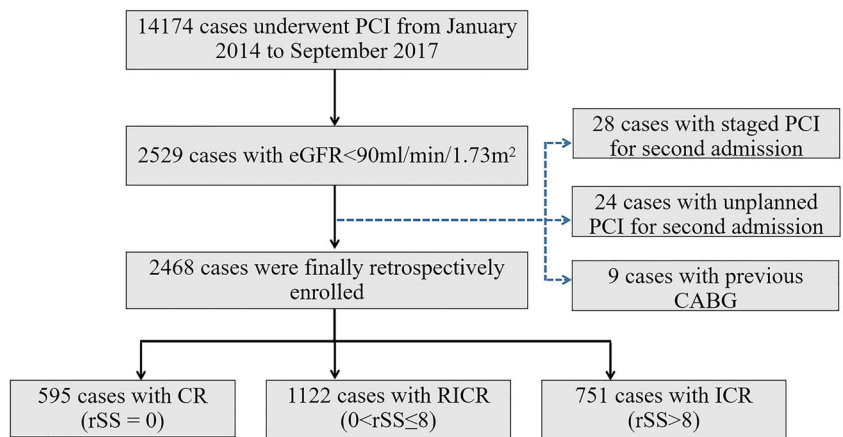


**FIGURE 2** Correlation between the baseline SYNTAX score and residual SYNTAX score after percutaneous coronary intervention



**FIGURE 3** Distribution of complete, reasonable incomplete, and incomplete revascularization according to the baseline SYNTAX score. CR, complete revascularization; ICR, incomplete revascularization; RICR, reasonable incomplete revascularization; rSS, residual SYNTAX score

**FIGURE 1** Study flowchart. CABG, coronary artery bypass grafting; CR, complete revascularization; eGFR, estimated glomerular filtration rate; ICR, incomplete revascularization; RICR, reasonable incomplete revascularization; rSS, residual SYNTAX score; PCI, percutaneous coronary intervention



diet in renal disease equation:  $eGFR \text{ (ml/min/1.73 m}^2\text{)} = 186.3 \times \text{serum creatinine}^{-1.154} \text{ (mg/dl)} \times \text{age}^{-0.203} \times 0.742 \text{ (if female)} \times 1.212 \text{ (if African American)}.$ <sup>20</sup> Because the SYNTAX score has been validated only for patients with native CAD, nine cases with a history of previous coronary artery bypass grafting (CABG) were excluded. After excluding another 28 cases with staged PCI and 24 cases with unplanned PCI

during the second admission, 2,468 patients were finally analyzed in this study (Figure 1).

The baseline SYNTAX score (bSS) was assessed visually by two of three experienced interventional cardiologists who were trained to perform SYNTAX score assessments and blinded to the treatment assignment and clinical outcomes. In the case of disagreement, the opinion of

**TABLE 1** Baseline characteristics according to the residual SYNTAX score

	CR (rSS = 0) (n = 595)	RICR (0 < rSS ≤ 8) (n = 1,122)	ICR (rSS >8) (n = 751)	p-Value
Demographics				
Age, year	63.7 ± 9.3	65.0 ± 8.5	66.2 ± 8.5	<.001
Male, n (%)	345 (58.0)	666 (59.4)	441 (58.7)	.815
BMI, kg/m <sup>2</sup>	25.9 ± 3.4	26.0 ± 3.3	26.1 ± 3.4	.911
Diabetes, n (%)	116 (19.5)	248 (22.1)	202 (26.9)	.001
Hypertension, n (%)	376 (63.2)	762 (67.9)	520 (69.2)	.022
Dyslipidemia, n (%)	222 (37.3)	446 (39.8)	305 (40.6)	.229
Current smoker, n (%)	55 (9.2)	142 (12.7)	78 (10.4)	.625
Prior MI, n (%)	36 (6.1)	97 (8.6)	75 (10.0)	.011
Previous PCI, n (%)	77 (13.0)	164 (14.6)	81 (10.8)	.180
Previous stroke	49 (8.2)	110 (9.8)	110 (14.6)	<.001
COPD, n (%)	11 (1.8)	21 (1.9)	8 (1.1)	.350
Clinical presentation, n (%)				.118
Stable angina	261 (43.9)	474 (42.2)	275 (36.6)	
Unstable angina	66 (11.1)	149 (13.3)	100 (13.3)	
NSTEMI	80 (13.4)	185 (16.5)	155 (20.6)	
STEMI	188 (31.6)	314 (28.0)	221 (29.4)	
eGFR, ml/min	76.3 ± 11.8	75.5 ± 13.2	74.1 ± 13.4	.006
Renal dysfunction, n (%)				.002
60 ≤ eGFR < 90	538 (90.4)	995 (88.7)	640 (85.2)	
30 ≤ eGFR < 60	54 (9.1)	116 (10.3)	101 (13.4)	
eGFR < 30	3 (0.5)	11 (1.0)	10 (1.3)	
LVEF	60.5 ± 9.6	59.5 ± 9.7	59.8 ± 9.6	.318
LVEF (%)				.461
Good LVEF (≥50%)	522 (87.7)	950 (84.7)	637 (84.8)	
Moderate LVEF (30–49%)	69 (11.6)	167 (14.9)	114 (15.2)	
Poor LVEF (<30%)	4 (0.7)	5 (0.4)	0 (0.0)	
LVEDD (mm)	47.8 ± 6.7	48.1 ± 6.1	48.3 ± 6.1	.510
Baseline laboratory				
Hemoglobin (mg/dl)	13.3 ± 1.7	13.1 ± 1.7	13.0 ± 1.8	.018
Creatinine (mg/dl)	0.97 ± 0.23	0.99 ± 0.38	1.0 ± 0.28	.160
Fasting glucose (mg/dl)	136.1 ± 66.7	136.4 ± 63.0	145.1 ± 71.7	.012
Total cholesterol (mg/dl)	170.9 ± 39.3	173.6 ± 42.9	175.4 ± 41.4	.199
TG (mg/dl)	154.6 ± 106.5	163.2 ± 122.4	162.1 ± 95.5	.360
HDL (mg/dl)	37.3 ± 9.3	36.8 ± 8.6	36.2 ± 8.6	.140
LDL (mg/dl)	99.3 ± 30.1	100.9 ± 31.6	102.6 ± 31.2	.224

Note: Continuous data are expressed as mean ± SD. Categorical data are expressed as n (%).

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; CR, complete revascularization; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; ICR, incomplete revascularization; LDL, low-density lipoprotein; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSTEMI, non ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; RICR, reasonable incomplete revascularization; TG, triglyceride.

the third observer was obtained and the final decision was made by consensus. Each lesion with stenosis >50% in diameter in vessels >1.5 mm in diameter was scored using the SYNTAX score algorithm (fully described elsewhere).<sup>21</sup> The intraobserver variability of the calculated bSS (quartile partitioning) based on reanalyzing 50 cases every 3 months indicated a high level of agreement ( $k$  statistic = 0.88; 95% confidence interval [CI], 0.78–0.98;  $p < .001$ ).<sup>22</sup> The rSS was calculated based on the other obstructive coronary disease cases after treatment with PCI.<sup>10</sup> In the case of staged PCI procedures (defined as a second planned PCI procedure after the initial intervention), the final planned procedure was used as the entry point for this study. All data were

entered into a dedicated computer database. The study protocol was approved by the ethics committee of Cangzhou Central Hospital, Hebei Medical University, and all patients provided written informed consent.

## 2.2 | Endpoints and definitions

Clinical follow-up was scheduled at 1, 3, 6, and 12 months, and then annually thereafter via clinical visit or telephone contact. The primary endpoints were all-cause mortality and cardiac mortality. Death that could not be attributed to a noncardiac cause was considered cardiac

**TABLE 2** Anatomical and procedural characteristics of lesions according to the residual SYNTAX score

	CR (rSS = 0) (n = 595)	RICR (0 < rSS ≤ 8) (n = 1,122)	ICR (rSS > 8) (n = 751)	p-Value
CAD extension, n (%)				<.001
One-vessel disease	428 (71.9)	92 (8.2)	8 (1.1)	
Two-vessel disease	142 (23.9)	556 (49.6)	145 (19.3)	
Three-vessel disease	25 (4.2)	474 (42.2)	598 (79.6)	
Left main disease, n (%)	17 (2.9)	46 (4.1)	96 (12.8)	<.001
Lesion anatomical characteristics, n (%)				
Lesion length >20 mm	219 (36.8)	615 (54.8)	490 (65.2)	<.001
Bifurcation or trifurcation	72 (12.1)	306 (27.3)	253 (33.7)	<.001
Aorto-ostial lesion	5 (0.8)	11 (1.0)	40 (5.3)	<.001
Heavy calcification	17 (2.9)	67 (6.0)	138 (18.4)	<.001
Severe tortuosity	15 (2.5)	64 (5.7)	72 (9.6)	<.001
Thrombus	117 (19.7)	129 (11.5)	85 (11.3)	.008
Chronic total occlusions	55 (9.2)	118 (10.5)	184 (24.5)	<.001
Target vessel number	1.29 ± 0.55	1.33 ± 0.56	1.18 ± 0.44	<.001
Target lesion location, n (%)				
LM	14 (2.4)	45 (4.0)	12 (1.6)	.288
LAD	377 (63.4)	703 (62.7)	250 (33.3)	<.001
LCX	156 (26.2)	311 (27.7)	231 (30.8)	.061
RCA	220 (37.0)	431 (38.4)	220 (29.2)	<.001
Procedural characteristics				
Stent per patient	1.70 ± 1.1	1.81 ± 0.96	1.67 ± 0.84	.005
Total length of stent, mm	45.02 ± 32.19	49.64 ± 29.89	46.51 ± 27.59	.005
Stent length >100 mm, n (%)	40 (6.7)	84 (7.5)	43 (5.7)	.414
Mean stent diameter, mm	3.03 ± 0.45	2.96 ± 0.48	2.93 ± 0.42	.029
Minimum stent diameter, mm	2.95 ± 0.45	2.86 ± 0.45	2.83 ± 0.43	<.001
Maximum stent diameter, mm	3.18 ± 0.45	3.11 ± 0.48	3.05 ± 0.48	<.001
Primary PCI, n (%)	84 (14.1)	100 (8.9)	74 (9.9)	.132
Baseline SYNTAX score	8.88 ± 5.90	13.16 ± 6.08	20.59 ± 6.97	<.001
Baseline SYNTAX score, n (%)				<.001
Low (<22)	576 (96.8)	1,007 (89.8)	475 (63.2)	
Median (22–32)	19 (3.2)	108 (9.6)	223 (29.7)	
High (>32)	0 (0.0)	7 (0.6)	53 (7.1)	
Residual SYNTAX score	0	4.32 ± 2.23	14.42 ± 5.64	<.001
Delta SYNTAX score	8.88 ± 5.90	8.85 ± 5.90	6.17 ± 4.64	<.001

Note: Continuous data are expressed as mean ± SD. Categorical data are expressed as n (%).

Abbreviations: CAD, coronary artery disease; CR, complete revascularization; ICR, incomplete revascularization; LAD, left anterior descending artery; LCX, left circumflex; LM, left main; RCA, right coronary artery; RICR, reasonable incomplete revascularization.

death. The secondary endpoints included myocardial infarction (MI), stroke, unplanned revascularization, and major adverse cardiovascular and cerebrovascular events (MACCE; a composite of all-cause death, MI, stroke, and unplanned revascularization). MI was defined according to the fourth universal definition of MI.<sup>23</sup> Revascularization was defined as unplanned revascularization for ischemic symptoms and events caused by PCI or CABG. All endpoints were assessed centrally by two independent cardiologists, and disagreements were resolved by consensus.

## 2.3 | Statistical analysis

Continuous variables are expressed as mean  $\pm$  SD, whereas categorical variables are presented as *n* (%). All variables were stratified according to tertiles of rSS. Comparisons of continuous variables were analyzed by an analysis of variance. Categorical data were compared using the chi-square or the Fisher exact test. Time-to-event variables were analyzed using Kaplan–Meier methodology and compared using the log-rank test. Patients lost to follow-up were considered at risk until the date of last contact, at which point they were censored. Multivariable Cox regression analyses were conducted using the enter method. In addition to rSS, variables historically known to be associated with these adverse events were included in the models. The proportional hazards assumption was verified for each endpoint using the supremum test. Receiver-operating characteristic (ROC) curves for both bSS and rSS were created, and the area under the curve was compared using the nonparametric test of DeLong et al.<sup>24</sup> Two-sided  $p < .05$  was considered statistically significant. All analyses were conducted using the SPSS 24.0 (IBM Corp., Armonk, NY) and R software version 3.6.0.

## 3 | RESULTS

### 3.1 | Patient demographics, lesion characteristics, and procedural results

Among the 2,468 enrolled patients, the mean bSS was  $14.4 \pm 7.7$  (range, 1.0–47.0) and the mean rSS was  $6.4 \pm 6.6$  (range, 0–44.5). The

correlation (Spearman coefficient, 0.695;  $p < .001$ ) and distribution of bSS and rSS are illustrated in Figure 2. CR (rSS = 0), RICR ( $0 < rSS \leq 8$ ), and ICR (rSS  $> 8$ ) were achieved in 595 (24.1%), 1,122 (45.5%), and 751 (30.4%) patients, respectively. Figure 3 shows the level of completeness of revascularization stratified by the rSS according to the original bSS tertiles. The frequency of patients with ICR progressively increased across bSS tertiles (0–22: 23.1%; 22–32: 63.7%;  $> 32$ : 88.3%;  $p < .001$  for linear trend).

Clinical and angiographic characteristics of patients stratified by the rSS are shown in Tables 1 and 2. A higher rSS was associated with progressively increasing clinical comorbidity, namely, older age ( $p < .001$ ), diabetes ( $p = .001$ ), prior MI ( $p = .011$ ), previous stroke ( $p < .001$ ), reduced eGFR ( $p = .009$ ), lower hemoglobin ( $p = .018$ ), and higher fasting glucose ( $p = .012$ ). Similarly, a higher rSS was associated with a progressively higher bSS, three-vessel disease, left main disease, long lesions, bifurcations or trifurcations, aorto-ostial lesions, heavy calcification, severe tortuosity, thrombus, and chronic total occlusions ( $p \leq .001$ –.008). Compared to patients with CR and ICR, patients with RICR had more target vessels ( $p < .001$ ) and more implanted stents with longer lengths ( $p = .005$ ). However, the ICR group had the lowest delta SYNTAX score ( $p < .001$ ).

### 3.2 | Clinical outcomes

Among the 2,468 enrolled patients, 2,425 (98.3%) patients finished 3 years of follow-up (range, 1.5–5 years). Among the three groups, the ICR group had the highest 5-year cumulative incidence of all-cause death (8.1% vs. 4.9% vs. 5.6%;  $p = .021$ ), cardiac death (5.8% vs. 2.5% vs. 3.3%;  $p = .010$ ), MI (8.8% vs. 4.8% vs. 3.0%;  $p < .001$ ), unplanned revascularization (16.1% vs. 12.3% vs. 6.5%;  $p < .001$ ), stroke (10.5% vs. 6.5% vs. 6.6%;  $p < .001$ ), and MACCE (31.4% vs. 21.8% vs. 17.6%;  $p < .001$ ). Despite having higher rates of unplanned revascularization (12.3% vs. 6.5%;  $p = .001$ ) and MACCE (21.8% vs. 17.6%;  $p = .005$ ), the RICR group had all-cause death (4.9% vs. 5.6%;  $p = .830$ ), cardiac death (2.5% vs. 3.3%;  $p = .798$ ), MI (4.8% vs. 3.0%;  $p = .020$ ), and stroke (6.5% vs. 6.6%;  $p = .644$ ) rates that were similar to those of the CR group (Table 3 and Figure 4).

**TABLE 3** The 5-year cumulative incidence of adverse events according to the residual SYNTAX score

	CR (rSS = 0) ( <i>n</i> = 595)	RICR (0 < rSS $\leq$ 8) ( <i>n</i> = 1,124)	ICR (rSS > 8) ( <i>n</i> = 751)	p-Value			
				Trend	RICR versus CR*	ICR versus CR*	ICR versus RICR*
All-cause death	5.6% (33)	4.9% (55)	8.1% (60)	.021	.830	.036	.022
Cardiac death	3.3% (20)	2.5% (28)	5.8% (43)	.010	.798	.027	.003
Myocardial infarction	3.0% (18)	4.8% (54)	8.8% (66)	<.001	.020	<.001	.065
Unplanned revascularization	6.5% (39)	12.3% (138)	16.1% (121)	<.001	.001	<.001	.031
Stroke	6.6% (39)	6.5% (73)	10.5% (79)	<.001	.644	.001	.001
MACCE	17.6 (105)	21.8% (245)	31.4% (235)	<.001	.005	<.001	<.001

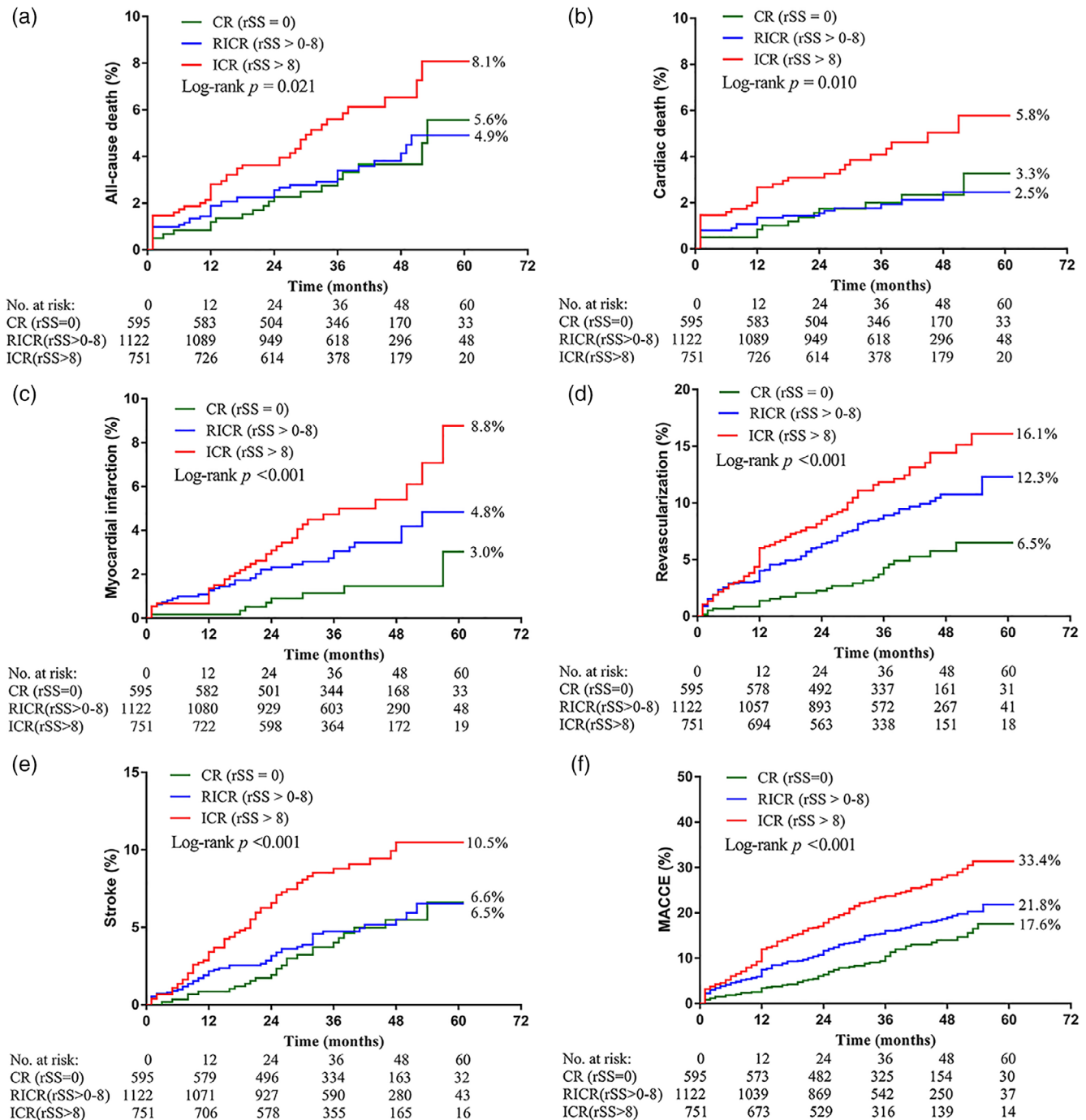
Note: Event rates are Kaplan–Meier estimates, % (*n*). \*Adjusted significance level is 0.017.

Abbreviations: CR, complete revascularization; ICR, incomplete revascularization; MACCE, major adverse cardiovascular and cerebrovascular events; RICR, reasonable incomplete revascularization.

### 3.3 | Multivariable analysis and ROC analysis

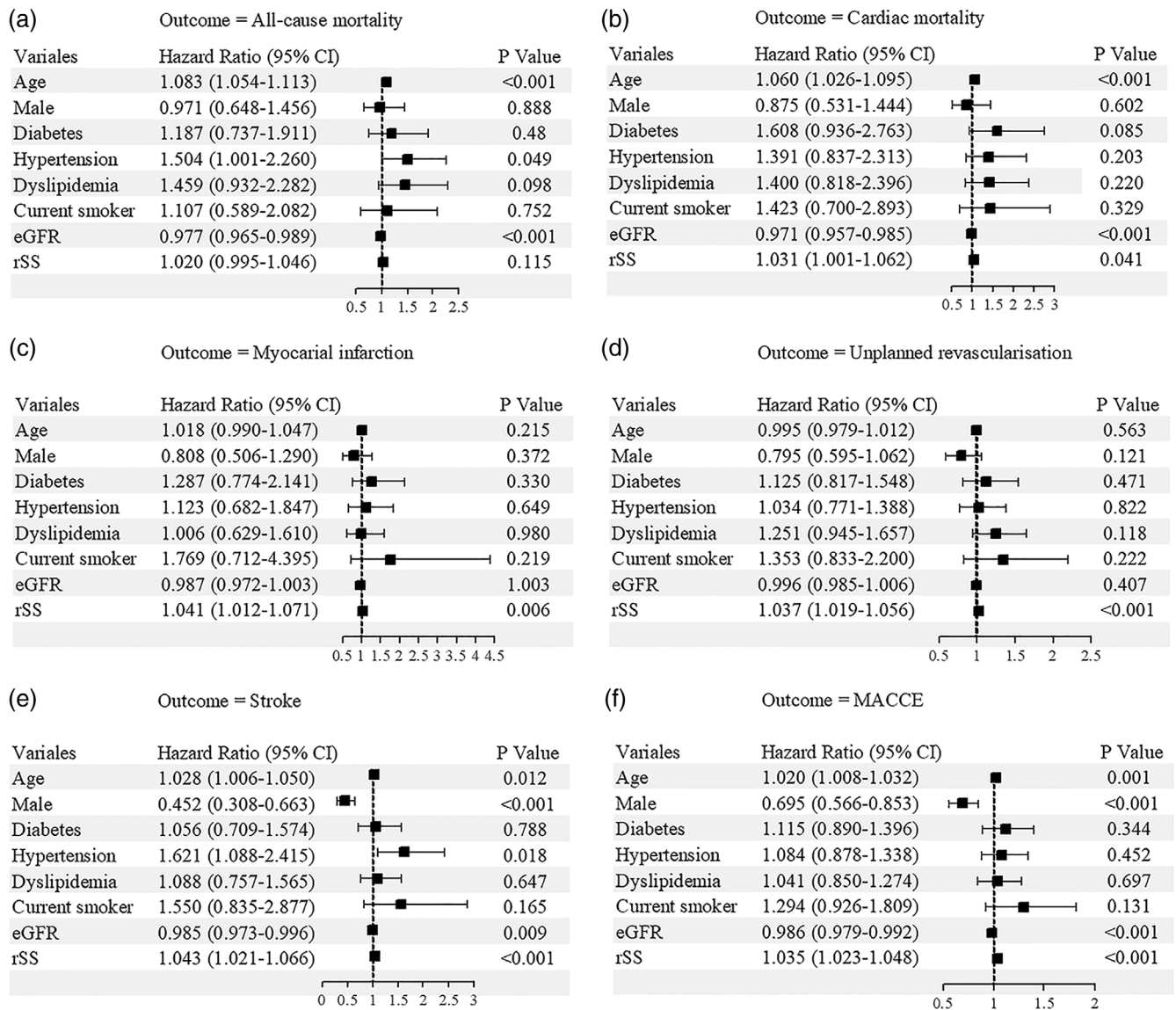
In the Cox multivariable analysis, rSS was an independent predictor of cardiac death (hazard ratio [HR], 1.031;  $p = .041$ ), MI (HR, 1.041;  $p = .006$ ), unplanned revascularization (HR, 1.037;  $p < .001$ ), stroke (HR, 1.043;  $p < .001$ ), and MACCE (HR, 1.035;  $p < .001$ ) at the 3-year follow-up (Figure 5).

The ROC curve analysis demonstrated a significant association between the rSS and all-cause death ( $p = .009$ ), cardiac death ( $p = .009$ ), MI ( $p = .001$ ), unplanned revascularization ( $p < .001$ ), stroke ( $p < .001$ ), and MACCE ( $p < .001$ ) at 3 years. The rSS cutoff values of 4 and 8.5 had the best prognostic accuracy for predicting the risk of all-cause death and cardiac death, respectively (Table 4).



**FIGURE 4** Kaplan-Meier curves showing event rates stratified by the residual SYNTAX score over the course of 5 years: (a) all-cause death; (b) cardiac death; (c) myocardial infarction; (d) revascularization; (e) stroke; and (f) major adverse cardiovascular and cerebrovascular events (MACCE). CR, complete revascularization; ICR, incomplete revascularization; RICR, reasonable incomplete revascularization; rSS, residual SYNTAX score





**FIGURE 5** Independent predictors of clinical outcomes at 3 years. CI, confidence interval; eGFR, estimated glomerular filtration rate; MACCE, major adverse cardiovascular and cerebrovascular events; rSS, residual SYNTAX score

**TABLE 4** ROC curve analysis of the residual SYNTAX scores for clinical outcomes at 3 years

Variables	AUC	p-Value	Optimal cutoff	Sensitivity (%)	Specificity (%)
All-cause death	0.576	.009	4	64.4	49.4
Cardiac death	0.593	.009	8.5	47.8	70.2
Myocardial infarction	0.610	.001	9	44.9	74.7
Unplanned revascularization	0.589	<.001	5.5	60.0	56.0
Stroke	0.598	<.001	8.5	44.9	70.6
MACCE	0.596	<.001	5.5	58.6	57.4

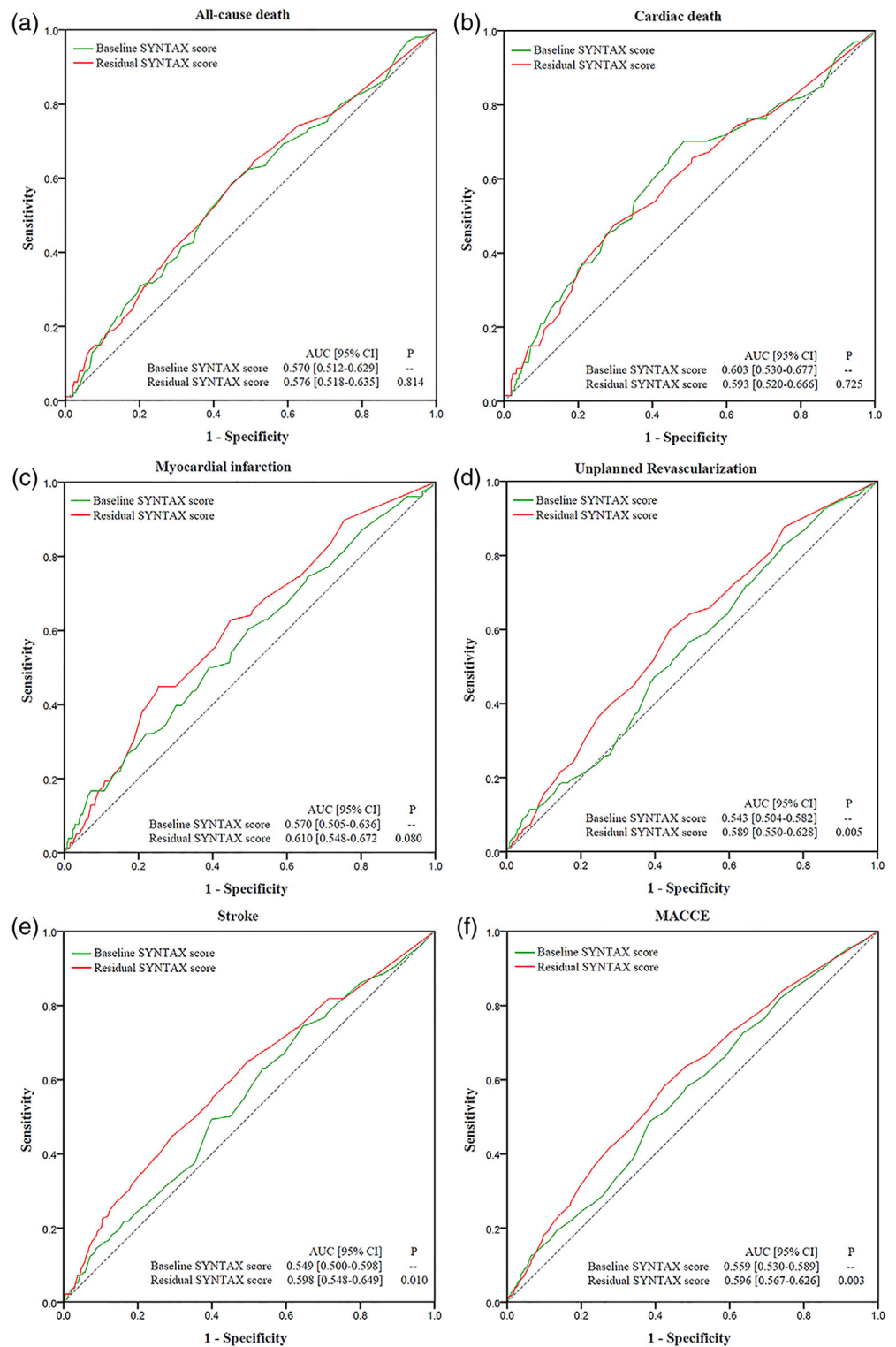
Abbreviations: AUC, area under the curve; MACCE, major adverse cardiovascular and cerebrovascular events; ROC, receiver-operating characteristic.

### 3.4 | Predictability of the rSS compared to the bSS

According to the ROC curve analysis, both the rSS and bSS were significantly associated with clinical outcomes at 3 years. Although the rSS

and bSS were similarly able to predict all-cause death, cardiac death, and MI, the rSS was superior for predicting unplanned revascularization (0.589 vs. 0.543;  $p = .005$ ), stroke (0.598 vs. 0.549;  $p = .010$ ), and MACCE (0.596 vs. 0.559;  $p = .003$ ) at the 3-year follow-up (Figure 6).

**FIGURE 6** Comparison of receiver-operating characteristic curves of the residual SYNTAX score and baseline SYNTAX score for the predictability of long-term outcomes. AUC, area under the curve; CI, confidence interval



## 4 | DISCUSSION

In this study, we assessed the impact of the rSS on long-term clinical outcomes of a large cohort of patients with CRI after PCI. During this study, we validated the prognostic value of the rSS for patients with CRI. We found that an rSS >8 was associated with progressively increasing rates of all adverse clinical outcomes, and

that an rSS <8 indicated comparable risks of all-cause death, cardiac death, and stroke with CR for patients with CRI. We also found that the rSS had stronger accuracy than the bSS for predicting the risk of unplanned revascularization, stroke, and MACCE.

Patients in our study were stratified according to the rSS after PCI. CR, defined as an rSS value of 0, was achieved in only 24.1% patients, this rate was obviously lower than that reported by other studies.<sup>5,10-17</sup>



CKD is a common comorbidity with cardiovascular diseases, and it increases mortality and morbidity.<sup>1</sup> Patients with CKD have clustering of significant cardiovascular risk factors and comorbidities and are more likely to have anatomically complex disease (e.g., calcification, bifurcation, long lesions, and multivessel disease).<sup>25–27</sup> Furthermore, CKD is known to be associated with higher rates of complications related to invasive procedures, including stent thrombosis and restenosis, and lower procedural success rates.<sup>1,2</sup> Patients with CKD are at increased risk for the development of contrast-associated acute kidney injury after PCI.<sup>28</sup> Therefore, interventional cardiologists may encounter more potential difficulties when treating highly complex CAD with CKD, and they tend to perform ICR treatment for these patients.

The concept of rSS was first developed by Stone and colleagues. The rSS was assessed in a large cohort of patients with moderate-risk and high-risk acute coronary syndrome undergoing PCI. This study demonstrated that the rSS was useful for quantifying and stratifying the degree and complexity of residual stenosis after PCI. Specifically, an rSS >8.0 after PCI was associated with poor 30-day and 1-year prognoses for patients with moderate-risk and high-risk acute coronary syndrome.<sup>10</sup> Farooq validated the prognostic impact of the rSS on adverse outcomes in the SYNTAX trial, which showed that the rSS is a powerful indicator of 5-year mortality.<sup>5</sup> The prognostic value of the rSS has also been confirmed for patients with multivessel CAD,<sup>13,17</sup> unprotected left main disease,<sup>12</sup> MI while undergoing primary PCI,<sup>18,29</sup> complex disease treated with second-generation drug-eluting stents,<sup>16</sup> and all PCI patients.<sup>15,19</sup> However, no studies or subgroup analyses have been performed to determine whether the rSS is meaningful for patients with CRI.

In this study, we validated the prognostic value of the rSS for adverse clinical outcomes of patients with CRI. Patients in the ICR group had the highest risk of adverse clinical outcomes, and patients in the RICR group and CR group had similar risks of all-cause death, cardiac death, MI, and stroke despite an increase in unplanned revascularization and MACCE in the RICR group. Therefore, the rSS can be an objective tool for quantitatively assessing the extent of ICR in patients with CRI in daily clinical practice. Furthermore, the rSS allowed for the determination of a threshold value of ICR that would not have a negative impact on long-term adverse cardiac events. Consistent with a previous study, we found that the ability of the rSS to predict mortality and MI was comparable with that of the bSS.<sup>16</sup> However, in contrast to that previous study, the rSS significantly improved the ability of the bSS to predict unplanned revascularization, stroke, and MACCE.<sup>16</sup>

Despite the greater anatomic complexity in the ICR group, the delta SYNTAX score from baseline to post-PCI, which represented the burden of coronary disease removed by PCI, did not significantly vary according to the rSS. These results suggest the potential difficulties that physician may encounter with highly complex CAD. Therefore, ICR is more likely because the anatomy is unfavorable for PCI. Advances in PCI technology developed to ensure that major epicardial vessels have been fully revascularized and aggressive secondary prevention may improve the long-term prognosis of patients with substantial ICR after PCI.

## 5 | LIMITATIONS

This study was limited by its post hoc nature. Validation was restricted to patients with CRI, the proportion of patients with CKD was small (11.9%), and the proportion of patients with Stages 4 or 5 renal insufficiency was even smaller (0.97%). We evaluated kidney function using the eGFR derived from serum creatinine rather than direct measurements of renal function such as iothalamate clearance. Additionally, the creatinine level might have been influenced by medications or clinical conditions. Third, rSS cannot fully represent coronary artery function. A previous study demonstrated that only 35% of lesions visually estimated to represent angiographic stenosis were functionally significant when tested by the fractional flow reserve, and low rates of clinical events were observed for lesions with normal fractional flow reserve.<sup>30</sup> Finally, participants in our study were enrolled at a single center. Further prospective, multicenter, randomized trials are required for better quantification of these findings.

## 6 | CONCLUSIONS

For a large cohort of patients with CRI after PCI, the rSS was an independent predictor of cardiac death, MI, unplanned revascularization, stroke, and MACCE at the 3-year follow-up. ICR (rSS >8) was associated with progressively increasing rates of adverse clinical outcomes, and RICR (rSS <8) was associated with similar risks of all-cause death, cardiac death, and stroke with CR despite its higher risks of MI, unplanned revascularization, and MACCE. The rSS may aid in determining a reasonable level of revascularization for patients with CRI after PCI.

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### CONFLICT OF INTEREST

All authors have no conflicts of interest to disclose.

### REFERENCES

1. Cai Q, Mukku VK, Ahmad M. Coronary artery disease in patients with chronic kidney disease: a clinical update. *Curr Cardiol Rev.* 2013;9:331-339.
2. Tsai TT, Messenger JC, Brennan JM, et al. Safety and efficacy of drug-eluting stents in older patients with chronic kidney disease: a report from the linked CathPCI Registry-CMS claims database. *J Am Coll Cardiol.* 2011;58:1859-1869.
3. Lehmann R, Fichtlscherer S, Schächinger V, et al. Complete revascularization in patients undergoing multivessel PCI is an independent predictor of improved long-term survival. *J Interv Cardiol.* 2010;23:256-263.
4. Hannan EL, Racz M, Holmes DR, et al. Impact of completeness of percutaneous coronary intervention revascularization on long-term outcomes in the stent era. *Circulation.* 2006;113:2406-2412.
5. 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.
6. Sarno G, Garg S, Onuma Y, et al. Impact of completeness of revascularization on the five-year outcome in percutaneous coronary intervention and coronary artery bypass graft patients (from the ARTS-II study). *Am J Cardiol*. 2010;106:1369-1375.
  7. De Bruyne B. Multivessel disease: from reasonably incomplete to functionally complete revascularization. *Circulation*. 2012;125:2557-2559.
  8. Gossel M, Faxon DP, Bell MR, Holmes DR, Gersh BJ. Complete versus incomplete revascularization with coronary artery bypass graft or percutaneous intervention in stable coronary artery disease. *Circ Cardiovasc Interv*. 2012;5:597-604.
  9. Rastan AJ, Walther T, Falk V, et al. Does reasonable incomplete surgical revascularization affect early or long-term survival in patients with multivessel coronary artery disease receiving left internal mammary artery bypass to left anterior descending artery? *Circulation*. 2009;120:S70-S77.
  10. Genereux 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.
  11. Schwietz T, Spyridopoulos I, Pfeiffer S, et al. Risk stratification following complex PCI: clinical versus anatomical risk stratification including "post PCI residual SYNTAX-score" as quantification of incomplete revascularization. *J Interv Cardiol*. 2013;26:29-37.
  12. Malkin CJ, Ghobrial MS, Raina T, Siotia A, Morton AC, Gunn J. Impact of incomplete revascularization in patients undergoing PCI for unprotected left main stem stenosis. *Catheter Cardiovasc Interv*. 2013;81:939-946.
  13. Malkin CJ, George V, Ghobrial MS, et al. Residual SYNTAX score after PCI for triple vessel coronary artery disease: quantifying the adverse effect of incomplete revascularisation. *EuroIntervention*. 2013;8:1286-1295.
  14. Capodanno D, Chisari A, Giacoppo D, et al. Objectifying the impact of incomplete revascularization by repeat angiographic risk assessment with the residual SYNTAX score after left main coronary artery percutaneous coronary intervention. *Catheter Cardiovasc Interv*. 2013;82:333-340.
  15. Park KW, Kang J, Kang SH, et al. The impact of residual coronary lesions on clinical outcomes after percutaneous coronary intervention: residual SYNTAX score after percutaneous coronary intervention in patients from the efficacy of Xience/Promus versus cypher in rEducing late loss after stENTing (EXCELLENT) registry. *Am Heart J*. 2014;167:384-392.e5.
  16. Xu B, Yang YJ, Han YL, et al. Validation of residual SYNTAX score with second-generation drug-eluting stents: one-year results from the prospective multicentre SEEDS study. *EuroIntervention*. 2014;10:65-73.
  17. Witberg G, Lavi I, Assali A, Vaknin-Assa H, Lev E, Kornowski R. The incremental impact of residual SYNTAX score on long-term clinical outcomes in patients with multivessel coronary artery disease treated by percutaneous coronary interventions. *Catheter Cardiovasc Interv*. 2015;86:3-10.
  18. Khan R, Al-Hawwas M, Hatem R, et al. Prognostic impact of the residual SYNTAX score on in-hospital outcomes in patients undergoing primary percutaneous coronary intervention. *Catheter Cardiovasc Interv*. 2016;88:740-747.
  19. Song Y, Gao Z, Tang X, et al. Impact of residual SYNTAX score on clinical outcomes after incomplete revascularisation percutaneous coronary intervention: a large single-Centre study. *EuroIntervention*. 2017;13:1185-1193.
  20. Inker LA, Astor BC, Fox CH, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. *Am J Kidney Dis*. 2014;63:713-735.
  21. 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.
  22. Genereux P, Palmerini T, Caixeta A, et al. SYNTAX score reproducibility and variability between interventional cardiologists, core laboratory technicians, and quantitative coronary measurements. *Circ Cardiovasc Interv*. 2011;4:553-561.
  23. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction (2018). *Glob Heart*. 2018;13:305-338.
  24. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics*. 1988;44:837-845.
  25. Mathew RO, Bangalore S, Lavelle MP, et al. Diagnosis and management of atherosclerotic cardiovascular disease in chronic kidney disease: a review. *Kidney Int*. 2017;91:797-807.
  26. Yan LQ, Guo LJ, Zhang FC, Gao W. The relationship between kidney function and angiographically-derived SYNTAX score. *Can J Cardiol*. 2011;27:768-772.
  27. Cao XF, Yan LQ, Han LX, et al. Association of mild to moderate kidney dysfunction with coronary artery calcification in patients with suspected coronary artery disease. *Cardiology*. 2011;120:211-216.
  28. Solomon RJ, Natarajan MK, Doucet S, et al. Cardiac Angiography in Renally Impaired Patients (CARE) study: a randomized double-blind trial of contrast-induced nephropathy in patients with chronic kidney disease. *Circulation*. 2007;115:3189-3196.
  29. Singbal Y, Fryer M, Garrahy P, Lim R. Baseline and residual SYNTAX score in predicting outcomes after acute infarct angioplasty. *EuroIntervention*. 2017;12:1995-2000.
  30. Tonino PA, De Bruyne B, Pijls NH, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. *N Engl J Med*. 2009;360:213-224.

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