Trends in Outcomes of Revascularization for Left Main Coronary Disease or Three-Vessel Disease With the Routine Incorporation of Fractional Flow Reserve in Real Practice

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Impact of fractional flow reserve guidance on revascularization strategies and outcomes for severe coronary artery disease was unclear. We evaluate changes in treatment strategy and clinical outcomes and to compare the effectiveness between percutaneous coronary intervention (PCI) with second-generation drug-eluting stents and coronary artery bypass graft surgery (CABG) in severe coronary artery disease patients before and after routine use of FFR. From January 2008 to December 2011, we enrolled 2,612 patients with significant left main coronary artery disease or 3-vessel disease. We obtained data of patients before (from January 2008 to December 2009) and after (January 2010 to December 2011) the routine use of FFR. We used propensity score matching to compare the rate of primary outcomes (death, myocardial infarction, stroke, or repeat revascularization [Major adverse cardiovascular and cerebral event; MACCE]) at 1 year. Introduction of routine FFR use reduced the proportion of patients receiving CABG from 54% to 43% (p <0.001). The risk of MACCE before routine FFR use was significantly higher in the PCI group than the CABG group (hazard ratio [HR] 1.82, 95% confidence interval [CI] 1.09 to 3.03, p = 0.021), whereas that after routine FFR use was not significantly different between the groups (HR 1.22, 95% CI 0.59 to 2.52, p = 0.59). The risk of MACCE in patients receiving revascularization lowered after routine FFR use compared with that before (HR 0.57, 95% CI 0.38 to 0.85, p = 0.005). In conclusion, routine incorporation of FFR resulted in improved PCI outcomes, comparable with concurrent CABG in patients with severe coronary artery disease who received revascularization. **(Am J Cardiol 2015;116:1163−1171)**

Recently, 2 large randomized trials with a long-term follow-up found that coronary artery bypass graft surgery (CABG) reduced adverse clinical events compared with percutaneous coronary intervention (PCI).[1,2] Accordingly, current guidelines have recommended CABG as the primary revascularization therapy in patients with severe coronary artery disease.[3,4] However, previous trials were limited because of the use of inferior stent technology, such as first-generation drug-eluting stent (DES), and because ischemia-guided PCI, particularly fractional flow reserve (FFR), was not applied while deciding revascularization. Therefore, we aimed to evaluate changes in treatment strategy and clinical outcomes and to compare the effectiveness between PCI with second-generation DES and CABG in patients with left main coronary artery (LMCA) stenosis or 3-vessel disease before and after routine FFR implementation in real practice.

Methods

From January 2008 to December 2011, patients with angiographically confirmed significant LMCA disease or 3-vessel disease, in which revascularization was deemed to be clinically indicated, were consecutively enrolled in this study from the Asan Left Main and Multivessel Registry. Significant left main disease was defined as the angiographic diameter stenosis of >50%. We excluded patients who underwent previous CABG or concomitant valvular or aortic surgery, those who had an acute myocardial infarction (MI) 24 hours before revascularization or presented with cardiogenic shock, and those who had a contraindication to the placement of a DES. Patients who did not receive revascularization because of poor clinical or coronary anatomical condition or who refused percutaneous or surgical procedures were also excluded. Our center's institutional review board approved the use of clinical data for this

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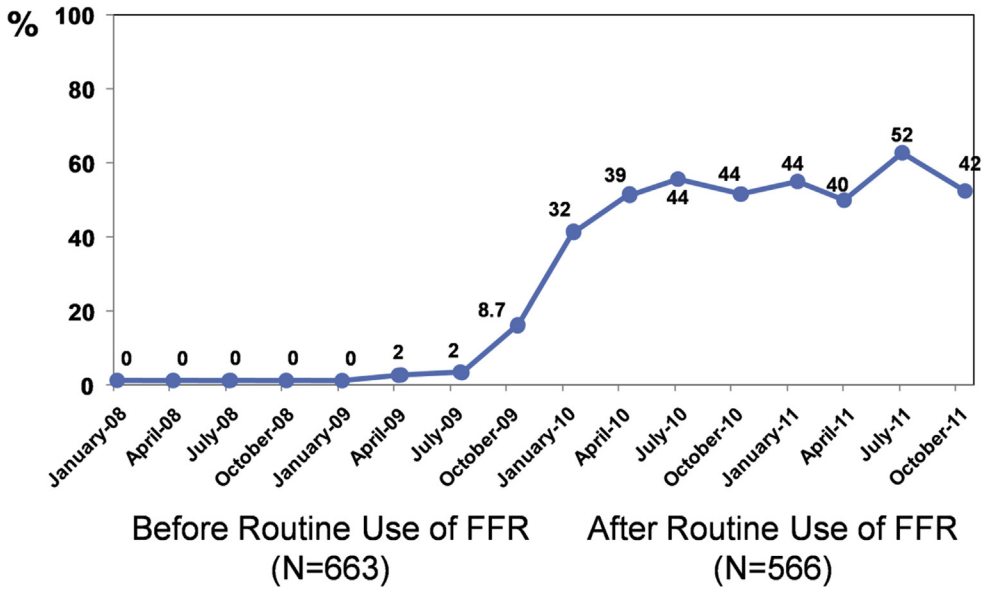

Figure 1. The rate of FFR during PCI.

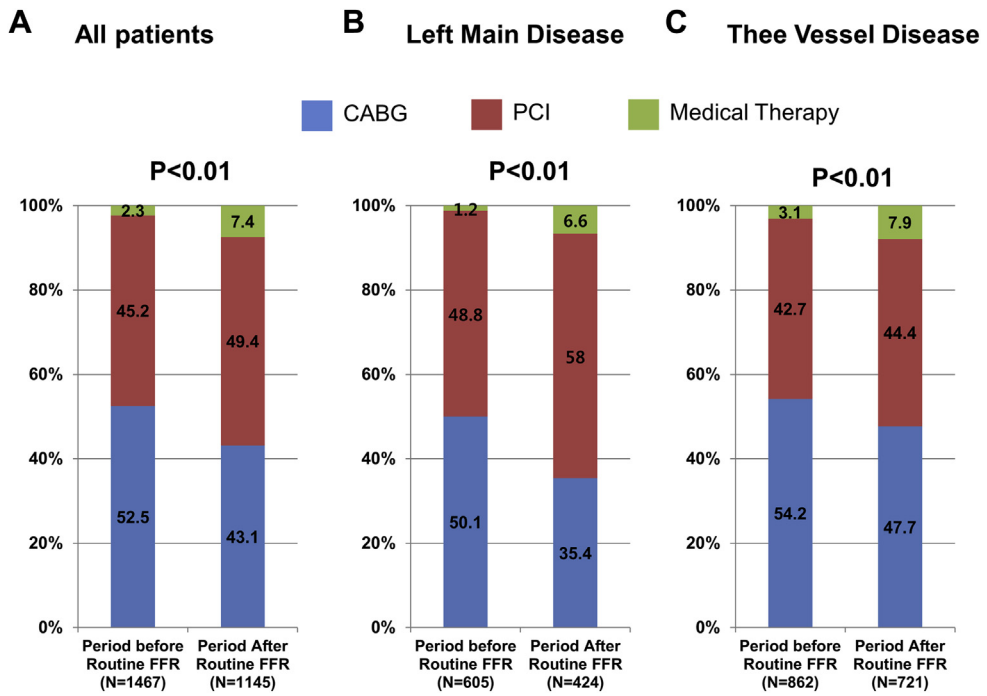

Figure 2. Changes in treatment strategy in all patients *(A)*, left main disease *(B)*, and three vessel disease *(C)*.

study, and all patients provided written informed consent for enrollment in our registry.

Since January 2010, clinical protocols of our institute were revised to mandate its use during coronary intervention, and thereby, all operators in our institution routinely use FFR for assessing the functional severity of intermediate coronary stenosis (visual estimated diameter stenosis, 50% to 80%) during coronary intervention without objective evidence of ischemia before PCI.[5] All patients having routine FFR measurement were applied in this manner. Accordingly, data of study patients before routine FFR use (from January 2008 to December 2009) and those after routine FFR use (from January 2010 to December 2011) were obtained. FFR was measured with a coronary pressure wire (St. Jude Medical, Minneapolis, Minnesota) as described previously.[6] PCI was performed in coronary stenosis with FFR <0.75, if PCI was feasible and was deferred in those with FFR >0.80. For FFR values between 0.75 and 0.80, revascularization was performed at the operator's discretion. The choice between PCI and CABG was at the

Table 1
Baseline characteristics in the crude population

Variables	Before Routine FFR (Year 2008-2009)			P-value*	After Routine FFR (Year 2010−2011)			P-value*
	CABG (N = 770)	PCI (N = 663)	Medical Therapy (N = 34)		CABG (N = 494)	PCI (N = 566)	Medical Therapy (N = 85)	
Age (years)	63.8 ± 9.4	64.0 ± 10.1	64.3 ± 9.9	0.88	63.9 ± 9.2	63.7 ± 10.0	63.9 ± 9.8	0.95
Men	570 (74.0%)	487 (73.5%)	28 (82.4%)	0.51	387 (78.3%)	435 (76.9%)	57 (67.1%)	0.08
Height (cm)	162.8 ± 8.2	163.1 ± 8.5	165.2 ± 7.8	0.23	162.9 ± 8.4	163.3 ± 8.1	162.1 ± 8.6	0.39
Weight (kg)	65.7 ± 10.0	66.2 ± 10.4	68.6 ± 9.6	0.20	65.1 ± 10.0	66.8 ± 10.1	67.4 ± 12.4	0.012†
Hypertension	480 (62.3%)	425 (64.1%)	21 (61.8%)	0.78	226 (45.7%)	369 (65.2%)	59 (69.4%)	<0.001†
Diabetes mellitus	323 (41.9%)	239 (36.0%)	15 (44.1%)	0.06†	173 (35.0%)	226 (39.9%)	29 (34.1%)	0.21
Current smoker	199 (25.8%)	192 (29.0%)	9 (26.5%)	0.42	125 (25.3%)	158 (27.9%)	20 (23.5%)	0.51
Hyperlipidaemia	370 (48.1%)	365 (55.1%)	15 (44.1%)	0.02†	320 (64.8%)	375 (66.3%)	52 (61.2%)	0.63
Previous myocardial infarction	44 (5.7%)	35 (5.3%)	4 (11.8%)	0.28	47 (9.5%)	36 (6.4%)	6 (7.1%)	0.16
Previous coronary intervention	109 (14.2%)	115 (17.3%)	15 (44.1%)	<0.001	83 (16.8%)	90 (15.9%)	19 (22.4%)	0.33
Previous congestive heart failure	10 (1.3%)	10 (1.5%)	0	0.74	20 (4.0%)	4 (0.7%)	4 (4.7%)	0.001†
Previous stroke	81 (10.5%)	48 (7.2%)	3 (8.8%)	0.10†	54 (10.9%)	52 (9.2%)	7 (8.2%)	0.56
Peripheral vascular disease	17 (2.2%)	13 (2.0%)	3 (8.8%)	0.031	43 (8.7%)	11 (1.9%)	3 (3.5%)	<0.001†
Chronic renal failure	46 (6.0%)	26 (3.9%)	1 (2.9%)	0.18	33 (6.7%)	27 (4.8%)	8 (9.4%)	0.16
Chronic lung disease	20 (2.6%)	14 (2.1%)	1 (2.9%)	0.82	8 (1.6%)	10 (1.8%)	1 (1.2%)	0.92
Left ventricular ejection fraction (%)	56.6 ± 10.7	58.2 ± 8.7	56.6 ± 9.9	0.01†	55.8 ± 10.3	58.6 ± 8.1	59.7 ± 7.9	<0.001†
Clinical presentation				<0.001†				0.001†
Stable angina pectoris	513 (66.6%)	422 (63.7%)	27 (79.4%)		365 (73.9%)	355 (62.7%)	59 (69.4%)	
Unstable angina pectoris	220 (28.6%)	173 (26.1%)	3 (8.8%)		96 (19.4%)	160 (28.3%)	24 (28.2%)	
Acute myocardial infarction	37 (4.8%)	68 (10.3%)	4 (11.8%)		33 (6.7%)	51 (9.0%)	2 (2.4%)	
SYNTAX score	22.5 ± 14.8	19.9 ± 8.9	NA	<0.001†	27.5 ± 13.3	22.1 ± 9.2	18.4 ± 9.0	<0.001†
No. of coronary arteries narrowed:				0.007				<0.001†
3	467 (60.6%)	368 (55.5%)	27 (79.4%)		344 (69.6%)	320 (56.5%)	57 (67.1%)	
Left main disease	303 (39.4%)	295 (44.5%)	7 (20.6%)		150 (30.4%)	246 (43.5%)	28 (32.9%)	
Coronary artery narrowed:								
Left anterior descending	749 (97.3%)	615 (92.8%)	33 (97.1%)	<0.001†	487 (98.6%)	524 (92.6%)	73 (85.9%)	<0.001†
Left circumflex	728 (94.5%)	535 (80.7%)	32 (94.1%)	<0.001†	485 (98.2%)	458 (80.9%)	69 (81.2%)	<0.001†
Right	709 (92.1%)	498 (75.1%)	32 (94.1%)	<0.001	471 (95.3%)	425 (75.1%)	66 (77.6%)	<0.001†
Fractional flow reserve	1 (0.1%) ‡	13 (2.0%)	1 (2.9%)	<0.001†	8 (1.6%)	237 (41.9%)	63 (74.1%)	<0.001†
Thallium or treadmill test	202 (26.2%)	185 (27.9%)	19 (55.9%)	0.001	223 (45.1%)	253 (44.7%)	68 (17%)	<0.001

N (%) or Mean ± SD.

CABG = coronary artery bypass graft surgery; FFR = fractional flow reserve; NA = not available; PCI = percutaneous coronary intervention; SYNTAX = The Synergy Between PCI with Taxus and Cardiac Surgery.

* P values were derived from 3 group-comparison using ANOVA test for continuous variables and chi square test for categorical variables, as appropriate.

† $P < 0.05$ for CABG versus PCI.

‡ Number (Percentage) of patients received FFR evaluation.

physician's discretion, primarily based on the angiography results. Patients whose revascularizations were intentionally deferred by attending physicians based on the angiographic or invasive/noninvasive functional studies were included in the medical treatment group. Stent implantation was performed according to the standard guidelines and techniques.[7] During the study period, DES was the default stent for patients with coronary artery stenosis. Each PCI patient received a loading dose of 200 mg aspirin and 300 mg clopidogrel before the procedure. After DES implantation, standard dual antiplatelet therapy consisting of 100 mg/day aspirin and 75 mg/day clopidogrel was recommended for at least 6 months, and patients at high risk of ischemic complications were administered clopidogrel for a longer period. CABG was performed using standard bypass techniques.[8]

The primary outcome of interest was the composite of all-cause death, MI, stroke, and any repeat revascularization (Major adverse cardiovascular and cerebral event [MACCE]). The principal secondary end points were the composite of death, MI, and stroke and individual components of these composite endpoints. Deaths were considered cardiac unless an unequivocal, noncardiac cause was established. MI was defined as an increase in the creatine kinase MB concentration to >5 times the upper limit of the normal range and any of the following: (1) new pathologic Q waves or new bundle branch block, (2) angiographically documented new graft or new native coronary occlusion, or (3) new loss of viable myocardium or new regional wall motion abnormalities, if occurring within 48 hours after the procedure or any increase in creatine kinase MB concentration to greater than the upper limit of the normal range plus ischemic symptoms or signs, if occurring >48 hours after the procedure.[9] Repeat revascularization included target vessel revascularization, regardless of whether the procedure was clinically or angiographically driven and nontarget vessel revascularization. Stroke, as indicated by neurologic deficits, was established by a neurologist on the basis of imaging studies. All outcomes of interest were carefully verified and adjudicated by independent clinicians.

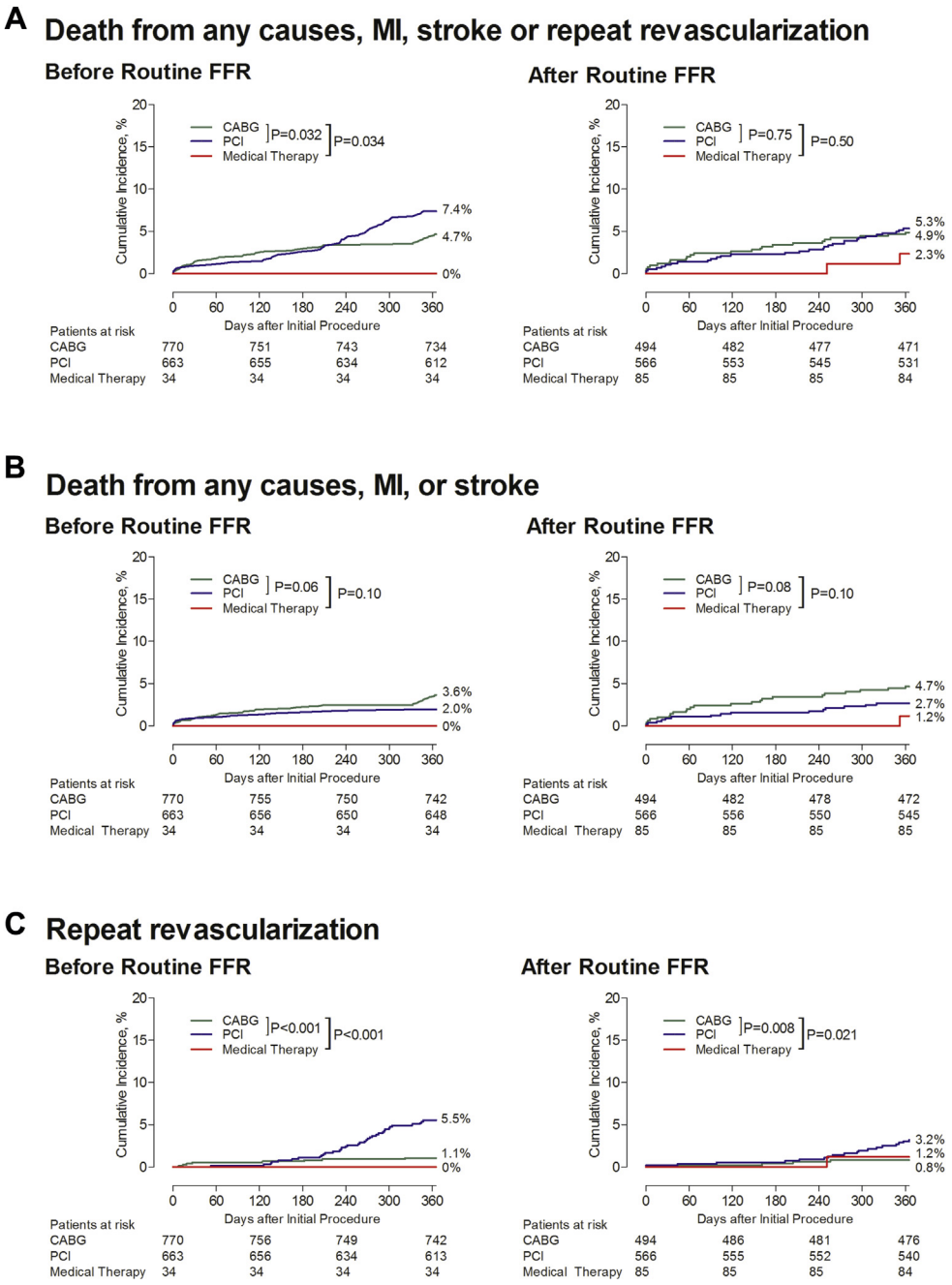

Figure 3. Kaplan-Meier curve for the composite of death, myocardial infarction, or repeat revascularization *(A)*, the composite of death, myocardial infarction, or stroke *(B)*, and repeat revascularization *(C)* in the CABG and PCI groups before and after routine use of FFR in the crude population.

All analyses were performed using R software, version 2.15.2 (R Foundation for Statistical Computing, Vienna, Austria) and SPSS software, version 19.0 (IBM Corp., Armonk, New York) by an independent statistician (S-BH). All reported p values are 2 sided, and p values <0.05 were considered statistically significant. All continuous variables are expressed as mean $\pm$ SD, and categorical variables are expressed as a number (percentage). Continuous variables were compared using the *t* test, the Mann-Whitney *U* test, or analysis of variance test (among 3 group comparisons), and categorical variables were compared using the chi-square or Fisher's exact test, as appropriate. To reduce the effect of selection bias and potential confounding, we used the propensity score (PS) matching method to adjust for baseline characteristics of patients. PS was estimated nonparametrically using variables that are known to be related to both group assignments and outcome variables. 1:1 PS matching was performed by a nearest neighbor matching without replacement. The considered caliper size was 0.1. Pairs on the PS logit were matched within a range of 0.1 SDs of logit-transformed PS. The PS logit distributions for each cohort showed sufficient overlaps with caliber size 0.1. The

Table 2
Clinical outcomes in the crude population at 1 year

Variables	Before Routine FFR (Year 2008−2009)			P-value	After Routine FFR (Year 2010−2011)			P-value
	CABG (N = 770)	PCI (N = 663)	Medical Therapy (N = 34)		CABG (N = 494)	PCI (N = 566)	Medical Therapy (N = 85)	
MACCE*	36 (4.7%)	49 (7.4%)†	0	0.034	24 (4.9%)	30 (5.3%)	2 (2.4%)	0.50
Death	21 (2.7%)	13 (2.0%)	0	0.42	16 (3.2%)	13 (2.3%)	1 (1.2%)	0.43
Cardiac death	11 (1.4%)	7 (1.1%)	0	0.66	11 (2.2%)	10 (1.8%)	0	0.37
Noncardiac death	10 (1.3%)	5 (0.8%)	0	0.50	5 (1.0%)	3 (0.5%)	1 (1.2%)	0.61
Myocardial infarction	3 (0.4%)	0	0	0.26	2 (0.4%)	2 (0.4%)	0	0.84
Stroke	5 (0.6%)	1 (0.2%)	0	0.31	5 (1.0%)	1 (0.2%)	0	0.13
Repeat revascularization	8 (1.0%)	36 (5.5%)†	0	<0.001	4 (0.8%)	18 (3.2%)†	1 (1.2%)	0.021
Target vessel	8 (1.0%)	29 (4.4%)	-	<0.001	4 (0.8%)	13 (2.3%)	-	0.06
Target lesion	8 (1.0%)	27 (4.1%)	-	<0.001	4 (0.8%)	8 (1.4%)	-	0.36
New lesion	4 (0.5%)	9 (1.4%)	-	0.10	1 (0.2%)	11 (1.9%)	-	0.008
The composite of death, MI, or stroke	28 (3.6%)	13 (2.0%)	0	0.10	23 (4.7%)	15 (2.7%)	1 (1.2%)	0.10

CABG = coronary artery bypass graft surgery; FFR = fractional flow reserve; MI = myocardial infarction; PCI = percutaneous coronary intervention.
* The composite of death, MI, stroke, or repeat revascularization.
† $P < 0.05$ for CABG versus PCI.

balance difference of covariates was measured by their standardized differences in means. For the matched pair comparison, the Wilcoxon signed-rank test for continuous variables and the McNemar's test for categorical variables were used. The Cox proportional hazards regression model with robust SEs that accounts for the clustering of the pairs was used to compare the clinical outcomes between the 2 groups. The proportional hazards assumption was confirmed by examination of log (−log [survival]) curves and by testing of partial (Schoenfeld) residuals. When the proportional hazards assumption is violated, we fitted an Aalen's additive hazard model.[10] In the additive hazard model, the results were consistent with primary analysis. R packages of timereg[11] and MatchIt[12] were used to fit the additive hazard model and to construct matched cohort and for balance checking.

Results

We enrolled 2,612 patients, including 1,264 who underwent CABG, 1,229 who underwent PCI, and 119 in whom revascularization was not performed. In addition, we obtained data before (1,467 patients) and after routine (1,145 patients) FFR use (Figure 1). Treatment strategies are shown in Figure 2. After routine FFR use, the proportion of patients receiving CABG decreased, whereas that of patients receiving PCI and in whom revascularization was deferred increased. Similarly, this trend was observed in the subgroup of LMCA disease or 3-vessel disease.

Patient characteristics are listed in Table 1. Before routine FFR use, a higher number of patients in the CABG group had diabetes, peripheral vascular disease, and history of stroke; less hyperlipidemia and MI presentation; and lower ejection fraction than that after routine FFR use. After routine FFR use, a higher number of patients in the CABG group had history of congestive heart failure and peripheral vascular disease; less hypertension; and lower weight and ejection fraction. After routine FFR use, more patients had hyperlipidemia, previous MI, previous congestive heart failure, peripheral vascular disease, and less hypertension than before routine FFR use (Supplementary Table 1).

After PS matching, there were 488 and 314 matched pairs of patients between the CABG and PCI groups, before and after routine FFR use, respectively, and 915 matched pairs of patients before and after routine FFR use, with no significant differences between groups for any of the covariates (Supplementary Tables 2 and 3). Revascularization was not performed in a total of 119 patients, the reasons for which are listed in Supplementary Table 4. Procedural characteristics are shown in Figure 1 and listed in Supplementary Table 5. Supplementary Figure 1 showed the summary of FFR-measured patients (lesions) and outcomes. FFR was measured in 323 patients and 450 lesions (15 before the routine FFR measurement and 308 after the routine FFR measurement). Of them, 64 patients were deferred without any revascularizations after FFR measurement. At 1 year, only 1 repeated revascularization occurred in deferred patients. Of the 259 patients (358 lesions) who received any revascularization after FFR measurement, 158 lesions were deferred and 191 lesions were revascularized (CABG was performed in 9 patients). At 1 year, 3 deaths (1 cardiac and 2 noncardiac death) occurred and repeated revascularizations occurred in 10 patients (12 lesions), of which only 3 repeated revascularizations were associated with deferred lesion after FFR measurement. Supplementary Table 6 demonstrated reasons for FFR not measured from 2010 to 2011. Tight stenosis (visual estimated diameter stenosis >80%) or total occlusion was the most frequent cause. After routine use of FFR, ~92% were second-generation DES, and few and short stents were placed in each patient. In the CABG group, more conduits were used, and off-pump CABG was more frequently performed.

Complete 1-year follow-up data were obtained for 2,605 patients (99.7%). At 1-year follow-up, 64 patients (2.5%) died, of which 24 (0.9%) were cardiovascular-related deaths. Seven patients (0.3%) had an MI and 68 (2.6%) had a repeat revascularization.

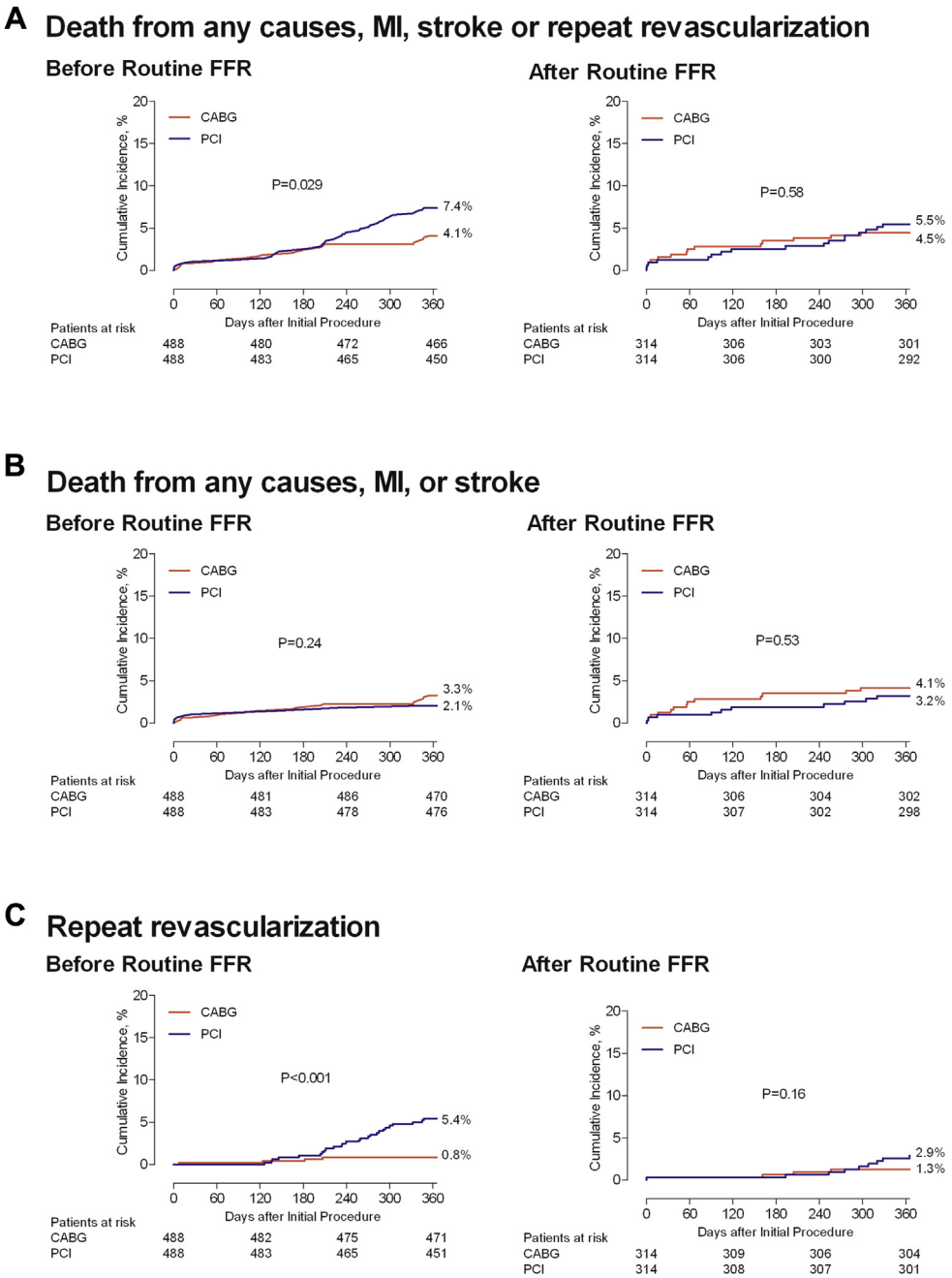

Figure 4. Kaplan-Meier curve for the composite of death, myocardial infarction, or repeat revascularization *(A)*, the composite of death, myocardial infarction, or stroke *(B)*, and repeat revascularization *(C)* in the CABG and PCI groups before and after routine use of FFR in the PS-matched population.

Regarding clinical outcomes, unadjusted event rates are shown in Figure 3 and listed in Table 2. Before routine FFR use, the rate of MACCE at 1 year was significantly higher in the PCI group, mainly because of the high rate of repeat revascularization. The composite of death, MI, and stroke was not significantly different between groups. However, there was no significant difference in the rates of MACCE and the composite of death, MI, and stroke at 1 year before and after routine FFR use. The repeat revascularization rate was still significantly higher in the PCI group, although it was reduced. The 1-year event rate in the medical therapy group was only 0% and 1.2% before and after the routine FFR use, respectively. Figure 4 and Table 3 summarizes the rates of clinical outcomes in the PS-matched population. The risks of MACCE and repeat revascularization were significantly higher in the PCI group before routine FFR use but did not differ significantly 1 year after the routine FFR use. The risk of composite of death, MI, or stroke was not significantly different between the PCI and CABG groups before and after FFR.

Subgroup analysis was performed. Supplementary Figure 2 showed the left main coronary disease and

Table 3
Hazard ratio for clinical outcomes after percutaneous coronary intervention compared with that after coronary artery bypass surgery in the propensity-score matched population

	Before Routine FFR (Year 2008–2009) N=976 (PCI: 488, CABG: 488)		After Routine FFR (Year 2010–2011) N=628 (PCI: 314, CABG: 314)		P-value
	Hazard Ratio (95% CI)*	P-value	Hazard Ratio (95% CI)		
MACCE†	1.82 (1.09–3.03)	0.021	1.22 (0.59–2.52)		0.59
Death	0.84 (0.41–1.72)	0.63	1.00 (0.37–2.69)		>0.99
The composite of death, MI, or stroke	0.62 (0.31–1.26)	0.19	0.77 (0.33–1.78)		0.54
Repeat revascularization	6.62 (2.28–19.2)	<0.001	2.25 (0.694–8.12)		0.18

CI = confidence interval; FFR = fractional flow reserve; MI = myocardial infarction.
* Hazard ratios are for PCI as compared with CABG group.
† The composite of death, MI, stroke, or repeat revascularization.

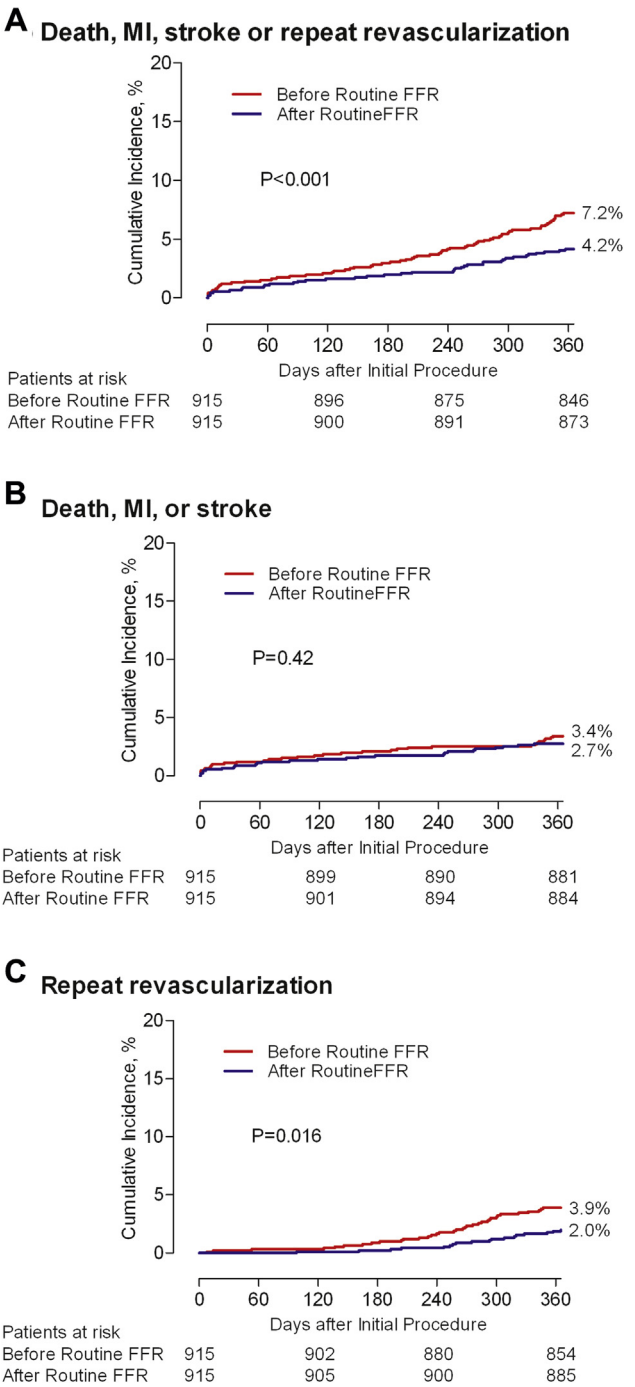

Figure 5. Kaplan-Meier curve for the composite of death, myocardial infarction, or repeat revascularization *(A)*, the composite of death, myocardial infarction, or stroke *(B)*, and repeat revascularization *(C)* before and after routine use of FFR in the PS-matched population.

3-vessel subgroup showed similar trends. In addition, Supplementary Table 7 demonstrated that PCI with FFR showed comparable clinical outcomes with CABG regarding the adjusted risk of MACCE at 1 year. However, PCI without FFR showed the trends of worse clinical outcomes.

Regarding clinical outcome comparison before versus after routine FFR use, Supplementary Figure 3 shows the

Table 4
Incidence and hazard ratio for clinical outcomes before and after the routine use of fractional flow reserve in the propensity-matched cohorts

	Before Routine FFR (Year 2008−2009) N = 915	After Routine FFR (Year 2010−2011) N = 915	HR (95% CI)*	P-value
MACCE†	66 (7.2)	38 (4.2)	0.57 (0.38−0.85)	0.005
Death	21 (2.3)	23 (2.5)	0.68 (0.36−1.26)	0.22
The composite of death, MI, or stroke	31 (3.4)	25 (2.7)	0.80 (0.47−1.37)	0.43
Repeat revascularization	35 (3.8)	18 (2.0)	0.50 (0.28−0.89)	0.019

CI = confidence interval; FFR = fractional flow reserve; HR = hazard ratio; MI = myocardial infarction.
* Hazard ratios are before routine FFR use compared with that after.
† The composite of death, MI, stroke, or repeat revascularization.

unadjusted rates of clinical outcomes. The rates of MACCE at 1 year, death from any cause or MI, and repeat revascularization were not significantly different before and after the routine FFR use. However, of the 915 propensity score-matched pairs, the risks of MACCE and repeat revascularization were significantly lower after the routine FFR use than that before (Figure 5 and Table 4). During the study period, the risk of death and the composite of death, MI, or stroke were not changed.

Discussion

In this study, we found that (1) the routine incorporation of FFR in real practice extended the role of PCI as a primary revascularization strategy, (2) FFR-guided PCI using second-generation DES showed similar clinical outcomes with concurrent CABG at 1 year, (3) patients in whom revascularization was deferred showed excellent clinical outcomes, and (4) overall MACCE rate decreased after implementing FFR guidance as a routine strategy in patients with severe coronary artery disease, primarily driven by the reduced repeat revascularization rates after PCI, with comparable safety, as reflected by the risk of death, MI, or stroke.

Two recently published, large, randomized trials demonstrated the superiority of CABG over PCI in the treatment of patients with the severe coronary artery disease. The Synergy Between PCI With Taxus and Cardiac Surgery (SYNTAX) trial showed a significantly higher rate of the composite of death, MI, stroke, and repeat revascularization in the PCI group in the 5-year follow-up. Although the difference was largely driven by repeat revascularization and the rates of cardiac death or MI were also significantly higher in the PCI group.[1] Another randomized trial, Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM), added further support to the findings of the SYNTAX trial. The FREEDOM trial randomized 1,900 diabetic patients to PCI or CABG and showed a significantly higher rate of the composite of death, MI, or stroke in the PCI group at the 5-year follow-up.[2] However, these trials were limited by factors that both trials used first-generation DES as the default stent and they used angiographic evaluation in the revascularization decision.

From 2010 to 2011, we exclusively used second-generation DES, and FFR was routinely incorporated in daily practice. In this cohort, the clinical outcomes with PCI improved compared with that before routine FFR measurement, and 1-year event rates of MACCE were similar between patients receiving PCI or CABG. This improvement in the PCI group may be primarily because of routine FFR measurement, which led to judicious PCI, whereby ischemia-producing lesions are revascularized and nonischemia-producing ones are treated medically. In addition, improved efficacy and safety profiles of second-generation DES are another important contributing factor. However, our findings should be confirmed or reputed in large ongoing randomized trials such as Evaluation of Everolimus-Eluting Stent System Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) study and Fractional Flow Reserve Versus Angiography for Multivessel Evaluation (FAME) 3 study.

As anticipated, we also observed significant changes in treatment strategies during the study period, with an increasing proportion of patients receiving PCI and deferral of revascularization and deceasing proportion of CABG. This could be because of a shift in the cardiovascular clinical practice pattern from CABG toward PCI in recent years.[13] However, we believe that the introduction of FFR would, at least, further accelerate such changes because FFR frequently reduced the complexity of angiographically diagnosed coronary artery disease in patients with multivessel or LMCA disease.[14,15] The angiography subanalysis of the FAME trial demonstrated that of the patients with angiographic triple-vessel disease, only 14% had functional triple-vessel disease, whereas 9% had no functionally significant stenosis. In our retrospective registry, similar proportion of patients (85 of 1,060 patients [8.0%]) received medical treatment only after routine use of FFR.

We also found that deferral of revascularization was safe for even patients with angiographically confirmed severe coronary artery disease, albeit with a few patients. Particularly, of the 67 patients in whom revascularization was deferred after FFR measurement, no cardiac death or MI occurred at the 1-year follow-up.

The present study had several limitations. First, despite appropriate statistical adjustments, unknown confounders may have affected the results. Second, the follow-up duration was limited to 1 year, which may be a disadvantage in CABG, because the benefits of CABG over PCI have not been fully evident within a 1-year period.[16] Third, FFR was

only used in ~42% of cases although it was mandated, which could have diluted the effect of routine FFR measurement. However, in daily practice, FFR measurement in all lesions is neither feasible nor necessary.

Disclosures

The authors have no conflicts of interest to disclose.

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.amjcard.2015.07.028.

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