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Prognostic Implication of Functional Incomplete Revascularization and Residual Functional SYNTAX Score in Patients With Coronary Artery Disease

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ABSTRACT

OBJECTIVES The aim of this study was to investigate the prognostic implication of functional incomplete revascularization (IR) and residual functional SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score (rFSS) in comparison with 3-vessel fractional flow reserve (FFR) and residual SYNTAX score.

BACKGROUND IR is associated with poor clinical outcomes in patients who underwent percutaneous coronary intervention.

METHODS A total of 385 patients who underwent 3-vessel FFR measurement after stent implantation were included in this study. The rFSS was defined as residual SYNTAX score measured only in vessels with FFR ≤0.8. The study population was divided into the functional IR group (rFSS ≥1) and the functional complete revascularization (CR) group (rFSS = 0). The primary outcome was major adverse cardiac events (MACEs; a composite of cardiac death, myocardial infarction, and ischemia-driven revascularization) at 2 years.

RESULTS Functional CR was achieved in 283 patients (73.5%). At 2-year follow-up, the functional IR group showed a significantly higher risk for MACEs (functional IR vs. CR, 14.6% vs. 4.2%; hazard ratio: 4.09; 95% confidence interval: 1.82 to 9.21; $p < 0.001$) than the functional CR group. In a multivariate-adjusted model, functional IR was an independent predictor of MACEs (adjusted hazard ratio: 4.17; 95% confidence interval: 1.85 to 9.44; $p < 0.001$). The rFSS showed a significant association with estimated 2-year MACE rate (hazard ratio: 1.09 per 1-U increase; 95% confidence interval: 1.02 to 1.17; $p = 0.018$). When added to clinical risk factors, rFSS showed the highest integrated discrimination improvement value for MACEs (3.5%; $p = 0.002$) among 3-vessel FFR, residual SYNTAX score, and rFSS.

CONCLUSIONS Patients with functional IR showed significantly higher rate of 2-year MACEs than those with functional CR. A combined anatomic and physiological scoring system (rFSS) after stent implantation better discriminated the risk for adverse events than anatomic or physiological assessment alone. (Clinical Implication of 3-Vessel Fractional Flow Reserve [FFR]; NCT01621438) (J Am Coll Cardiol Intv 2018;11:237–45)

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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

CR = complete revascularization

FFR = fractional flow reserve

HR = hazard ratio

IR = incomplete revascularization

MACE = major adverse cardiac event(s)

MI = myocardial infarction

PCI = percutaneous coronary intervention

rFSS = residual functional SYNTAX score

rSS = residual SYNTAX score

Patients with incomplete revascularization (IR) after percutaneous coronary intervention (PCI) are reported to have worse clinical outcomes than those with complete revascularization (CR) (1–5). However, most previous studies determined the completeness of revascularization using anatomic stenosis severity, without consideration of the functional significance of remaining stenoses. It is well-known that discrepancy exists between anatomic lesion severity and the functional significance assessed by fractional flow reserve (FFR) (6–11). Moreover, FFR-guided revascularization strategy has been reported to be better than angiography-guided revascularization or medical treatment (12,13).

The SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score is a comprehensive angiographic scoring system based on coronary anatomy and lesion characteristics (14). Previously, Nam et al. (15) integrated the SYNTAX score and FFR to develop the concept of the functional SYNTAX score. They calculated the SYNTAX score only in vessels with low FFR (FFR ≤0.8) and showed that the functional SYNTAX score better predicted clinical outcomes than the SYNTAX score. The residual functional SYNTAX score (rFSS), which is the sum of residual SYNTAX score (rSS) of the vessels with low FFR, can provide integrated anatomic and functional information on the residual disease burden after PCI. However, its prognostic value has not yet been investigated.

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The aim of this study was to investigate the prognostic implication of functional IR and rFSS in comparison with rSS and FFR in all 3 major coronary arteries.

METHODS

STUDY POPULATION. The 3V-FFR-FRIENDS (3-Vessel Fractional Flow Reserve for the Assessment of Total Stenosis Burden and Its Clinical Impact in Patients With Coronary Artery Disease) study is a prospective, multicenter, observational study that recruited patients with coronary artery disease who underwent FFR measurement in all major coronary arteries (16). In brief, inclusion criteria for this study were age at least 18 years and >30% stenosis in all major epicardial coronary arteries. Patients with left ventricular systolic dysfunction (ejection fraction <35%), ST-segment elevation myocardial infarction (MI) within 72 h, previous coronary artery bypass graft surgery, chronic kidney disease (serum creatinine ≥2.0 mg/dl), or abnormal epicardial coronary flow (TIMI [Thrombolysis In Myocardial Infarction] flow grade <3, including chronic total occlusion) and those who underwent planned coronary artery bypass graft surgery after diagnostic angiography were excluded. For lesions with significant per vessel FFR (≤0.80), PCI was recommended as per the current guideline. However, the decision for PCI was at the discretion of the operators. In case of PCI, measurement of post-PCI FFR was mandatory per the study protocol.

The present study was a pre-specified substudy of the 3V-FFR-FRIENDS study, and 385 patients who underwent PCI for functionally significant lesions were included in the present study. The study population was divided into the functional CR group (rFSS = 0, n = 283) and the functional IR group (rFSS ≥1, n = 102). The Institutional Review Board or ethics committee of each center approved the study protocol, and all patients provided written informed consent before enrollment.

QUANTITATIVE CORONARY ANGIOGRAPHY AND SYNTAX SCORE. Coronary angiography was performed using standard techniques and analyzed by an independent core laboratory at Seoul National University Hospital using validated software (CAAS II, Pie Medical System, Maastricht, the Netherlands). Angiographic views were obtained after administration of intracoronary nitrate (100 or 200 μg). Minimum luminal diameter, reference diameter, and lesion length were measured, and percentage diameter stenosis was calculated. The SYNTAX score, rSS, and rFSS were calculated in an independent core laboratory by a blinded investigator (17). The rFSS was calculated as the sum of the rSS of lesions in vessels with FFR ≤0.8. The intraindividual variability in the calculation of the SYNTAX score was determined in 20 randomly selected patients. Repeated measurements showed excellent correlation ($r = 0.984$; $p < 0.001$; p for difference = 0.781), and the mean difference was -0.100 ± 1.586 in the Bland-Altman analysis.

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MEASUREMENTS OF FFR. For FFR measurement, a pressure-temperature sensor guidewire (Abbott Vascular, Santa Clara, California) was positioned at the distal segment of a target vessel. Intracoronary nitrate (100 or 200 μg) was administered before each FFR measurement. Intravenous infusion of adenosine (140 μg/kg/min via peripheral vein) was used to induce hyperemia. Hyperemic proximal aortic pressure and distal coronary arterial pressure were obtained during sustained hyperemia and FFR was calculated as the mean of distal coronary arterial pressure/proximal aortic pressure during hyperemia. Treatment strategies of intervention were performed according to the operator's discretion. Three-vessel FFR was calculated as the sum of the 3 epicardial coronary vessels' FFR values after PCI (16). All FFR tracings were validated at the independent core laboratory at Seoul National University Hospital, blinded to clinical and angiographic findings.

OUTCOMES AND FOLLOW-UP. The primary endpoint of this study was major adverse cardiac events (MACE) at 2 years, a composite of cardiac death, MI, and any ischemia-driven revascularization. All deaths were considered cardiac unless a definitive noncardiac cause was established. MI was defined as an elevation of creatine kinase myocardial band or troponin level greater than the upper limit of normal with concomitant ischemic symptoms or electrocardiography findings indicative of ischemia. Periprocedural MI was not included as clinical event. Ischemia-driven revascularization was defined as a revascularization procedure with at least 1 of the following: 1) recurrence of angina; 2) positive noninvasive test results; and 3) positive invasive physiological test results. Clinical data were obtained by outpatient clinic visits or by telephone contact, if necessary. All clinical events were adjudicated by an independent clinical events committee.

STATISTICAL ANALYSIS. Categorical variables were tested using the chi-square test or Fisher exact test, as appropriate, and are presented as numbers and relative frequencies. Continuous variables were compared using the Student *t* test. Correlations among 3-vessel FFR, rSS, and rFSS were tested using the Spearman correlation coefficient. To evaluate the association among the 3 scoring systems (3-vessel FFR, rSS, and rFSS) and estimated MACE risk, probability of risk was estimated using the Cox proportional hazards model. The estimated MACE risk was plotted using the locally weighted scatterplot smoothing regression line. The cumulative incidence of clinical events was presented as Kaplan-Meier estimates and compared using a log-rank test. Cox proportional hazards regression was used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) to compare the risk for clinical events between the functional CR and IR groups.

A multivariate Cox proportional hazards regression model was used to identify independent predictors of clinical events. Covariates that were either statistically significant on univariate analysis or clinically relevant were considered candidate variables. Variables selected for a multivariate model were carefully chosen, given the number of events available, to ensure parsimony of the final models (18). The incremental prognostic value of 3-vessel FFR, rSS, and rFSS, in addition to clinical risk factors, was assessed using the Brier score, Harrell's C index, net reclassification improvement, and the integrated discrimination improvement index (19). Clinical risk factors included age, sex, hypertension, diabetes mellitus,

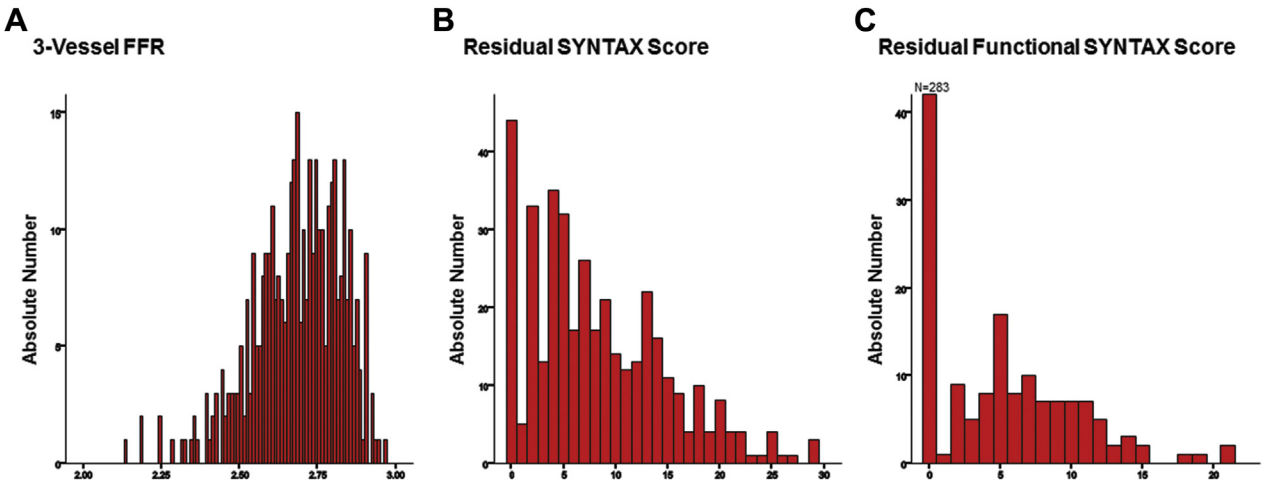
TABLE 1 Baseline Characteristics of Study Population

	Total (n = 385)	Functional CR (n = 283)	Functional IR (n = 102)	p Value
Per patient				
Age (yrs)	61.5 ± 9.6	61.8 ± 9.7	60.5 ± 9.3	0.234
Male	295 (76.6)	218 (77.0)	77 (75.5)	0.858
Hypertension	234 (60.8)	174 (61.5)	60 (58.8)	0.724
Diabetes mellitus	137 (35.6)	104 (36.7)	33 (32.4)	0.500
Hyperlipidemia	204 (53.0)	142 (50.2)	62 (60.8)	0.085
Acute coronary syndrome	169 (43.9)	126 (44.5)	43 (42.2)	0.767
Angiographic disease severity				0.005
1-vessel disease	131 (34.0)	108 (38.2)	23 (22.5)	
2-vessel disease	143 (37.1)	104 (36.7)	39 (38.2)	
3-vessel disease	111 (28.8)	71 (25.1)	40 (39.2)	
Multivessel disease	254 (66.0)	175 (61.8)	79 (77.5)	0.006
Number of stents used	1.4 ± 0.8	1.4 ± 0.8	1.4 ± 0.7	0.932
Number of treated vessels				0.644
1-vessel PCI	296 (76.9)	221 (78.1)	75 (73.5)	
2-vessel PCI	76 (19.7)	53 (18.7)	23 (22.5)	
3-vessel PCI	13 (3.4)	9 (3.2)	4 (3.9)	
Total stent length (mm)	36.3 ± 23.5	35.9 ± 23.5	37.4 ± 21.2	0.575
Residual SYNTAX score	7.0 (4.0-13.0)	5.0 (2.0-10.0)	12.5 (8.0-17.0)	<0.001
Residual functional SYNTAX score	0 (0-2.0)	0 (0-0)	7.0 (5.0-10.0)	<0.001
3-vessel FFR	2.70 ± 0.14	2.73 ± 0.11	2.53 ± 0.13	<0.001
Per lesion				
Diameter stenosis (%)	53.1 ± 21.4	51.5 ± 21.4	57.6 ± 20.7	<0.001
Lesion length (mm)	13.6 ± 10.8	13.2 ± 10.6	14.7 ± 11.3	0.054
Treated lesion				
LAD	249 (64.7)	186 (65.7)	63 (61.8)	0.551
LCX	102 (26.5)	79 (27.9)	23 (22.5)	0.356
RCA	134 (34.8)	87 (30.7)	47 (46.1)	0.008

Values are mean ± SD, n (%), or median (interquartile range).

CR = complete revascularization; FFR = fractional flow reserve; IR = incomplete revascularization; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; PCI = percutaneous coronary intervention; RCA = right coronary artery; SYNTAX = Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery.

FIGURE 1 Distribution of 3-Vessel Fractional Flow Reserve, Residual SYNTAX Score, and Residual Functional SYNTAX Score



Distribution of **(A)** 3-vessel fractional flow reserve (FFR), **(B)** residual SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score (rSS), and **(C)** residual functional SYNTAX score (rFSS) are presented.

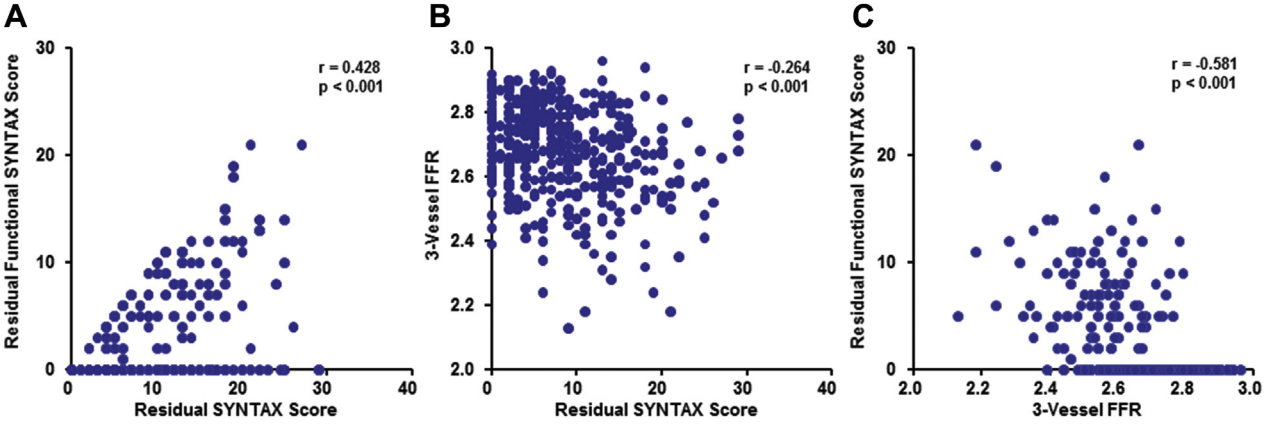
hyperlipidemia, history of MI, history of revascularization, and acute coronary syndrome.

Statistical analyses were performed using R statistical software version 3.2.5 (R Foundation for Statistical Computing, Vienna, Austria). Values of $p < 0.05$ were considered to indicate statistical significance.

RESULTS

BASELINE CHARACTERISTICS. The mean 3-vessel FFR, rSS, and rFSS were 2.70 ± 0.14, 8.3 ± 6.5, and 2.0 ± 4.0, respectively (Table 1). There were no differences in baseline patient characteristics, number of treated vessel, and number of stents used between the functional IR group and the functional CR group. However, the functional IR group had a higher prevalence of multivessel disease, higher percentage diameter stenosis, higher rSS, and lower 3-vessel FFR than the functional CR group (Table 1). Functional CR could not be achieved in 52 patients even after successful PCI for target lesions. In deferred lesions, the reasons for not treating the functionally significant

FIGURE 2 Correlations Among 3-Vessel Fractional Flow Reserve, Residual SYNTAX Score, and Residual Functional SYNTAX Score



Correlations **(A)** between residual SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score (rSS) and residual functional SYNTAX score (rFSS), **(B)** between rSS and 3-vessel FFR (fractional flow reserve), and **(C)** between 3-vessel FFR and rFSS are presented.

lesion were diffuse narrowing without focal stenosis (25 of 50 [50%]), reverse mismatch between angiographic severity and functional significance (17 of 50 [34%]), small vessel (4 of 50 [8%]), heavily calcified lesion (2 of 50 [4%]), or angulated lesion (2 of 50 [4%]) in which the operators considered that the benefit of PCI might not outweigh the risk of the procedure.

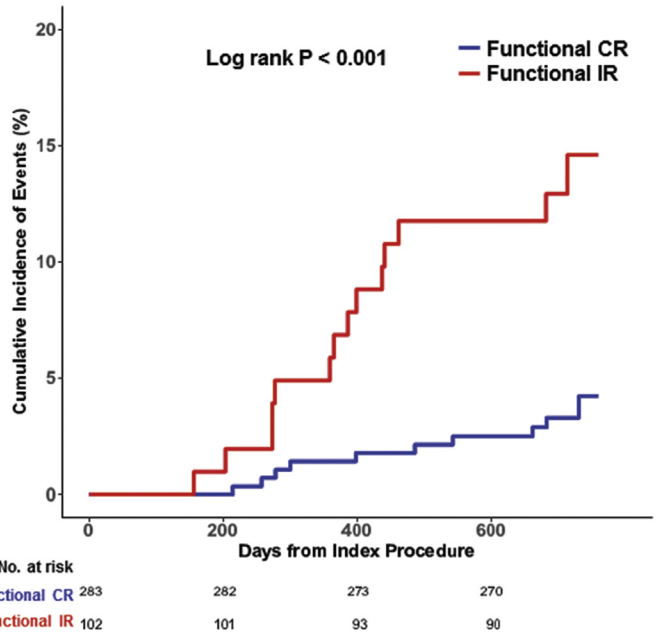
DISTRIBUTIONS AND CORRELATIONS OF ANATOMIC AND PHYSIOLOGICAL SCORING SYSTEMS. Distributions of 3-vessel FFR, rSS, and rFSS are shown in Figure 1. Correlations between different scoring systems are presented in Figure 2. The rFSS had significant correlations with rSS ($r = 0.428$; $p < 0.001$) and 3-vessel FFR ($r = -0.581$; $p < 0.001$). In addition, 3-vessel FFR was negatively correlated with rSS ($r = -0.264$; $p < 0.001$).

CLINICAL OUTCOMES. Compared with the functional CR group, the functional IR group showed a higher incidence of MACEs (14.6% vs. 4.2%; hazard ratio [HR]: 4.09; 95% confidence interval [CI]: 1.82 to 9.21; $p < 0.001$) (Figure 3). When comparing individual components of MACEs, the functional IR group showed higher cardiac death or MI (6.2% vs. 0.8%) and ischemia-driven revascularization (13.7% vs. 4.2%). All-cause death (1.0% vs. 1.4%) and cardiac death (1.0% vs. 0%) rates were similar between the 2 groups (Table 2). Among patients with ischemia-driven revascularization, PCI was performed in 47.8% (11 of 23) because of acute coronary syndromes, 39.1% (9 of 23) because of objective signs of inducible ischemia on noninvasive tests, and 13.1% (3 of 23) because of progressed angiographic stenosis with aggravation of symptoms.

The presence of functional IR was an independent predictor of MACEs (adjusted HR: 4.17; 95% CI: 1.85 to 9.44; $p < 0.001$) in a multivariate Cox proportional hazards model (Table 3). The rFSS as a continuous variable was also independently associated with MACEs (adjusted HR: 1.09; 95% CI: 1.02 to 1.18; $p = 0.018$) (Table 3).

INCREMENTAL PROGNOSTIC VALUES OF 3-VESSEL FFR, rSS, AND rFSS IN ADDITION TO CLINICAL RISK FACTORS. Three-vessel FFR showed significant association with the estimated MACEs rates (Figure 4A). The rSS and rFSS also showed significant association with the estimated MACE rate as continuous values (Figures 4B and 4C). When each of the different scoring systems (3-vessel FFR, rSS, and rFSS) was added to clinical risk factors for prediction of 2-year MACE, the model with rFSS showed the highest C index (0.701; 95% CI: 0.592 to 0.810; $p < 0.001$) (Figure 5). In addition, only the model with rFSS showed significantly improved net reclassification improvement, compared with other models with 3-vessel FFR or rSS (Figure 5).

FIGURE 3 Comparison of 2-Year Clinical Outcomes Between the Functional Complete Revascularization Group and the Functional Incomplete Revascularization Group



Kaplan-Meier survival curves are presented for cumulative incidence of 2-year major adverse cardiac events according to functional complete revascularization (CR) and incomplete revascularization (IR) groups.

DISCUSSION

In the present study, we investigated the prognostic implication of functional IR and rFSS, and the main

TABLE 2 Cumulative Incidences of Clinical Outcomes Between Functional Complete Revascularization Group and Functional Incomplete Revascularization Group

	Functional CR	Functional IR
Major adverse cardiac events*	10 (4.2)	14 (14.6)
Cardiac death or myocardial infarction	2 (0.8)	5 (6.2)
Cardiac death	0 (0)	1 (1.0)
All-cause death	4 (1.4)	1 (1.0)
Myocardial infarction	2 (0.8)	4 (5.2)
Ischemia-driven revascularization	10 (4.2)	13 (13.7)

Values are n (%). Cumulative incidences of events are presented as Kaplan-Meier estimates. *Major adverse cardiac events were defined as a composite of cardiac death, myocardial infarction, and ischemia-driven revascularization.

Abbreviations as in Table 1.

TABLE 3 Independent Predictors of Major Adverse Cardiac Events

	Adjusted HR (95% CI)	p Value
Model 1*		
Functional IR	4.17 (1.85–9.44)	<0.001
Acute coronary syndrome	1.37 (0.60–3.10)	0.452
Diabetes mellitus	0.79 (0.32–1.94)	0.600
Age (per year)	1.02 (0.97–1.06)	0.424
Model 2†		
rFSS (as a continuous value)	1.09 (1.02–1.18)	0.018
Acute coronary syndrome	1.40 (0.62–3.12)	0.413
Diabetes mellitus	0.83 (0.33–2.09)	0.697
Age (per year)	1.02 (0.97–1.06)	0.453

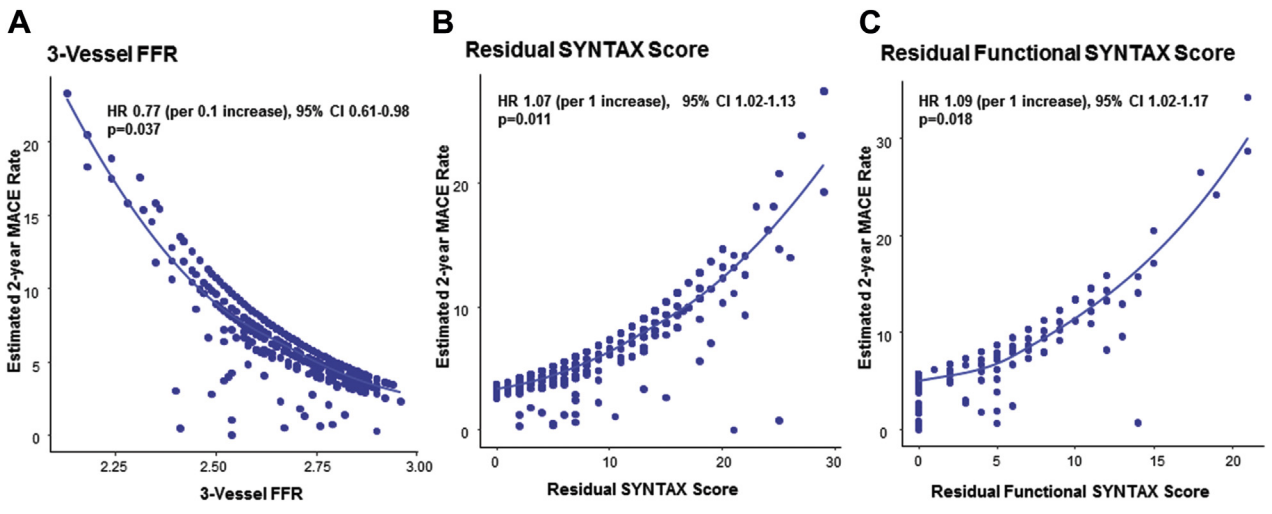
*Harrell's C index of the Cox regression model for MACEs including functional IR was 0.714 (95% CI: 0.596 to 0.832). †Harrell's C index of the Cox regression model for MACEs including rFSS was 0.685 (95% CI: 0.567 to 0.803).

CI = confidence interval; HR = hazard ratio; rFSS = residual functional SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score; other abbreviations as in Table 1.

findings are as follows: 1) the MACE rate was significantly higher in patients with functional IR than in those with functional CR; 2) functional IR was an independent predictor of MACEs in a multivariate-adjusted model; and 3) 3-vessel FFR was significantly correlated with the estimated 2-year MACE rate. The rSS and rFSS also showed significant associations with the estimated 2-year MACE rate. When 3-vessel FFR, rSS, and rFSS were added to clinical risk factors, the model with rFSS showed the highest discrimination ability for MACEs.

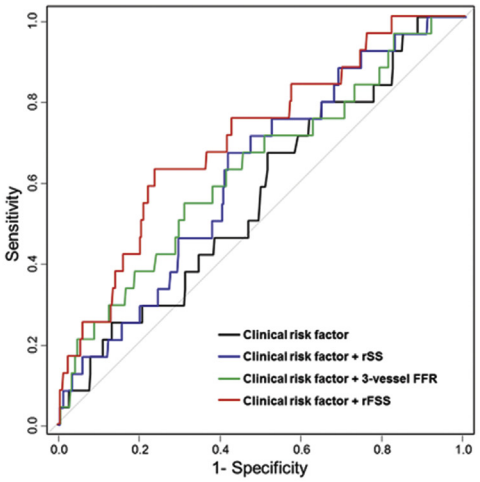
Previous studies reported higher risk for adverse cardiovascular events in patients with anatomic IR, compared with anatomic CR (20–23). The rSS, which represents the quantitative extent of IR, was reported to be an independent predictor of clinical outcomes (24–26). In concordance with previous studies, rSS was significantly associated with the 2-year rate of MACEs in our study. However, CR and rSS are determined by angiographic residual stenosis, and the discrepancy between anatomic lesion severity and functional significance is well known (6–11). Furthermore, recent post hoc analysis of the FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) trial showed that residual angiographic stenoses did not have additional prognostic implication after the achievement of functional CR (27). In this regard, the present study focused on the prognostic implication of functional IR. Patients with functional IR showed significantly higher risk for MACEs compared with those with functional CR. In addition, functional IR was an independent predictor of MACEs. These results

FIGURE 4 Estimated 2-Year Major Adverse Cardiac Event Rate According to 3-Vessel Fractional Flow Reserve, Residual SYNTAX Score, and Residual Functional SYNTAX Score



Estimated 2-year major adverse cardiac event (MACE) risk was plotted according to **(A)** 3-vessel fractional flow reserve (FFR), **(B)** residual SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score (rSS), and **(C)** residual functional SYNTAX score (rFSS). CI = confidence interval; HR = hazard ratio.

FIGURE 5 Comparison of Predictive Models With 3-Vessel Fractional Flow Reserve, Residual SYNTAX Score, and Residual Functional SYNTAX Score in Addition to Clinical Risk Factors



Model	Brier Score	C index	95% CI	P value	NRI (Category free)	P value	IDI	P value
Clinical risk factor*	0.0582	0.563	0.447-0.679	0.301	Reference		Reference	
Clinical risk factor + rSS	0.0578	0.618	0.509-0.728	0.053	0.336 (-0.065 - 0.737)	0.101	0.7%	0.122
Clinical risk factor + 3-vessel FFR	0.0575	0.625	0.503-0.747	0.041	0.342 (-0.049 - 0.733)	0.087	1.0%	0.047
Clinical risk factor + rFSS	0.0562	0.701	0.592-0.810	<0.001	0.679 (0.275 - 1.083)	0.001	3.5%	0.002

Brier score, discriminant function (C index), net reclassification improvement (NRI), and integrated discrimination index (IDI) were compared among 4 models. The reference model included clinical risk factors only, including age, sex, hypertension, diabetes mellitus, hyperlipidemia, history of myocardial infarction, history of revascularization, and acute coronary syndrome. Brier score, C index, NRI, and IDI values of models with 3-vessel fractional flow reserve (FFR), residual SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score (rSS), or residual functional SYNTAX score (rFSS) in addition to clinical risk factor were compared. Among these, the model with the rFSS showed the highest C index, NRI, and IDI values. CI = confidence interval.

suggest the prognostic implication of functional IR and stress the importance of functional assessment after PCI.

Previously, Nam et al. (15) presented the concept of functional SYNTAX score, which incorporated both anatomic and functional significance of lesions in pre-PCI evaluation of patients with multivessel coronary artery disease. The rFSS can provide integrated anatomic and functional information on the residual disease burden after PCI. The rSS and 3-vessel FFR represent residual anatomic and functional disease burden, respectively. When the prognostic implications of 3 different scoring systems (3-vessel FFR, rSS, and rFSS) were investigated in our study, all 3 systems showed significant associations with the risk for 2-year MACEs. These results suggest that both comprehensive anatomic and physiological assessment systems can be helpful in risk assessment after PCI. However, when each of the 3 scoring systems was added to clinical risk factors, the model with rFSS showed the highest C index for 2-year MACEs. In addition, only rFSS among the 3 scoring systems improved discrimination ability for MACEs when added to clinical risk factors. These results imply that combining both anatomic and functional information can better estimate patient risk after PCI than anatomic or functional assessments alone.

STUDY LIMITATIONS. First, the study population was relatively small. In addition, the overall event rate was generally lower than that of previous studies. This difference was probably due to the difference in baseline angiographic characteristics between our study and previous studies.

Second, this study was not a randomized study, and the decision for revascularization was left to the operator's discretion. Therefore, the optimal treatment strategy for patients with functional IR could not be evaluated.

Third, the lack of intravascular imaging data precluded a detailed analysis for the cause of functional IR.

Fourth, the difference of 2-year MACE rates between the functional CR and IR groups was driven mainly by ischemia-driven revascularization.

CONCLUSIONS

Patients with functional IR showed significantly higher rate of 2-year MACEs compared with those with functional CR. The combined anatomic and physiological scoring system (rFSS) provided better discrimination ability for the risk for adverse events than anatomic or physiological assessments alone.

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PERSPECTIVES

WHAT IS KNOWN? Although the benefits of an FFR-guided revascularization strategy have been well validated, the prognostic impact of functional IR and rFSS on clinical outcomes has not been evaluated.

WHAT IS NEW? The rFSS, which integrates residual anatomic and functional disease burden after stent implantation, showed significant and independent association with the risk for MACEs. Patients with functional IR, which was defined using the rFSS, showed significantly higher rates of 2-year MACEs than those with functional CR.

WHAT IS NEXT? Risk stratification of revascularized patients using the rFSS showed better discrimination of future adverse cardiac events. Further study is warranted to validate this concept and to find the optimal treatment strategy for patients with functional IR.

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