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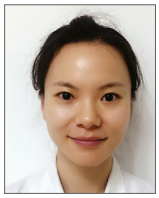
Impact of residual SYNTAX score on clinical outcomes after incomplete revascularisation percutaneous coronary intervention: a large single-centre study



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KEYWORDS

- chronic coronary total occlusion
- clinical research
- multiple vessel disease
- risk stratification

Abstract

Aims: This study aimed to assess the prognostic capacity of the residual SYNTAX score (rSS) in a large cohort of patients undergoing percutaneous coronary intervention (PCI) in clinical practice.

Methods and results: Ten thousand three hundred and forty-four (10,344) consecutive patients were prospectively enrolled. Complete revascularisation (CR; rSS=0), reasonable incomplete revascularisation (RICR; 0<rSS≤8), and ICR (rSS>8) were achieved in 5,375 (51.9%), 3,401 (32.9%), and 1,568 (15.2%) patients, respectively. During two-year follow-up, ICR patients had the highest incidence of major adverse cardiovascular and cerebrovascular events (MACCE; 20.0% vs. 13.6% vs. 8.7%, respectively; p<0.001). There was no difference in the incidence of all-cause death (1.2% vs. 1.0%; p=0.45), cardiac death (0.6% vs. 0.5%; p=0.31), and myocardial infarction (2.2% vs. 1.6%; p=0.07) between RICR and CR patients, while the rate of repeat revascularisation was significantly higher in RICR patients (9.8% vs. 5.8%; p<0.001). After multivariate analysis, rSS was an independent predictor of two-year cardiac death, myocardial infarction, revascularisation, and MACCE (p<0.05).

Conclusions: Despite an increase in revascularisation, RICR was associated with a similar mortality and myocardial infarction to CR patients. rSS is a prognostic indicator after PCI in daily practice, and may be used to determine a reasonable level of revascularisation.

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Abbreviations

CR	complete revascularisation
CTO	chronic total occlusion
ICR	incomplete revascularisation
MACCE	major adverse cardiovascular and cerebrovascular events
MI	myocardial infarction
PCI	percutaneous coronary intervention
RICR	reasonable incomplete revascularisation
rSS	residual SYNTAX score
SS	SYNTAX score

Introduction

For patients with multivessel coronary disease, percutaneous coronary intervention (PCI) frequently involves incomplete revascularisation (ICR) because of coronary anatomy complexity or co-existing serious medical conditions[1,2]. The prognostic impact of ICR after PCI remains inconsistent among studies[3-6], which may relate to the lack of consensus on the definition of incomplete revascularisation (ICR)[7].

Recently, the residual SYNTAX score (rSS), which is calculated by subtracting the value of the lesions treated during PCI from the pre-revascularisation SYNTAX score (SS), was developed to quantify and describe the extent of ICR more accurately[8-17]. rSS was reported to increase the prognostic capacity after PCI in different population cohorts[8-17], and an rSS≥8 was identified as a level of ICR strongly associated with increased mortality and adverse ischaemic events[8,9]. However, the utility of rSS among unselected real-world PCI patients remains unclear. Therefore, in the present study we assessed the prognostic capacity of rSS in a large cohort of patients undergoing PCI in daily clinical practice.

Methods

STUDY POPULATION

From January 2013 to December 2013, 10,724 consecutive patients who underwent PCI were enrolled at Fu Wai Hospital, National Center for Cardiovascular Diseases, Beijing, China. After excluding patients with a history of previous coronary artery bypass grafting, 10,344 patients were finally analysed in this study. The rSS[8] was assessed by two of the three experienced cardiologists in an independent angiographic core laboratory, who were blinded to clinical outcomes. In case of disagreement, the opinion of the third observer was obtained and the final decision was made by consensus. The intraobserver variability for calculation of the rSS (tertile partitioning), based on re-analysing 50 cases at a three-month interval, indicated a high level of agreement (κ statistic=0.879; 95% confidence interval [CI]: 0.81-0.94; p<0.001)[18,19]. The Institutional Review Board approved the study protocol, and all patients provided written informed consent before the intervention.

PROCEDURE AND MEDICATIONS

The decision on PCI strategy and stent type was left to the discretion of the treating physician. If patients were not taking long-term aspirin or $P2Y_{12}$ inhibitors, they received oral aspirin (300 mg) and clopidogrel (300 mg loading dose) or ticagrelor (180 mg loading dose) at least 24 hours before the procedure. Patients with acute coronary syndrome (ACS) scheduled for PCI received the same dose of aspirin and ticagrelor or clopidogrel (300 mg or 600 mg loading dose) as soon as possible. During the procedure, unfractionated heparin (100 U/kg) was administered to all patients, and use of glycoprotein IIb/IIIa inhibitors was per the operator's judgement. After the procedure, aspirin was prescribed at a dose of 100 mg daily indefinitely, while clopidogrel (75 mg daily) or ticagrelor (90 mg twice daily) was advised for at least one year after PCI.

PATIENT FOLLOW-UP

All patients were evaluated by clinical visit or by phone at one, three, six, and 12 months, and annually thereafter. Patients were advised to return for coronary angiography if clinically indicated by symptoms or documentation of myocardial ischaemia.

ENDPOINTS AND DEFINITIONS

Death that could not be attributed to a non-cardiac aetiology was considered cardiac death. Myocardial infarction (MI) was defined by the reported third universal definition of myocardial infarction[20]. Revascularisation was defined as repeat revascularisation for ischaemic symptoms and events driven by PCI or surgery of any vessel. Stent thrombosis was defined as definite or probable based on Academic Research Consortium definitions according to the level of certainty[21]. Major adverse cardiovascular and cerebrovascular events (MACCE) were defined as the occurrence of death, MI, revascularisation, stent thrombosis and stroke during follow-up. Procedural success was defined as residual stenosis <50% and without in-hospital MACCE. All endpoints were assessed centrally by two independent cardiologists, and disagreement was resolved by consensus.

STATISTICAL ANALYSIS

Continuous variables are reported as mean (±standard deviation), while categorical variables are reported as counts or percentage. All variables were stratified according to rSS (three groups). For the baseline characteristics, generalised linear models were used to compare continuous variables across rSS groups with rSS class as a covariable, while the Cochran-Armitage test for trends was used for categorical data. Clinical outcomes were determined using Kaplan-Meier methodology. To test for potential associations of rSS with rates of long-term mortality, a stepwise Cox multivariable regression analysis was used, with variable entry/stay criteria of 0.1/0.15. In addition, variables historically associated with long-term mortality were included in the model. The proportional hazard assumption was verified for each endpoint using the supremum test. A p-value <0.05 was considered statistically significant. Statistical analyses were performed using two statistical software packages (SPSS, Version 23; IBM Corp., Armonk, NY, USA; SAS v9.2; SAS Institute, Cary, NC, USA).

Results

PATIENT AND BASELINE CHARACTERISTICS

The mean baseline SS was 13.6±9.1 (range 1.0-58.0). The correlation (Spearman coefficient 0.597; p<0.001) and distribution of the baseline and residual SYNTAX score are shown in **Figure 1**. The CR (rSS=0), reasonable ICR (RICR) (0 <rSS ≤8), and ICR (rSS>8) were achieved in 5,375 (51.9%), 3,401 (32.9%), and 1,568 (15.2%) patients, respectively. The distribution of the CR, RICR, and ICR of the baseline SS is shown in **Figure 2**. The frequency of patients with CR and RICR decreased across tertiles of the baseline SS. By contrast, the frequency of ICR progressively increased across the baseline SS tertiles (0-22, 10.6% vs. 22-32, 46.9% vs. >32, 67.0%; p<0.001 for linear trend).

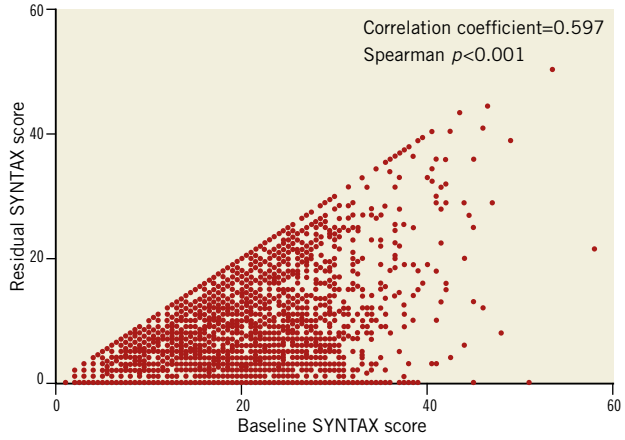

Figure 1. *Correlation between the baseline and residual SYNTAX score. Relationship between the baseline (x-axis) and residual (y-axis) SYNTAX score for individual patients.*

Patients in higher rSS levels were associated with increasing clinical comorbidities, including older age (p<0.001), decreased renal function (p<0.001), lower left ventricular ejection fraction (p<0.001), diabetes mellitus (p<0.001), hypertension (p<0.001), previous stroke history (p<0.001), peripheral vascular disease (p=0.003), previous MI history (p<0.001), and previous PCI history (p<0.001). Similarly, higher rSS was associated with increasing higher baseline SS (p<0.001), three-vessel disease (p<0.001), chronic total occlusion (CTO) lesions (p<0.001), and intra-aortic balloon pump use (p<0.001) in procedures **(Table 1)**.

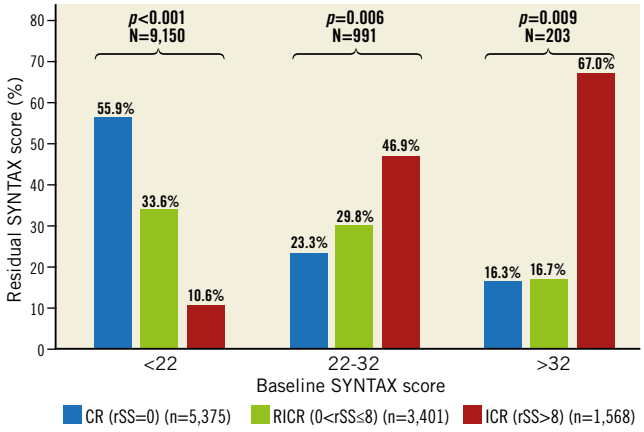

Figure 2. *Distribution of complete, reasonable complete, and incomplete revascularisation of the baseline SYNTAX score.*

CLINICAL OUTCOMES

The two-year follow-up was completed for 10,287 (99.4%) patients. There were significant differences between the rates of all-cause death, cardiac death, MI, repeat revascularisation and MACCE among different rSS groups (p<0.001) **(Table 2, Figure 3)**; ICR patients had the highest incidence of adverse clinical events (MACCE: 20.0% vs. 13.6% vs. 8.7%; p<0.001). When only comparing RICR with CR patients, the incidences of all-cause death (1.2% vs. 1.0%; p=0.45), cardiac death (0.6% vs. 0.5%; p=0.31), and MI (2.2% vs. 1.6%; p=0.07) were similar between the groups, while the MACCE rate remained significantly higher in RICR patients (13.6% vs. 8.7%; p<0.001), mainly driven by the increased risk of repeat revascularisation (9.8% vs. 5.8%; p<0.001) **(Table 2)**. After multivariate analysis, rSS was an independent predictor of two-year cardiac death, MI, revascularisation and MACCE (p<0.05), but was not an independent predictor of two-year all-cause death (p>0.05) **(Table 3)**.

SUBGROUP ANALYSIS

Overall, RICR had a similar effect on cardiac death compared with CR (0.6% vs. 0.5%, hazard ratio [HR] 1.30, 95% CI: 0.74-2.30; p=0.37), which was also observed in a subgroup of patients with impaired left ventricular function (left ventricular ejection fraction <50%, n=525/10,344 [5.1%], p=0.80 for interaction; diabetes mellitus, n=3,108/10,344 [30.0%], p=0.83 for interaction; three-vessel disease, n=4,216/10,344 [40.7%], p=0.37 for interaction; CTO disease, n=1,979/10,344 [19.1%], p=0.60 for interaction). In the meantime, except for the CTO subgroup, ICR had a higher risk of two-year cardiac death in impaired left ventricular function, diabetes mellitus, and three-vessel disease patients. The risk of MACCE was higher in RICR patients compared with CR patients in the whole population, as well as in the subgroup of impaired left ventricular function, diabetes mellitus, three-vessel disease, and CTO, which was predominantly a result of revascularisation **(Figure 4)**.

Discussion

In the present study, we assessed the effects of rSS on clinical outcomes in a large registry cohort of real-world patients undergoing contemporary PCI treatment. The major findings of this study were as follows: 1) rSS was able to risk-stratify patients and predict two-year composite adverse cardiac events after PCI (patients with a higher rSS had a higher incidence of adverse clinical events); 2) compared with CR patients, RICR (0<rSS≤8) patients had a similar risk of mortality or MI, although they had a higher risk of repeat revascularisation; 3) the finding that RICR

Table 1. Baseline characteristics according to residual SYNTAX score.

		CR (rSS=0) (n=5,375)	RICR (0<rSS≤8) (n=3,401)	ICR (rSS>8) (n=1,568)	*p*-value for linear trends
Age, yrs		57±10	58±10	60±10	<0.001
Male, n (%)		4,140 (77.0)	2,618 (77.0)	1,210 (77.2)	0.935
BMI, kg/m^2		25.9±3.2	26.0±3.1	26.0±3.1	0.246
eGFR, ml/min		92.7±14.5	90.7±15.1	88.8±16.6	<0.001
eGFR <90, n (%)		1,870 (34.8)	1,366 (40.2)	708 (45.2)	<0.001
LVEF, %		63.1±7.0	62.7±7.3	61.9±8.0	<0.001
LVEF <40, n (%)		53 (1.0)	37 (1.1)	27 (2.7)	0.001
Clinical history, n (%)					
Diabetes mellitus		1,398 (26.0)	1,156 (34.0)	554 (35.3)	<0.001
Hypertension		3,321 (61.8)	2,259 (66.4)	1,061 (67.7)	<0.001
Hyperlipidaemia		3,545 (66.0)	2,346 (69.0)	1,051 (67.0)	0.082
Previous stroke		491 (9.1)	404 (11.9)	214 (13.6)	<0.001
Peripheral vascular disease		121 (2.3)	92 (2.7)	57 (3.6)	0.003
COPD		114 (2.1)	83 (2.4)	39 (2.5)	0.287
Family history of CAD		1,298 (24.2)	840 (24.7)	414 (26.4)	0.087
Current smoker		3,057 (56.9)	1,940 (57.0)	891 (56.8)	0.978
Previous MI		884 (16.4)	671 (19.7)	366 (23.3)	<0.001
Previous PCI		1,203 (22.4)	889 (26.1)	424 (27.0)	<0.001
Clinical presentation, n (%)					
ACS		3,334 (62.0)	2,012 (59.2)	891 (56.8)	<0.001
Stable angina		1,620 (30.1)	1,110 (32.6)	529 (33.7)	0.002
Silent ischaemia		421 (7.8)	279 (8.2)	148 (9.4)	0.056
Angiographic and procedural characteristics					
CAD extension, n (%)	LM disease	131 (2.4)	89 (2.6)	36 (2.3)	0.946
	2-vessel disease	1,920 (35.7)	1,153 (33.9)	362 (23.1)	<0.001
	3-vessel disease	1,228 (22.8)	1,856 (54.6)	1,132 (72.2)	<0.001
Chronic total occlusion lesions		858 (16.0)	619 (18.2)	502 (32.0)	<0.001
No. of target lesions per patient		1.4±0.6	1.5±0.7	1.4±0.6	0.013
No. of stents per patient		1.8±1.1	1.9±1.1	1.7±1.2	0.164
Types of stent, n (%)	BMS	27 (0.5)	17 (0.5)	13 (0.8)	0.205
	DES	5,198 (96.7)	3,235 (95.1)	1,338 (85.3)	<0.001
PTCA, n (%)		104 (1.9)	74 (2.2)	52 (3.3)	0.003
IVUS use, n (%)		302 (5.6)	190 (5.6)	88 (5.6)	0.975
IABP use, n (%)		57 (1.1)	42 (1.2)	40 (2.6)	<0.001
Procedural success, n (%)		5,329 (99.1)	3,326 (97.8)	1,403 (89.5)	<0.001
Baseline SYNTAX score		9.0±6.5	12.7±6.6	21.3±7.2	<0.001
Residual SYNTAX score		0	4.1±2.1	14.8±6.0	<0.001

ACS: acute coronary syndrome; BMI: body mass index; BMS: bare metal stent; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; DES: drug-eluting stent; eGFR: estimated glomerular filtration rate; IABP: intra-aortic balloon pump; IVUS: intravascular ultrasound; LVEF: left ventricular ejection fraction; MI: myocardial infarction; PCI: percutaneous coronary intervention; PTCA: percutaneous transluminal coronary angioplasty

had a similar effect on cardiac death compared with CR was consistent in subgroups of left ventricular function, diabetes mellitus, and three-vessel disease patients.

Complete revascularisation was achieved in 51.9% of patients in our cohort, which was higher than that previously reported[8,17]. We found that patients with greater residual coronary lesions after PCI, as quantified by the rSS, had higher clinical risks including older age, decreased renal function, lower left ventricular ejection fraction, more comorbidities, and higher baseline SS. These associations reflected a clinical phenomenon whereby clinicians tended to perform ICR treatment when patients had high baseline clinical risks, as previously reported[8,17].

Patients in our all-comers cohort with high rSS after PCI were at significantly greater risk of MACCE, while patients with RICR

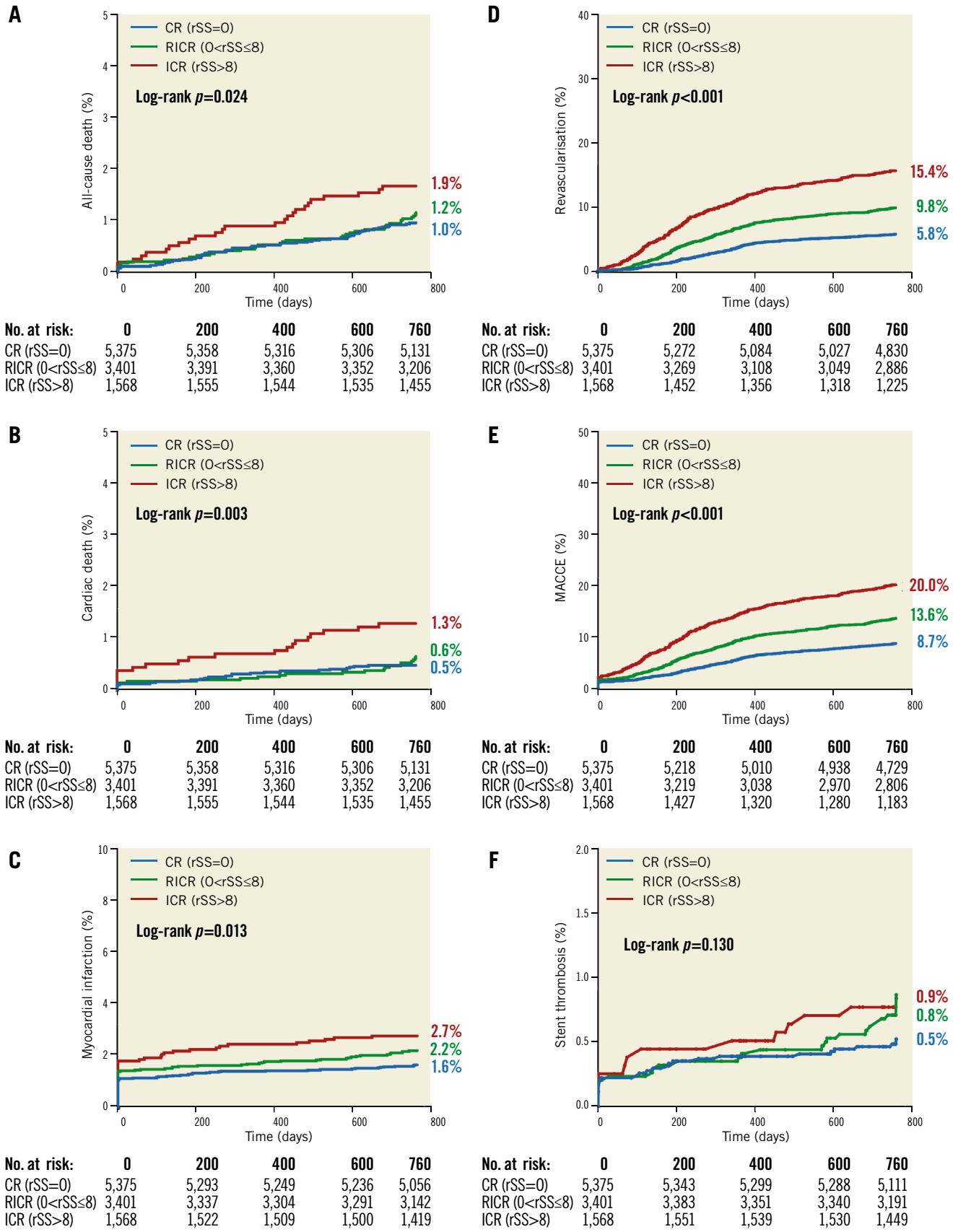

Figure 3. *Kaplan-Meier curves showing event rates stratified by the residual SYNTAX score over two years. A) All-cause death. B) Cardiac death. C) Myocardial infarction. D) Revascularisation. E) Major adverse cardiovascular and cerebrovascular events (MACCE). F) Stent thrombosis. CR: complete revascularisation; ICR: incomplete revascularisation; RICR: reasonable incomplete revascularisation*

Table 2. Adverse ischaemic outcomes at two years of follow-up according to residual SYNTAX score.

	CR (rSS=0) (n=5,375)	RICR (0<rSS≤8) (n=3,401)	ICR (rSS>8) (n=1,568)	*p*-value	*p*-value CR vs. RICR	*p*-value CR vs. ICR	*p*-value RICR vs. ICR
All-cause death	54 (1.0)	40 (1.2)	29 (1.8)	0.024	0.447	0.007	0.058
Cardiac death	26 (0.5)	22 (0.6)	20 (1.3)	0.003	0.312	0.001	0.024
Myocardial infarction	88 (1.6)	74 (2.2)	43 (2.7)	0.013	0.068	0.004	0.217
Revascularisation	311 (5.8)	334 (9.8)	242 (15.4)	<0.001	<0.001	<0.001	<0.001
Stroke	60 (1.1)	54 (1.6)	27 (1.7)	0.072	0.058	0.055	0.709
MACCE	466 (8.7)	462 (13.6)	314 (20.0)	<0.001	<0.001	<0.001	<0.001
Stent thrombosis	28 (0.5)	29 (0.9)	13 (0.8)	0.132	0.075	0.188	1.000
Definite thrombosis	15 (0.3)	11 (0.3)	6 (0.4)	0.797	0.693	0.600	0.795
Probable thrombosis	13 (0.2)	18 (0.5)	7 (0.4)	0.081	0.040	0.185	0.831

(0<rSS≤8) had the same mortality risk as CR (rSS=0) patients after PCI. These findings were in accordance with previous studies evaluating the prognostic utility of rSS in different population cohorts[8-17]. For example, in a landmark study first describing rSS assessed in a large cohort of moderate- and high-risk patients with ACS, rSS was associated with one-year adverse events, with an rSS=8 identified as the cut-off value with greater major adverse cardiac events (MACE) and mortality at 30 days and one year, respectively[8]. The prognostic value of rSS was subsequently validated in heterogeneous patient populations including multivessel disease, unprotected left main disease, ST-segment elevation myocardial infarction, and complex lesions with second-generation drug-eluting stents[9-16].

Table 3. Independent predictors of two-year adverse outcomes at multivariable analysis.

Residual SYNTAX score (three groups)*				
	Univariable analyses		Multivariable analyses	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
All-cause death	1.34 (1.07-1.68)	0.012	1.16 (0.92-1.47)	0.199
Cardiac death	1.61 (1.20-2.18)	0.002	1.40 (1.03-1.90)	0.031
Myocardial infarction	1.30 (1.09-1.56)	0.003	1.23 (1.03-1.47)	0.025
Revascularisation	1.69 (1.56-1.84)	<0.001	1.71 (1.57-1.86)	<0.001
MACCE	1.58 (1.47-1.69)	<0.001	1.54 (1.44-1.66)	<0.001

*Three groups: comparing CR, reasonable ICR and ICR. The following variables were included in each model: 1) for all-cause death and cardiac death: male, age, diabetes, hypertension, hyperlipidaemia, current smoking, renal dysfunction, left ventricular ejection fraction <40%, acute cardiovascular syndrome and drug-eluting stent; 2) for myocardial infarction and MACCE: male, age, diabetes, hypertension, hyperlipidaemia, current smoking, renal dysfunction, previous myocardial infarction, previous percutaneous coronary intervention, left ventricular ejection fraction <40%, acute cardiovascular syndrome and drug-eluting stent; 3) for unplanned revascularisation: male, age, diabetes, hypertension, hyperlipidaemia, current smoking, renal dysfunction, previous percutaneous coronary intervention, left ventricular ejection fraction <40%, acute cardiovascular syndrome and drug-eluting stent. CI: confidence interval; HR: hazard ratio

There is only one prior report of rSS validated in one all-comers population, where the population came from the multicentre EXCELLENT registry that enrolled 5,159 patients from 29 centres in Korea between April 2008 and May 2010[17]. In that study, rSS was an independent predictor of clinical outcomes at one year, while there was no further benefit after lowering the rSS to <7 in patients with higher baseline SS. By comparison, our study used a larger sample size of 10,344 patients from one-centre data (this reduces the potential confounder of operator experience). Both studies demonstrated that the rSS, an index for quantifying the remaining coronary lesions after PCI, is a useful tool to evaluate patient prognosis after PCI. Further, we demonstrated that RICR was associated with similar mortality and MI compared with CR, despite an increase in revascularisation. Thus, measuring the completeness of revascularisation by rSS can be used to ensure revascularisation in daily clinical practice. Importantly, this outcome was also observed in different subgroups of patients, including those with impaired left ventricular function, diabetes mellitus, and three-vessel disease. In the CTO subgroup, ICR was associated with a modest effect on cardiac death (HR 1.94, 95% CI: 0.75-5.02; p=0.17), compared with a significant effect in no CTO patients (HR 2.60, 95% CI: 1.23-5.50, p=0.010), as previously reported[9]. Hannan et al[22] also reported that patients with successful CTO revascularisation in conjunction with ICR of other diseased lesions had a similar risk to patients with CR of all diseased lesions, suggesting that RICR may be a treatment target for high-risk CTO patients. Moreover, preprocedural assessment such as myocardial viability testing was required to ensure revascularisation in CTO patients.

Study limitations

There are a number of limitations in our study. First, the non-randomised design using unmeasured confounders may preclude any definitive conclusion. Second, the two-year follow-up duration was comparatively short for evaluating long-term outcomes. Third, patients enrolled in this study had lower levels of complex coronary artery disease and incidence of mortality compared with the SYNTAX trial. Fourth, rSS is based on angiographic interpretation that has inherent limitations[23], and our findings may have

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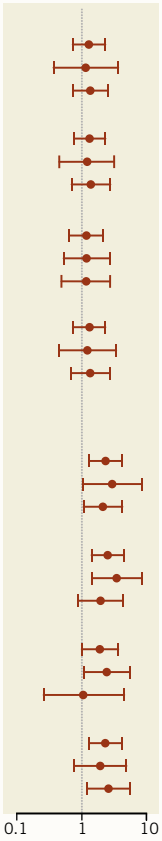
CR vs. RICR	CR	RICR	HR (95% CI)	*p*-value	$p_{interaction}$
Cardiac death	26/5,375 (0.5%)	22/3,401 (0.6%)	1.30 (0.74-2.30)	0.37	0.80
LVEF <50%	6/237 (2.5%)	5/175 (2.9%)	1.14 (0.35-3.72)	0.84	
LVEF ≥50%	20/5,138 (0.4%)	17/3,226 (0.5%)	1.36 (0.71-2.59)	0.36	
Cardiac death	26/5,375 (0.5%)	22/3,401 (0.6%)	1.32 (0.75-2.33)	0.34	0.83
Diabetes	8/1,398 (0.6%)	8/1,156 (0.7%)	1.21 (0.45-3.22)	0.71	
No diabetes	18/3,977 (0.5%)	14/2,245 (0.6%)	1.38 (0.69-2.77)	0.37	
Cardiac death	26/5,375 (0.5%)	22/3,401 (0.6%)	1.18 (0.64-2.15)	0.31	0.96
3VD	8/1,228 (0.7%)	14/1,856 (0.8%)	1.19 (0.52-2.74)	0.62	
No 3VD	18/4,147 (0.4%)	8/1,545 (0.5%)	1.16 (0.49-2.7)	0.15	
Cardiac death	26/5,375 (0.5%)	22/3,401 (0.6%)	1.31 (0.74-2.31)	0.35	0.86
CTO	8/858 (0.9%)	7/619 (1.1%)	1.21 (0.44-3.35)	0.71	
No CTO	18/4,517 (0.4%)	15/2,782 (0.5%)	1.35 (0.68-2.69)	0.39	
CR vs. ICR	**CR**	**ICR**	**HR (95% CI)**	***p*-value**	$p_{interaction}$
Cardiac death	26/5,375 (0.5%)	20/1,568 (1.3%)	2.36 (1.31-4.24)	0.04	0.60
LVEF <50%	6/237 (2.5%)	8/109 (7.3%)	2.98 (1.03-8.59)	0.04	
LVEF ≥50%	20/5,138 (0.4%)	12/1,459 (0.8%)	2.12 (1.04-4.33)	0.04	
Cardiac death	26/5,375 (0.5%)	20/1,568 (1.3%)	2.52 (1.40-4.53)	<0.01	0.35
Diabetes	8/1,398 (0.6%)	11/554 (2.0%)	3.50 (1.41-8.70)	<0.01	
No diabetes	18/3,977 (0.5%)	9/1,014 (0.9%)	1.97 (0.88-4.38)	0.10	
Cardiac death	26/5,375 (0.5%)	20/1,568 (1.3%)	1.93 (1.01-3.74)	0.04	0.37
3VD	8/1,228 (0.7%)	18/1,132 (1.6%)	2.45 (1.07-5.64)	0.04	
No 3VD	18/4,147 (0.4%)	2/436 (0.5%)	1.06 (0.25-4.55)	0.90	
Cardiac death	26/5,375 (0.5%)	20/1,568 (1.3%)	2.32 (1.28-4.21)	<0.01	0.60
CTO	8/858 (0.9%)	9/502 (1.8%)	1.94 (0.75-5.02)	0.17	
No CTO	18/4,517 (0.4%)	11/1,066 (1.0%)	2.60 (1.23-5.50)	0.01	



B

CR vs. RICR	CR	RICR	HR (95% CI)	*p*-value	$p_{interaction}$
MACCE	466/5,375 (8.7%)	462/3,401 (13.6%)	1.62 (1.42-1.86)	<0.01	0.85
LVEF <50%	32/237 (13.5%)	32/175 (18.3%)	1.38 (0.84-2.25)	0.20	
LVEF ≥50%	434/5,138 (8.4%)	430/3,226 (13.3%)	1.63 (1.42-1.86)	<0.01	
MACCE	466/5,375 (8.7%)	462/3,401 (13.6%)	1.76 (1.50-2.06)	<0.01	0.03
Diabetes	152/1,398 (10.9%)	161/1,156 (13.9%)	1.30 (1.05-1.63)	0.019	
No diabetes	314/3,977 (7.9%)	301/2,245 (13.4%)	1.76 (1.50-2.06)	<0.01	
MACCE	466/5,375 (8.7%)	462/3,401 (13.6%)	2.12 (1.63-2.76)	<0.001	0.50
3VD	150/1,228 (12.2%)	290/1,856 (15.6%)	1.43 (1.11-1.85)	0.01	
No 3VD	316/4,147 (7.6%)	172/1,545 (11.1%)	1.67 (1.44-1.94)	<0.01	
MACCE	466/5,375 (8.7%)	462/3,401 (13.6%)	1.62 (1.40-1.88)	<0.01	0.71
CTO	96/858 (11.2%)	102/619 (16.5%)	1.53 (1.16-2.02)	<0.01	
No CTO	370/4,517 (8.2%)	360/2,782 (12.9%)	1.62 (1.40-1.88)	<0.01	
CR vs. ICR	**CR**	**ICR**	**HR (95% CI)**	***p*-value**	$p_{interaction}$
MACCE	466/5,375 (8.7%)	462/1,568 (13.6%)	2.47 (2.12-2.87)	<0.01	0.74
LVEF <50%	32/237 (13.5%)	30/109 (27.5%)	2.20 (1.34-3.63)	<0.01	
LVEF ≥50%	434/5,138 (8.4%)	284/1,459 (19.5%)	2.47 (2.13-2.87)	<0.01	
MACCE	466/5,375 (8.7%)	462/1,568 (13.6%)	2.59 (2.17-3.10)	<0.01	0.22
Diabetes	152/1,398 (10.9%)	121/554 (21.8%)	2.15 (1.69-2.73)	<0.01	
No diabetes	314/3,977 (7.9%)	193/1,014 (19.0%)	2.59 (2.16-3.10)	<0.01	
MACCE	466/5,375 (8.7%)	462/1,568 (13.6%)	2.12 (1.63-2.76)	<0.01	0.50
3VD	150/1,228 (12.2%)	247/1,132 (21.8%)	2.30 (1.71-3.11)	<0.01	
No 3VD	316/4,147 (7.6%)	67/436 (15.4%)	2.54 (2.16-2.99)	<0.01	
MACCE	466/5,375 (8.7%)	462/1,568 (13.6%)	2.31 (1.94-2.75)	<0.01	0.77
CTO	96/858 (11.2%)	123/502 (24.5%)	2.41 (1.84-3.14)	<0.01	
No CTO	370/4,517 (8.2%)	191/1,066 (17.9%)	2.31 (1.94-2.75)	<0.01	

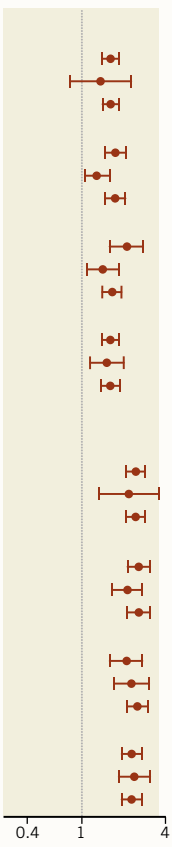


Figure 4. *Subgroup analysis of all-cause death and MACCE. A) Subgroup analysis of all-cause death. B) Subgroup analysis of MACCE. CTO: chronic total occlusion; LVEF: left ventricular ejection fraction*

varied if the SS had been assessed by less well-trained readers. However, rSS was assessed by an independent angiographic core laboratory in this study, with good reproducibility for rSS evaluation[15]. Finally, the patients in this study only included those receiving PCI treatment. Thus, use of rSS should also be validated in patients receiving coronary artery bypass graft therapy.

Conclusions

In this large cohort of real-world patients receiving PCI, RICR was associated with similar mortality and MI compared with CR, despite an increase in revascularisation. Thus, RICR may be a treatment target for high-risk patients. rSS was a prognostic indicator after PCI in daily practice, and may be useful for determining a reasonable level of revascularisation.

Impact on daily practice

The utility of rSS in real-world PCI patients is unclear. In this study, rSS was able to risk-stratify patients and predict two-year composite adverse cardiac events after PCI. ICR patients (rSS>8) had a higher incidence of adverse clinical events compared with CR patients (rSS=0), while RICR patients (0<rSS≤8) had similar risks of mortality and MI, despite a higher risk of repeat revascularisation. We suggest that RICR (0<rSS≤8) is a potential treatment target for high-risk PCI patients.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

References

1. McLellan CS, Ghali WA, Labinaz M, Davis RB, Galbraith PD, Southern DA, Shrive FM, Knudtson ML; Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH) Investigators. Association between completeness of percutaneous coronary revascularization and postprocedure outcomes. *Am Heart J.* 2005;150:800-6.

2. Bourassa MG, Yeh W, Holubkov R, Sopko G, Detre KM. Long-term outcome of patients with incomplete vs complete revascularization after multivessel PTCA. A report from the NHLBI PTCA Registry. *Eur Heart J.* 1998;19:103-11.

3. Rosner GF, Kirtane AJ, Genereux P, Lansky AJ, Cristea E, Gersh BJ, Weisz G, Parise H, Fahy M, Mehran R, Stone GW. Impact of the presence and extent of incomplete angiographic revascularization after percutaneous coronary intervention in acute coronary syndromes: the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial. *Circulation.* 2012; 125:2613-20.

4. Hannan EL, Wu C, Walford G, Holmes DR, Jones RH, Sharma S, King SB 3rd. Incomplete revascularization in the era of drug-eluting stents: impact on adverse outcomes. *JACC Cardiovasc Interv.* 2009;2:17-25.

5. Kim YH, Park DW, Lee JY, Kim WJ, Yun SC, Ahn JM, Song HG, Oh JH, Park JS, Kang SJ, Lee SW, Lee CW, Park SW, Park SJ. Impact of angiographic complete revascularization after drug-eluting stent implantation or coronary artery bypass graft surgery for multivessel coronary artery disease. *Circulation.* 2011;123:2373-81.

6. Gao Z, Xu B, Yang YJ, Yuan JQ, Chen J, Chen JL, Qiao SB, Wu YJ, Yan HB, Gao RL. Long-term outcomes of complete versus incomplete revascularization after drug-eluting stent implantation in patients with multivessel coronary disease. *Catheter Cardiovasc Interv.* 2013;82:343-9.

7. Patel MR, Dehmer GJ, Hirshfeld JW, Smith PK, Spertus JA. ACCF/SCAI/STS/AATS/AHA/ASNC/HFSA/SCCT 2012 Appropriate use criteria for coronary revascularization focused update: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, Society for Cardiovascular Angiography and Interventions, Society of Thoracic Surgeons, American Association for Thoracic Surgery, American Heart Association, American Society of Nuclear Cardiology, and the Society of Cardiovascular Computed Tomography. *J Am Coll Cardiol.* 2012;59: 857-81.

8. Généreux P, Palmerini T, Caixeta A, Rosner G, Green P, Dressler O, Xu K, Parise H, Mehran R, Serruys PW, Stone GW. 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;59:2165-74.

9. Farooq V, Serruys PW, Bourantas CV, Zhang Y, Muramatsu T, Feldman T, Holmes DR, Mack M, Morice MC, Stahle E, Colombo A, de Vries T, Morel MA, Dawkins KD, Kappetein AP, Mohr FW. 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;128:141-51.

10. Malkin CJ, George V, Ghobrial MS, Krishnan A, Siotia A, Raina T, Morton AC, Gunn J. Residual SYNTAX score after PCI for triple vessel coronary artery disease: quantifying the adverse effect of incomplete revascularisation. *EuroIntervention.* 2013;8: 1286-95.

11. 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.

12. Capodanno D, Chisari A, Giacoppo D, Bonura S, Lavanco V, Capranzano P, Caggegi A, Ministeri M, Tamburino C. 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;82:333-40.

13. 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;81:939-46.

14. Khan R, Al-Hawwas M, Hatem R, Azzalini L, Fortier A, Joliecoeur EM, Tanguay JF, Lavoie-L'Allier P, Ly HQ. 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.

15. Xu B, Yang YJ, Han YL, Lu SZ, Li B, Liu Q, Zhu GY, Cui JY, Li L, Zhao YL, Kirtane AJ; SEEDS Investigators. 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.

16. Schwietz T, Spyridopoulos I, Pfeiffer S, Laskowski R, Palm S, DE Rosa S, Jens K, Zeiher AM, Schächinger V, Fichtlscherer S, Lehmann R. 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.

17. Park KW, Kang J, Kang SH, Ahn HS, Kang HJ, Koo BK, Chae IH, Youn TJ, Oh BH, Park YB, Kandzari D, Kim HS. 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.

18. Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A, Dawkins K, van den Brand M, Van Dyck N, Russell ME, Mohr FW, Serruys PW. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. *EuroIntervention.* 2005;1:219-27.

19. Généreux P, Palmerini T, Caixeta A, Cristea E, Mehran R, Sanchez R, Lazar D, Jankovic I, Corral MD, Dressler O, Fahy MP, Parise H, Lansky AJ, Stone GW. SYNTAX score reproducibility and variability between interventional cardiologists, core laboratory technicians, and quantitative coronary measurements. *Circ Cardiovasc Interv.* 2011;4:553-61.

20. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD; ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction, Thygesen K, Alpert JS, White HD, Jaffe AS, Katus HA, Apple FS, Lindahl B, Morrow DA, Chaitman BA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow RO, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, Hamm CW, Uretsky BF, Steg PG, Wijns W, Bassand JP, Menasche P, Ravkilde J, Ohman EM, Antman EM, Wallentin LC, Armstrong PW, Simoons ML, Januzzi JL, Nieminen MS, Gheorghiade M, Filippatos G, Luepker RV, Fortmann SP, Rosamond WD, Levy D, Wood D, Smith SC, Hu D, Lopez-Sendon JL, Robertson RM, Weaver D, Tendera M, Bove AA, Parkhomenko AN, Vasilieva EJ, Mendis S; ESC Committee for Practice Guidelines (CPG). Third universal definition of myocardial infarction. *Eur Heart J.* 2012;33:2551-67.

21. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, Steg PG, Morel MA, Mauri L, Vranckx P, McFadden E, Lansky A, Hamon M, Krucoff MW, Serruys PW; Academic Research Consortium. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation.* 2007;115:2344-51.

22. Hannan EL, Zhong Y, Jacobs AK, Stamato NJ, Berger PB, Walford G, Sharma S, Venditti FJ, King SB 3rd. Patients With Chronic Total Occlusions Undergoing Percutaneous Coronary Interventions: Characteristics, Success, and Outcomes. *Circ Cardiovasc Interv.* 2016;9:e003586.

23. Tonino PA, Fearon WF, De Bruyne B, Oldroyd KG, Leesar MA, Ver Lee PN, Maccarthy PA, Van't Veer M, Pijls NH. Angiographic versus functional severity of coronary artery stenoses in the FAME study fractional flow reserve versus angiography in multivessel evaluation. *J Am Coll Cardiol.* 2010;55:2816-21.