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Objectifying the level of incomplete revascularization by residual SYNTAX score and evaluating the impact of incomplete revascularization on exercise tolerance in patients with coronary atherosclerotic heart disease treated by percutaneous coronary intervention

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Abstract

The prognostic impact of incomplete revascularization (ICR) on patients underwent percutaneous coronary intervention (PCI) was vague. Our research aimed to objectify the level of ICR by residual SYNTAX score (rSS) and evaluate the impact of ICR on exercise tolerance.

We enrolled 87 patients who completed cardiopulmonary exercise testing (CPET) within 12 months after PCI, retrospectively. According to rSS, patients were divided into rSS = 0 group, 0 < rSS ≤ 8 group, and rSS > 8 group. The CPET variables–including peak metabolic equivalent (MET_{peak}), percentages of predicting value of MET_{peak} (MET_{peak}%pred), MET at anaerobic threshold (AT), peak oxygen uptake (VO_{2peak}), percentages of predicting value of VO_{2peak} (VO_{2peak}%pred), VO_2 at AT–were collected and compared.

Among rSS = 0, 0 < rSS ≤ 8 and rSS > 8 groups, patients with higher rSS had progressively lower MET_{peak}, MET_{peak}%pred, VO_{2peak}%pred, VO_2 at AT, and MET at AT, which indicate reduced exercise tolerance. And further multiple comparisons showed that there were no statistically significant differences between rSS = 0 and 0 < rSS ≤ 8 groups, while the aforementioned CPET variables were significantly lower in rSS > 8 group compared with rSS = 0 group. Logistic regression analysis showed that rSS was an independent risk factor for reduced exercise tolerance.

- There was no significant difference in exercise tolerance between rSS = 0 and 0 < rSS ≤ 8 groups. However, the exercise tolerance of patients in rSS = 0 and 0 < rSS ≤ 8 groups was better than that of patients in rSS > 8 group;
- rSS was an independent risk factors for reduced exercise tolerance.

Abbreviations: AT = anaerobic threshold, bSS = baseline SYNTAX score, CABG = coronary artery bypass grafting, CAD = coronary atherosclerotic heart disease, CPET = cardiopulmonary exercise testing, CR = complete revascularization, ICR = incomplete revascularization, IQR = interquartile ranges, LCX = left circumflex, LSD-t = least significant difference t-test, MET_{peak}% pred = percentages of predicting value of MET_{peak}, MET_{peak} = peak metabolic equivalent, PCI = percutaneous coronary intervention, $P_{ET}CO_2$ = partial pressure of end-tidal carbon dioxide production, RCA = right coronary artery, rICR = reasonable incomplete revascularization, rSS = residual SYNTAX score, SD = standard deviation, sICR = ICR with severe residual lesion of coronary artery, VCO_2 = carbon dioxide production, VE = minute ventilation, VO_{2peak}%pred = percentages of predicting value of VO_{2peak}, VO_{2peak} = peak oxygen uptake.

Keywords: coronary atherosclerotic heart disease, residual SYNTAX score, cardiopulmonary exercise testing, exercise tolerance

Editor: Ovidiu Constantin Baltatu.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

The authors have no conflicts of interest to declare.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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How to cite this article: Xue L, Guo D, Wang L, Cao C, Li Q, Zou S. Objectifying the level of incomplete revascularization by residual SYNTAX score and evaluating the impact of incomplete revascularization on exercise tolerance in patients with coronary atherosclerotic heart disease treated by percutaneous coronary intervention. Medicine 2020;99:38(e22221).

Received: 4 December 2019 / Received in final form: 15 August 2020 / Accepted: 18 August 2020

http://dx.doi.org/10.1097/MD.0000000000022221

1. Introduction

Coronary artery revascularization is a crucial treatment for patients with coronary atherosclerotic heart disease (CAD). Achieving complete revascularization (CR) is intuitively desirable in patients with CAD undergoing revascularization. However, for patients with multi-coronary disease, percutaneous coronary intervention (PCI) frequently involves incomplete revascularization (ICR) because of coronary anatomy complexity or severe comorbidities.[1,2] There is no universally accepted definition for ICR. Actually, definitions of ICR in prior studies have varied according to the degree of coronary stenosis severity (e.g., ≥50% vs ≥70%) or the vessel size diameter (e.g., ≥1.5 or ≥2.5 mm) required to be treated.[3–6] Thus, previous studies have reported inconsistent results regarding the prognostic impact of ICR on patients underwent PCI.[3,4,7,8]

Residual SYNTAX score (rSS) is a systematic angiographic score that measures the extent and complexity of residual coronary lesions after PCI using the original lesion stratification of the SYNTAX score. Furthermore, rSS allowed for a threshold value of ICR to be determined that would not have a negative impact on long-term mortality, which is the concept of "reasonable" incomplete revascularization (rICR).[9,10] Several studies revealed that, long-term mortality of patients with rICR was comparable with that of subjects with CR, but when patients residual lesions of coronary arteries exceeded the threshold of rICR, their adverse long-term clinical outcomes may increase progressively.[11,12] Ying et al indicated that rSS may be used to determine a reasonable level of revascularization.[13] However, there have been no standard definition for rICR, some studies reported a cut-off of rSS < 5 although in others the cut-off was rSS < 8.[11,12,14–16]

Some variables including peak metabolic equivalent (MET-peak), peak oxygen uptake (VO2peak) of cardiopulmonary exercise testing (CPET) are also associated with the prognosis of patients with CAD.[17,18] One MET increment in cardiorespiratory fitness (VO_{2peak}, 3.5 ml/kg/minutes) was related to a decreased risk of CAD death and all-cause death.[19] After rSS was proposed, researchers used it to objectify the level of revascularization and evaluate its impact on patients outcomes,[11,14,20] while few researchers paid attention to its impact on patients exercise tolerance. It is important to know whether ICR affects exercise tolerance and, if so, what level of ICR is acceptable. To address this question, we used rSS to objectify the level of ICR and evaluate the impact of ICR on exercise tolerance in patients with CAD treated by PCI.

2. Method

2.1. Study population

The study was approved by the ethics committee of Peking University People's Hospital. Patients with CAD (including stable angina, unstable angina, ST-segment elevated myocardial infarction and non-ST-segment elevated myocardial infarction) who completed CPET within 12 months after PCI were enrolled retrospectively from January 2011 to January 2018. Inclusion criteria were:

1. age ≥18 years;
2. by visual estimation, there should be at least 1 coronary vessel lesion with diameter stenosis ≥50% in vessels ≥1.5 mm in diameter, treated by PCI.
3. patients completed CPET within 12 months after PCI treatment.

Exclusion criteria were:

1. previous coronary artery bypass grafting (CABG);
2. chronic lung disease;
3. severe valve dysfunction.

Baseline demographic and clinical parameters, including name, gender, age, body mass index, medical history, medications, were obtained from hospital records retrospectively.

2.2. SYNTAX scoring

The patients angiographic images were reviewed and the baseline SYNTAX score (bSS) and rSS were calculated visually using a web-based calculator (www.syntaxscore.com, version 2.28) by 2 experienced operators. When an approach of staged PCI was chosen, the rSS was calculated based on the remaining obstructive coronary lesions after the completion of all elective PCI procedures before conducting CPET.

2.3. CPET

Patients underwent symptom-limited treadmill testing on the cardiopulmonary apparatus (COSMED QUARK PFT 4 ERGO). For safety reasons, all tests were supervised by an experienced physician with the assistance of an experienced nurse. Standard criteria for termination were employed, including severe angina, dyspnea, >2.0 mm abnormal ST depression, a drop in systolic blood pressure >20 mm Hg, serious rhythm disturbances, or degree of effort reached Borg 19 to 20.[21–23] The electrocardiogram, blood pressure, heart rate, MET, VO_2, minute ventilation (VE), carbon dioxide production (VCO_2), and partial pressure of end-tidal carbon dioxide production ($P_{ET}CO_2$) were registered during the exercise test.

2.4. Study protocol and procedure

Our study included 2 parts. In the first part, patients were divided into rSS = 0 group, 0 < rSS ≤ 8 group, and rSS > 8 group according to rSS. The CPET variables within 1 year were collected and compared, including MET_{peak}, percentages of predicting value of MET_{peak} (MET_{peak}%pred), MET at anaerobic threshold (AT), VO_{2peak}, percentages of predicting value of VO_{2peak} (VO_{2peak}%pred), VO_2 at AT. In the second part we conducted logistic regression analysis to analyze risk factors of exercise tolerance after PCI in CAD patients. In our study, CR was defined as a post-PCI rSS = 0. rICR was defined as 0 < rSS ≤ 8, and rSS > 8 was considered to be ICR with severe residual lesion of coronary artery (sICR).

2.5. Statistical analyses

Statistical analyses were conducted using SPSS system software, version 20.0.0. Continuous variables were presented as mean with standard deviation (SD) or median with interquartile ranges (IQR), and were compared using the Student *t* test, Analysis of Variance or the Mann–Whitney rank sum test, as appropriate. If there were statistically significant differences among 3 groups, the least significant difference t-test (LSD-t) would be applied for multiple comparisons. Categorical variables were expressed as counts (percentages) and were compared using the Chi-Squared

Table 1

Baseline characteristics among different rSS groups.

	rSS=0; n=26	0<rSS≤8; n=35	rSS>8; n=26	Z/F/χ^2	*P* value
Age (years)	54.85±11.38	55.34±9.78	53.77±8.61	0.189	.828
Male gender [NO. (%)]	21 (80.8)	31 (88.6)	25 (96.2)	-	.205
BMI (kg/m^2)	25.02±3.02	25.31±3.01	26.48±3.29	1.651	.198
Smoker [NO. (%)]	15 (57.7)	23 (65.7)	20 (76.9)	2.187	.335
Medical history					
Hypertension [NO. (%)]	17 (65.4)	22 (62.9)	15 (57.7)	0.342	.843
DM [NO. (%)]	4 (15.4)	12 (34.3)	16 (61.5)	12.066	.002
Hyperlipidemia [NO. (%)]	12 (46.2)	21 (60.0)	10 (38.5)	2.927	.231
Medication					
Aspirin [NO. (%)]	26 (100.0)	33 (94.3)	23 (88.5)	-	.464
Clopidogrel [NO. (%)]	25 (96.2)	33 (94.3)	23 (88.5)	0.382	.818
Statins [NO. (%)]	26 (100.0)	35 (100.0)	23 (88.5)	-	.082
β-blocker [NO. (%)]	24 (92.3)	29 (82.9)	22 (84.6)	-	.629
Nitrates [NO. (%)]	8 (30.8)	9 (25.7)	10 (38.5)	1.134	.567
ACEI/ARB [NO. (%)]	17 (65.4)	17 (48.6)	15 (57.7)	1.743	.414
CCB [NO. (%)]	3 (11.5)	5 (14.3)	4 (15.4)	-	1.000
LVEF (%)	65.80 (59.65–71.47)	70.15 (66.94~74.02)	63.00 (50.68–72.80)	8.115	.017
Time of CPET after PCI (months)	3.00 (0.53–10.75)	2.25 (1.00–9.13)	3.00 (1.04–8.50)	0.957	.620
Target lesion location					
LM [NO. (%)]	1 (3.8)	5 (14.3)	6 (23.1)	-	.124
LAD [NO. (%)]	22 (84.6)	33 (94.3)	25 (96.2)	-	.366
LCX [NO. (%)]	9 (34.6)	24 (68.6)	23 (88.5)	16.885	.000
RCA [NO. (%)]	8 (30.8)	21 (60.0)	23 (88.5)	17.996	.000
Three-vessel disease [NO. (%)]	3 (11.5)	14 (40.0)	21 (80.8)	32.656	.000
Total occlusion [NO. (%)]	12 (46.2)	6 (17.1)	18 (69.2)	17.034	.000
bSS	9.50 (7.25–22.50)	14.00 (9.75–18.25)	23.75 (19.25–25.38)	19.644	.000

ACEI = angiotensin converting enzyme inhibitors, ARB = angiotensin receptor blocker, BMI = body mass index, bSS = baseline SYNTAX score, CCB = calcium channel blockers, CPET = cardiopulmonary exercise testing, DM = diabetes mellitus, LAD = left anterior descending artery, LCX = left circumflex, LM = left main, LVEF = left ventricular ejection fraction, PCI = percutaneous coronary intervention, RCA = right coronary artery, rSS = residual SYNTAX score.

or Fishers exact test. A *P* value <.05 was considered statistically significant. Multivariable analysis was performed using binary logistic regression to determine independent predictors for exercise tolerance reduction.

3. Results

Among the 100 patients who met the inclusion criteria, 4 patients were excluded from the study because of previous CABG surgery, 9 patients were excluded due to chronic lung disease, and the left 87 patients were enrolled in the study.

The baseline clinical and anatomic characteristics of the study population are summarized in Table 1, separately for each rSS group (rSS=0, 0<rSS ≤ 8, rSS>8). Patients with high rSS (rSS>8) were more frequently had a history of diabetes mellitus ($P<.05$). A grater rSS was associated with progressively higher bSS ($P<.05$), with a rSS>8 associated with significantly more total occlusion, 3-vessel disease, left circumflex (LCX) and right coronary artery (RCA) lesions ($P<.05$). The indices of treadmill exercise testing are presented in Table 2, and there was no significant difference among different rSS groups.

The indices of CPET among different rSS groups are presented in Table 3. Patients with higher rSS had progressively lower MET_{peak}, MET_{peak}%pred, VO_{2peak}%pred, VO_2 at AT, and MET at AT, which reflect patients exercise tolerance ($P<.05$). Further multiple comparisons (LSD-t) were applied for MET_{peak}, MET_{peak}%pred, VO_{2peak}%pred, VO_2 at AT, and MET at AT among different rSS groups. The result showed that there was no

Table 2

Indices of treadmill exercise test among different rSS groups.

	rSS=0; n=26	0<rSS≤8; n=35	rSS>8; n=26	Z/F/χ^2	*P* value
Exercise duration (seconds)	667.50 (478.75–756.00)	695.00 (462.50–792.00)	657.50 (491.50–753.25)	0.103	.950
ST-segment depression ≥0.1 mV [NO. (%)]	5 (19.2)	8 (22.9)	5 (19.2)	0.206	1.000
duration of ST-segment depression (seconds)	242.50 (90.00–516.00)	434.50 (272.00–510.50)	535.00 (510.50–705.50)	2.888	.236
Rest systolic BP (mm Hg)	120.08±18.32	120.91±18.08	121.31±19.48	0.028	.972
Peak systolic BP (mm Hg)	158.96±23.84	163.50±23.51	156.24±22.22	0.738	.481
Rest diastolic BP (mm Hg)	73.79±11.69	78.69±11.01	75.62±11.08	1.436	.244
Peak diastolic BP (mm Hg)	81.63±12.91	82.82±16.36	81.80±16.26	0.053	.949
Rest HR (bpm)	69.65±12.92	73.17±12.00	69.85±10.83	0.859	.427
Peak HR (bpm)	134.23±17.06	135.91±21.65	128.19±19.55	1.201	.306

BP = blood pressure, bpm = beats per minutes, HR = heart rate, rSS = residual SYNTAX score.

Table 3

Indices of CPET among different rSS groups.

	rSS = 0; n = 26	0 < rSS ≤ 8; n = 35	rSS > 8; n = 26	Z/F/χ^2	*P* value
MET_{peak} (mets)	7.24 ± 1.67	6.85 ± 1.60	6.00 ± 1.34	4.439	.015
MET_{peak}%pred (%)	88.96 ± 16.44	81.31 ± 19.05	70.77 ± 15.07	7.235	.001
MET at AT (mets)	4.77 ± 0.99	4.73 ± 0.96	4.11 ± 1.11	3.575	.032
VO_2 at AT (ml/min/kg)	16.72 ± 3.48	16.58 ± 3.34	14.36 ± 3.87	3.737	.028
VO_{2peak} (ml/min/kg)	23.98 ± 4.04	23.95 ± 4.72	21.56 ± 3.97	2.839	.064
VO_{2peak}%pred (%)	83.27 ± 16.24	80.71 ± 16.57	72.77 ± 12.71	3.334	.040
VE/VCO_2	32.26 ± 4.50	33.14 ± 4.88	34.02 ± 4.96	0.883	.417
EOV [NO. (%)]	3 (11.5)	2 (5.7)	2 (11.5)	-	.795
Rest $P_{ET}CO_2$	30.38 ± 2.53	31.20 ± 2.83	30.69 ± 2.45	0.737	.482
Peak $P_{ET}CO_2$	39.13 ± 3.26	39.54 ± 4.16	38.27 ± 3.98	0.768	.467
$\Delta P_{ET}CO_2$	8.75 ± 3.30	8.34 ± 3.44	7.58 ± 3.10	0.828	.441

AT = anaerobic threshold, CPET = cardiopulmonary exercise testing, EOV = exercise oscillatory ventilation, MET = metabolic equivalent, MET_{peak} %pred = percentages of predicting value of peak MET, MET_{peak} = peak MET, $P_{ET}CO_2$ = partial pressure of end-tidal carbon dioxide production, rSS = residual SYNTAX score, VCO_2 = carbon dioxide production, VE = minute ventilation, VO_{2peak}%pred = percentages of predicting value of peak VO_2, VO_{2peak} = peak VO_2.

statistically significant difference between rSS = 0 and 0 < rSS ≤ 8 group, while all the aforementioned variables were significantly lower in rSS > 8 group compared with rSS = 0 group ($P < .05$). And there were statistical differences between 0 < rSS ≤ 8 and rSS > 8 group in terms of MET_{peak}, MET_{peak}%pred, VO_2 at AT, and MET at AT ($P < .05$).

A decrease in VO_{2peak}%pred is a critical indicator of reduced exercise tolerance. Thus, in the second part of our present study, we divided patients into normal exercise tolerance (VO_{2peak}%pred >84%) and reduced exercise tolerance (VO_{2peak}%pred ≤84%) groups according to VO_{2peak}%pred,[21] to determine the risk factors of reduction in exercise tolerance. The clinical and anatomic characteristics between 2 groups are presented in Table 4.

On univariate analysis above, the difference of rSS between VO_{2peak}%pred > 84% and VO_{2peak}%pred ≤ 84 group was statistically significant (Table 4). Along with rSS, variables which were found to be significant by other studies, such as history of

Table 4

Clinical and angiographic characteristics according to VO_{2peak}%pred.

	VO_{2peak}%pred > 84%; N = 32	VO_{2peak}%pred ≤ 84%; N = 55	Z/t/χ^2	*P* value
Age≥65 years [NO. (%)]	6 (18.8)	5 (9.1)	0.946	.331
Male gender [NO. (%)]	28 (87.5)	49 (89.1)	0.000	1.000
BMI (kg/m^2)	25.38 ± 3.25	25.91 ± 2.91	−0.771	.443
Smoker [NO. (%)]	20 (62.5)	38 (69.1)	0.395	.529
Medical history				
Hypertension [NO. (%)]	21 (65.6)	33 (60.0)	0.272	.602
DM [NO. (%)]	11 (34.4)	21 (38.2)	0.126	.723
Hyperlipidemia [NO. (%)]	17 (53.1)	26 (47.3)	0.277	.599
Prior MI [NO. (%)]	16 (50.0)	35 (63.6)	1.551	.213
Medication				
Aspirin [NO. (%)]	31 (96.9)	51 (94.4)	0.000	1.000
Clopidogrel [NO. (%)]	31 (96.9)	50 (92.6)	0.118	.731
Statins [NO. (%)]	31 (100.0)	53 (96.4)	–	.534
β-blocker [NO. (%)]	29 (90.6)	46 (83.6)	0.347	.556
Nitrates [NO. (%)]	10 (31.2)	17 (30.9)	0.001	.974
ACEI/ARB [NO. (%)]	19 (59.4)	30 (54.5)	0.192	.661
CCB [NO. (%)]	5 (15.6)	7 (12.7)	0.003	.956
LVEF (%)	66.58 (59.22–70.63)	67.90 (61.40–72.70)	0.072	.788
Time of CPET after PCI (months)	3.25 (1.63–9.88)	2.00 (0.67–7.00)	3.576	.059
Target lesion location				
LM [NO. (%)]	4 (12.5)	8 (14.5)	0.000	1.000
LAD [NO. (%)]	28 (87.5)	52 (94.5)	0.572	.449
LCX [NO. (%)]	20 (62.5)	36 (65.5)	0.077	.781
RCA [NO. (%)]	17 (53.1)	35 (63.6)	0.930	.335
Three-vessel disease [NO. (%)]	13 (40.6)	25 (45.5)	1.719	.423
Total occlusion [NO. (%)]	12 (37.5)	24 (43.6)	0.314	.575
bSS	14.25 (8.00–23.50)	18.00 (11.00–22.50)	9.30	.335
rSS	3.00 (0.00–6.00)	6.00 (1.00–10.00)	5.776	.016

ACEI = angiotensin converting enzyme inhibitors, ARB = angiotensin receptor blocker, BMI = body mass index, bSS = baseline SYNTAX score, CCB = calcium channel blockers, CPET = cardiopulmonary exercise testing, DM = diabetes mellitus, LAD = left anterior descending artery, LCX = left circumflex, LM = left main, LVEF = left ventricular ejection fraction, MI = myocardial infarction, PCI = percutaneous coronary intervention, RCA = right coronary artery, rSS = residual SYNTAX score.

diabetes mellitus and prior myocardial infarction, were also included within the logistic regression model.[24] The rSS was found to be an independent predictor of reduced exercise tolerance (OR = 1.126, 95%CI: 1.021–1.242, $P < .05$).

4. Discussion

There is no universally accepted definition for ICR in prior studies. The concept of rSS was proposed by ACUITY investigators, and CR was defined as rSS = 0, while ICR was defined as rSS > 0 in ACUITY trial.[20] In 2013, Farooq et al[11] assessed the prognostic value of rSS in the randomized PCI cohort of the SYNTAX Trial at the 5-year follow-up, and the result showed that there were no significant differences in 5-year death between CR and 0 < rSS ≤ 8 patients, and an rSS > 8 was identified as a level of ICR strongly associated with increased mortality and adverse ischemic events. Witberg et al[12] used 3 different methods for defining rICR, and the result indicated that an rSS value <8 is a suitable threshold for the definition of rICR.

In our study, CR was defined as a post-PCI rSS = 0. rICR was defined as 0 < rSS ≤ 8, and rSS > 8 was considered to be sICR. Patients were divided into different groups according to rSS, and the CPET variables were compared among different groups. In present study, patients with higher rSS had progressively lower MET_{peak}, MET_{peak}%pred, VO_{2peak}%pred, VO_2 at AT, and MET at AT ($P < .05$), which indicate reduced exercise tolerance. And further multiple comparisons showed that there were no statistically significant differences between rSS = 0 and 0 < rSS ≤ 8 group, while the aforementioned variables were significantly lower in rSS > 8 group compared with rSS = 0 group ($P < .05$). Therefore, we believe that a rSS of ≤8 (rICR) was associated with exercise tolerance comparable with subjects with rSS = 0 (CR), while a rSS > 8 after PCI was associated with adverse exercise tolerance. This finding is in accordance with aforementioned studies which suggest rICR was an acceptable burden of CAD post revascularization to be associated with similar outcomes to subjects in whom CR was achieved. Only when the residual lesions of coronary arteries exceeded the threshold of rICR, they were associated with progressively increasing adverse long-term clinical outcomes, including mortality.[11,12]

In the second part of present study, we aimed to determine the risk factors of exercise tolerance reduction in CAD patients treated by PCI. rSS, history of diabetes mellitus, and prior myocardial infarction were included within the logistic regression, and the rSS was found to be an independent predictor of reduced exercise tolerance (OR = 1.126, 95%CI: 1.021–1.242, $P < .05$).

The rSS may improve the allocation of coronary patients to the optimal mode of revascularization. We believe that the favorable outcome and exercise tolerance after PCI seen in patients with low rSS demonstrates that different degrees of ICR after PCI are associated with different outcomes and different exercise tolerance, and we should not define ICR as a class effect. Thus, for high-risk PCI patients, especially for the aged and the ones suffering from complicated comorbidities, a rICR (0 < rSS ≤ 8) instead of an anatomic complete 1 would be a more reasonable strategy to use during stent implantation.

The importance of defining "reasonable" ICR also lies in its potential to aid in the selection of the revascularization procedure (PCI or CABG) in patients with complex multivessel disease. The heart team will need to estimate which coronary lesions will not likely be amenable to PCI, and if the sum of the lesions would exceed a score of 8, the patient should ideally be referred to CABG in order to achieve optimal revascularization and exercise tolerance.

5. Study limitations

Several limitations of the present study should be discussed. Firstly, our results are limited due to the study design—a single center retrospective study, which raises the possibility of selection bias. In addition, our cohort size was underpowered to conduct subgroup (stable angina, unstable angina, ST-segment elevated myocardial infarction or non-ST-segment elevated myocardial infarction) analyses. Moreover, future prospective studies are needed to assess the correlation between patients exercise tolerance and prognosis.

6. Conclusions

Our results suggest that:

1. There was no significant difference in exercise tolerance between CR (rSS = 0) and rICR (0 < rSS ≤ 8) groups in CAD patients treated by PCI. However, the exercise tolerance of CR and rICR groups was better than sICR (rSS > 8) group;
2. rSS was an independent risk factors for VO_{2peak}%pred reduction in patients with CAD after PCI.

Acknowledgments

The authors thank staff in the Department of Cardiology, Catheterization Laboratory and Cardiopulmonary Exercise Laboratory, Peking University People's Hospital for their research contributions.

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