



Original article

Treatment strategy modification and its implication on the medical cost of fractional flow reserve-guided percutaneous coronary intervention in Japan



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ABSTRACT

Background: Fractional flow reserve (FFR)-guided percutaneous coronary intervention (PCI) could improve outcome compared with angiography-guided PCI. However, the economic impact of FFR-guided PCI remains largely unknown in the medical system in Japan. We evaluated the impact of treatment strategy modification by FFR measurement on the direct medical cost using a model analysis with a decision tree model in Japan.

Methods: For the clinical parameters set in the model, the findings from CVIT-DEFER registry were adopted. Cost parameters were considered on the assumption that coronary angiography, FFR measurement, and the treatment are performed at Diagnosis Procedure combination (DPC) hospitals, and the costs were calculated based on the medical fee reimbursement systems in Japan.

Results: The probability of deferral of PCI in patients who were allocated to PCI based on coronary angiography was set as 90.1% based on the CVIT-DEFER registry. In the model analysis, the cost of tests was increased by 185,660 JPY per patient by the addition of FFR measurement, but the cost of treatment with PCI was reduced by 561,425 JPY per patient, and the entire cost of treatment was reduced by 322,675 JPY, resulting in the expected reduction in the total expected medical cost by 137,015 JPY per patient.

Conclusion: Under contemporary Japanese practice, FFR-guided PCI has potential to reduce the medical cost by effective reassessment of coronary stenosis and reducing inappropriate application of PCI.

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Introduction

The optimal treatment strategy for patients with stable coronary artery disease (SCAD) largely depends on the severity assessment of the stenosis, particularly when deciding whether medical therapy (MT) alone or percutaneous coronary intervention (PCI) plus MT is

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appropriate. However, as coronary angiography evaluates lesions based on projection images, the assessment of functional severity of stenosis is difficult in many cases. In addition, ischemia evaluation has been the cornerstone in dictating indication of the revascularization procedures, but its real-world application has been a major challenge. Inohara et al. reported that results of an evaluation for the appropriateness of PCI in 10,050 PCI cases (SCAD: 4950) registered in the Japan Cardiovascular Database between September 2008 and March 2013 and PCI for SCAD was judged as inappropriate in approximately 30% of cases [1].

Fractional flow reserve (FFR) is now widely used as an index for the functional severity of coronary stenosis [2]. The FAME and FAME2 study demonstrated that the clinical outcome improved and the medical cost was reduced in the FFR-guided group compared with angiography-guided group [3–6]. Based on these findings, FFR measurements before PCI have been recommended as class 1A for SCAD patients in the European guidelines [7]. Since FFR measurement is capable of correcting visual assessment by coronary angiography and reducing inappropriate PCI without disadvantage, reduction in the medical cost related to PCI is expected with its application but measurement rate of FFR is still lower in Japan (8.2% of total amount of coronary angiography) [8]. Herein, we aimed to clarify the economic impact of FFR measurement, including the material cost of the pressure measurement wire, through a model analysis with a decision tree model.

In Japan, FFR measurement has been covered by the national insurance system and became available for daily medical practice since the revision of the medical fee reimbursement system in 2012. In addition, CVIT-DEFER Registry study led by the Japanese Association of Cardiovascular Intervention and Therapeutics (CVIT) has evaluated the actual usage and long-term outcomes of FFR measurement in Japan.

Methods

Analysis overview

Using a decision tree model, the impact of FFR measurement on the medical cost was evaluated by comparing the expected medical costs for patients with SCAD diagnosed by coronary angiography alone (angiography-guided group) with those for patients with FFR measurement (FFR-guided group). For the treatment strategy for SCAD patients, coronary artery bypass graft (CABG), PCI, or medical treatment was applied. The decision tree of the FFR-guided group was prepared based on the findings from the CVIT-DEFER registry study [9–11]. The analysis was conducted from the health care payer's perspective and only direct medical costs were considered in the analysis.

Database

The CVIT-DEFER Registry study was a prospective observational study that enrolled 3228 patients with FFR measurement registered from 168 institutions between December 2012 and September 2013 [9]. The mean age of the patients in the study was 69.5 years and 73.8% were male. Approximately half of the patients had a history of PCI and the majority had stable coronary artery disease, including 63.2% with stable angina pectoris. The FFR measurement of many branches was carried out in 17.8% of cases. This study reported that discrepancy between assessment results of significant stenosis based on coronary angiography and FFR was not rare in Japan, and there was a high frequency of overestimation by coronary angiography in the right coronary artery (RCA) and left circumflex artery (LCX), as well as high frequency of underestimation in the left anterior descending (LAD) [9,10]. The tendency of deferred PCI in cases with an FFR value >0.80 was reproduced with

each treatment strategy based on coronary angiography alone in consideration of the proportion of patients with an FFR value >0.80 and ≤ 0.80 (Fig. 1).

Clinical parameters

For the clinical parameters of this analysis, the results from the CVIT-DEFER registry study were utilized [10]; on analysis of the treatment strategy, 80 (2.2%), 2374 (64.0%), and 1255 (33.8%) of the 3228 patients were allocated to CABG, PCI, and MT, respectively, based on coronary angiography alone, and the percentages of patients with FFR > 0.80 were 25.0, 53.4, and 68.1%, respectively. PCI was deferred and switched to MT in 1143 (90.1%) of the patients with FFR > 0.80 who were allocated to PCI based on coronary angiography alone ($2374 \times 53.4\% = 1268$). The percentages of patients with the other patterns after treatment strategy modification were also set based on the CVIT-DEFER registry study results as shown in Fig. 1.

The probability of revascularization within one year after deferral of PCI considered in the scenario analysis was set at 3.1% based on the one-year follow-up data from the CVIT-DEFER registry study [9]: The incidence of myocardial infarction or target vessel revascularization (TVR) within one year was 3.1% in patients in whom PCI was deferred because the FFR value was >0.80 and 4.8% in patients in whom PCI was performed as scheduled, demonstrating the absence of a major difference.

Cost parameters

The costs for coronary angiography and FFR measurement used in the analysis were calculated from the medical fee reimbursement system in Japan. The cost of coronary angiography was set at 54,000 JPY by adding 14,000 JPY for coronary angiography to the cost of "tests using the cardiac catheter method in diagnostic angiography (D206)", which is 40,000 JPY. The cost of FFR measurement was set at 185,660 JPY by summing 6000 JPY for the medical fee of FFR measurement with the increase with change to the DPC category, 179,660 JPY. As the costs other than those for coronary angiography and FFR measurement were assumed to be the same in both groups, they were not taken into consideration.

For the costs of CABG, PCI, and MT, an analysis of the medical costs for the patients extracted from the claims database provided by Medical Data Vision Co., Ltd. (Tokyo, Japan, EBM Provider[®]) were conducted, and the results were used in the model analysis. The EBM Provider[®] is a claims database in which 300 DPC hospitals in Japan were registered as of May 2017, and data of approximately 19 million patients after April 2008 are available. The patient inclusion criteria for the analysis to estimate the expected costs of CABG, PCI, and MT were as follows: (1) A record with the standard disease name similar with 'SCAD' is retained and (2) coronary angiography (D206) was performed in the month in which the above diagnosis was made. The exclusion criteria were as follows: (1) Of patients meeting the above inclusion criteria, those with the possibility that coronary angiography was performed to evaluate the acute phase, or (2) coronary angiography subjected to the inclusion criteria and CABG or PCI were performed within the same hospitalization period. The expected medical costs for cases treated with CABG and PCI were defined as follows: The total cost of 3 months from the coronary angiography-applied date for patients treated with CABG or PCI within 2 months after the earliest coronary angiography subjected to the inclusion criteria in the EBM Provider[®] (excluding costs related with the coronary angiography subjected to the inclusion criteria). When both CABG and PCI were performed within the same hospitalization period, the patient was considered as a CABG case. The expected medical cost of MT was defined as the total cost for 3 months from the

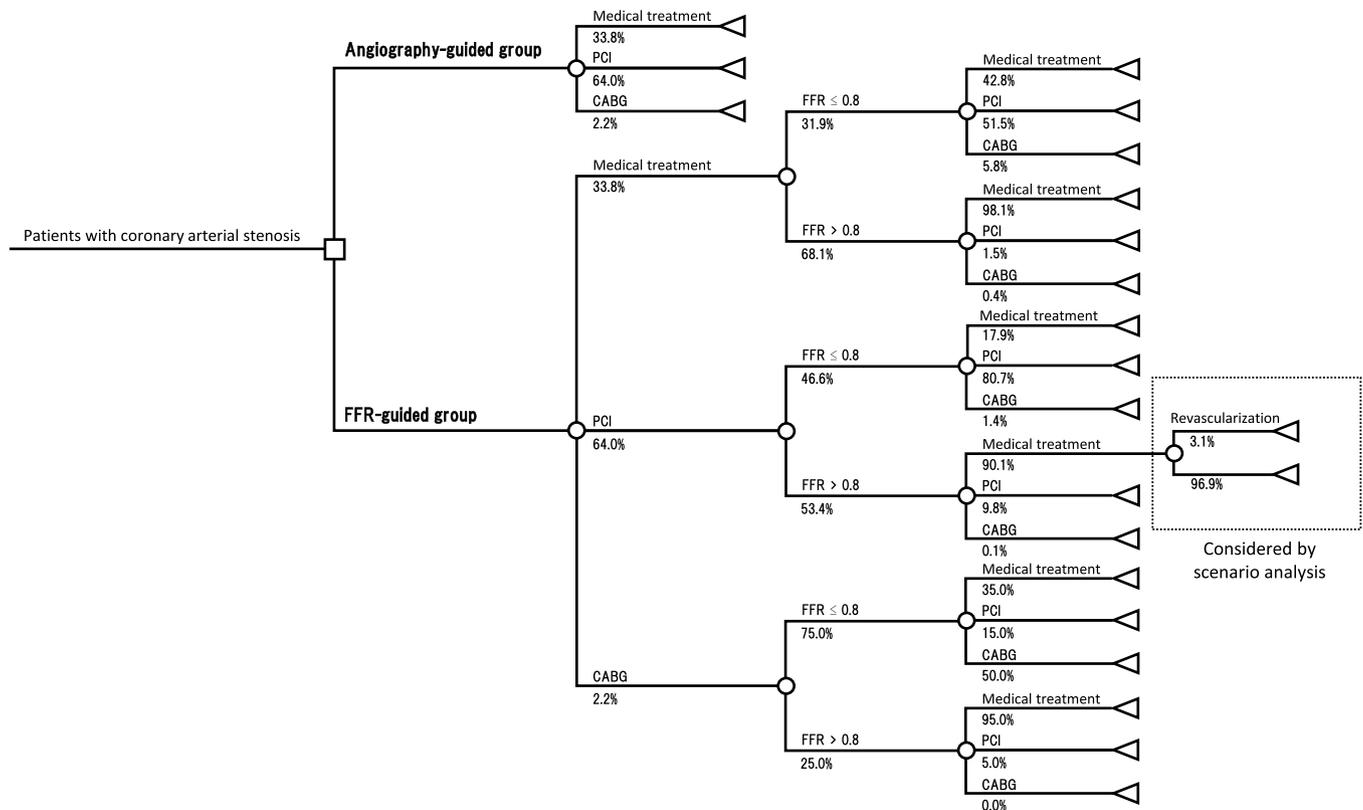


Fig. 1. Decision tree model structure. The impact of FFR measurement on the medical cost was evaluated by comparing the expected medical costs for patients with SCAD diagnosed by coronary angiography alone (angiography-guided group) with those for patients with FFR measurement (FFR-guided group) using a decision tree model. For the treatment strategy for SCAD patients, CABG, PCI, or medical treatment was applied. The decision tree of the FFR-guided group was prepared based on the findings from the CVIT-DEFER registry study. The tendency of deferred PCI in cases with an FFR value >0.80 was reproduced with each treatment strategy based on coronary angiography alone in consideration of the proportion of patients with an FFR value >0.80 and ≤ 0.80 . CABG, coronary artery bypass graft; FFR, fractional flow reserve; PCI, percutaneous coronary intervention; SCAD, stable coronary artery disease.

coronary angiography-applied date in patients who did not meet either of the CABG and PCI cases (excluding costs related with the target coronary angiography subjected to the inclusion criteria).

Results

Claims database analysis for treatment costs estimation

Of 172,589 patients extracted from the EBM Provider who were examined by coronary angiography and met the inclusion criteria, 75,413 patients who did not meet the exclusion criteria and could be followed for 3 months from the first coronary angiography-applied date were included in this analysis. Of the 75,413 patients included in analysis, 1106 (1.5%), 11,412 (15.1%), and 62,895 (83.4%) patients were classified into the CABG, PCI, and MT groups, respectively. The patient backgrounds and results of medical cost analysis in each group are shown in Tables 1 and 2. The proportion of males was 70–75% in all groups and the mean age was 70 years old.

As a result of the medical cost analysis, the mean medical costs during 3 months from the first coronary angiography (excluding costs related with the first coronary angiography and FFR) in the CABG, PCI, and MT groups were 4,535,997, 1,555,464, and 562,079 JPY, respectively.

Analysis for expected medical cost using the decision tree model

Base-case analysis

The expected medical costs for SCAD patients for whom the treatment strategy was decided based on coronary angiography

alone (angiography-guided group) and those for whom FFR measurement result was used (FFR-guided group) were calculated using the decision tree model. The results are shown in Table 3. The cost of tests was increased by 185,660 JPY per patient by the addition of FFR measurement, but the cost of treatment with PCI was reduced by 473,012 JPY per patient, and the entire cost of treatment combining CABG and MT was reduced by 310,266 JPY, resulting in the expected reduction in the total expected medical cost by 124,606 JPY per patient.

In scenario analysis, taking the probability of revascularization within one year after deferral of PCI of 3.1% into consideration, the total expected medical cost of the FFR-guided group increased by 14,848 JPY, and the cost reduction by FFR measurement was 109,758 JPY (Table 4).

Sensitivity analysis

The results of the one-way sensitivity analysis are shown in Fig. 2 (Parameter list for sensitivity analysis are shown in Supplementary Table 1). The base-case analysis result that the total expected medical cost was lower in the FFR-guided group than in the angiography-guided group in all parameters was not reversed, confirming the robustness of the analysis. The most influential parameter in the analysis was the probability of selecting CABG based on coronary angiographic diagnosis alone.

The parameters with a large influence on the results of one-way sensitivity analysis and having a meaning of consideration were subjected to threshold analysis. The results are shown in Fig. 3. Regarding the threshold of the parameters at which cost reduction by FFR measurement is expected, the threshold of 'PCI treatment cost' was 1,145,707 JPY or higher, that of 'the probability

Table 1
Patient background characteristics in the claims data analysis.

Item	CABG group	PCI group	Medical treatment group
N, %	1106	11,412	62,895
Sex			
Male (n, %)	813 (73.51%)	8642 (75.73%)	44,380 (70.56%)
Female (n, %)	293 (26.49%)	2770 (24.27%)	18,515 (29.44%)
Age	70.3 (9.0)	70.4 (10.0)	70.3 (11.0)
History of smoking			
Yes (n, %)	494 (44.67%)	4960 (43.46%)	25,562 (40.64%)
No (n, %)	504 (45.57%)	5064 (44.37%)	29,256 (46.52%)
Unknown (n, %)	108 (9.76%)	1388 (12.16%)	8077 (12.84%)
Concomitant drugs			
Antidiabetic drug (n, %)	863 (78.03%)	3006 (26.34%)	17,559 (27.92%)
Insulin preparation (n, %)	845 (76.40%)	1048 (9.18%)	7953 (12.64%)
Antihypertensive drug (n, %)	1103 (99.73%)	7726 (67.70%)	46,175 (73.42%)
Drug to treat dyslipidemia (n, %)	790 (71.43%)	7188 (62.99%)	33,389 (53.09%)
Antiplatelet drug (n, %)	1072 (96.93%)	10,611 (92.98%)	40,483 (64.37%)
Test			
CT	269 (24.32%)	390 (3.42%)	5153 (8.19%)
Myocardial scintigraphy	52 (4.70%)	277 (2.43%)	1682 (2.67%)
Cardiopulmonary treadmill exercise test	3 (0.27%)	38 (0.33%)	533 (0.85%)
Comorbidities			
Prior PCI (n, %)	25 (2.26%)	894 (7.83%)	10,452 (16.62%)
Prior CABG (n, %)	0 (0.00%)	23 (0.20%)	362 (0.58%)
Past medical history of myocardial infarction (n, %)	104 (9.40%)	1863 (16.32%)	13,805 (21.95%)
Past medical history of stroke (n, %)	96 (8.68%)	1086 (9.52%)	6565 (10.44%)
Hemodialysis (n, %)	156 (14.10%)	900 (7.89%)	3551 (5.65%)
Peripheral arterial disease (n, %)	378 (34.18%)	2867 (25.12%)	17,506 (27.83%)
Stable angina (n, %)	22 (1.99%)	256 (2.24%)	593 (0.94%)
Unstable angina (n, %)	19 (1.72%)	170 (1.49%)	3368 (5.35%)
Asymptomatic myocardial ischemia (n, %)	84 (7.59%)	1524 (13.35%)	3681 (5.85%)
Acute myocardial infarction (n, %)	9 (0.81%)	177 (1.55%)	2918 (4.64%)
Old myocardial infarction (n, %)	237 (21.43%)	2759 (24.18%)	16,101 (25.60%)
Diabetes (n, %)	677 (61.21%)	6491 (56.88%)	33,621 (53.46%)
Hypertension (n, %)	972 (87.88%)	9091 (79.66%)	50,262 (79.91%)
Hyperlipidemia (n, %)	885 (80.02%)	8961 (78.52%)	43,453 (69.09%)

CABG, coronary artery bypass graft; CT, computed tomography; PCI, percutaneous coronary intervention.

of selecting PCI based on the coronary angiographic diagnosis alone' was 51.5% or higher, that of 'the probability of FFR > 0.80 in patients for which PCI was selected based on the coronary angiographic diagnosis alone' was 27.6% or higher, and that of 'the probability of revascularization within one year' was 23.0% or lower.

Discussion

In the present analysis, the impact on the direct medical cost by FFR measurement under the contemporary Japanese reimbursement system was assessed through the decision tree model. Overall, a reduction in the total medical cost by 124,606 JPY may be expected even though the test cost was increased by the addition of FFR measurement. In one-way sensitivity analysis, the result of the base-case analysis: cost-saving by FFR measurement is expected, was not reversed in all parameters, confirming the robustness of this analysis. In addition, the medical cost-reduction by FFR measurement was noted even though the probability of

revascularization within one year after deferral of PCI of 3.1% was taken into consideration.

Previously the FAME study also reported the possibility of medical cost reduction by FFR measurement, in which the amount of contrast medium used, number of stents used, total costs related with the procedures, and duration of hospital stay were significantly lower in the FFR-guided group than in the angiography-guided group [3,4]. The FAME study was not a model analysis, and it analyzed actual healthcare resource utilization during the follow-up period in the study employing a study design different from that in our study, but the medical cost-reduction by FFR measurement confirmed in the FAME study supports our analysis results.

The parameters having a large influence on the results on one-way sensitivity analysis were subjected to threshold analysis. Regarding the thresholds of the parameters at which cost reduction by FFR-based modification of the treatment strategy is expected, the threshold of 'PCI treatment cost' was 1,145,707 JPY or higher, that of 'the probability of selecting PCI based on the coronary angiographic diagnosis alone' was 51.5% or higher, that of 'the probability of FFR > 0.80 in patients for whom PCI was selected based on the coronary angiographic diagnosis alone' was

Table 2
Analysis results of expected treatment cost from the claims data analysis.

	N	Mean (JPY)	SD (JPY)	95% confidence interval (JPY)
CABG				
Total cost	1106	4,535,997	2,005,481	4,417,803–4,654,191
Inpatient cost	1106	4,440,034	–	–
Outpatient cost	1106	95,963	–	–
PCI				
Total cost	11,412	1,555,464	892,421	1,539,090–1,571,838
Inpatient cost	11,412	1,476,088	–	–
Outpatient cost	11,412	79,375	–	–
Medical treatment				
Total cost	62,895	562,079	1,232,352	552,448–571,710
Inpatient cost	62,895	465,398	–	–
Outpatient cost	62,895	96,681	–	–

CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention.

Table 3
Base-case analysis results.

	Angiography-guided group	FFR-guided group	Difference
Test cost			
Angiography	54,000	54,000	0
FFR	0	185,660	185,660
Treatment cost			
CABG	99,792	90,455	–9337
PCI	995,497	522,485	–473,012
Medical treatment	189,983	362,066	172,083
Total medical cost	1,339,272	1,214,666	–124,606

CABG, coronary artery bypass graft; FFR, fractional flow reserve; PCI, percutaneous coronary intervention.

Table 4
Scenario analysis results.

	Angiography-guided group	FFR-guided group	Difference
Test cost			
Angiography	54,000	54,000	0
FFR	0	185,660	185,660
Treatment cost			
CABG	99,792	90,455	-9337
PCI	995,497	522,485	-473,012
Medical treatment	189,983	362,066	172,083
Revascularization cost after deferred PCI	0	14,848	14,848
Total medical cost	1,339,272	1,229,514	-109,758

CABG, coronary artery bypass graft; FFR, fractional flow reserve; PCI, percutaneous coronary intervention.

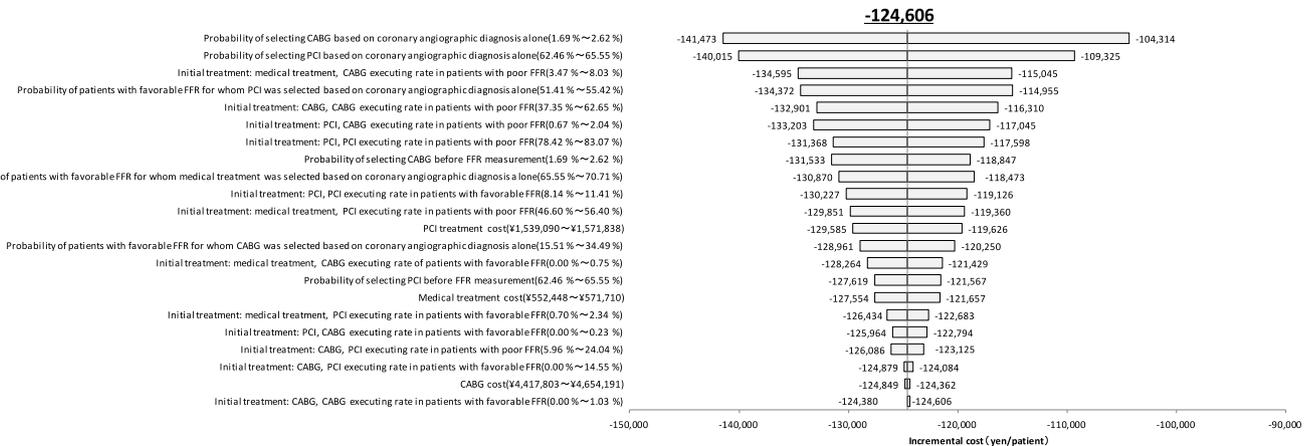


Fig. 2. One-way sensitivity analysis. The base-case analysis result that the total expected medical cost was lower in the FFR-guided group than in the angiography-guided group in all parameters was not reversed, confirming the robustness of the analysis. The most influential parameter in the analysis was the probability of selecting CABG based on coronary angiographic diagnosis alone. CABG, coronary artery bypass graft; FFR, fractional flow reserve; PCI, percutaneous coronary intervention.

27.6% or higher, and that of ‘the probability of revascularization within one year’ was 23.0% or lower.

As the cost of treatment with PCI has decreased yearly, and the difference between the value adopted in the base-case analysis (1,555,464 JPY) and threshold value described above (1,145,707 JPY) is small, the expected medical costs for the FFR-guided and angiography-guided groups may become comparable or reversed in the future, but reduction in invasiveness and burden of PCI by FFR measurement must be clinically significant [12].

Regarding the results of threshold analysis of ‘the probability of selecting PCI based on the coronary angiographic diagnosis alone’ and ‘the probability of FFR > 0.80 in patients for whom PCI was selected based on the coronary angiographic diagnosis alone’, both parameters indicated that the cost-reduction effects by FFR measurement may decrease when the appropriateness of PCI performed or assessment for the severity of stenosis in the target lesion based on coronary angiographic diagnosis is more favorable than that applied in this analysis. However, as the target populations of this analysis were all patients registered in the CVIT-DEFER registry study, cases in which appropriateness of PCI was sufficiently assessed by coronary angiography alone may have been included. From the viewpoint of appropriate use of FFR measurement, if there is a screening enabling identification of a subgroup for which additional FFR measurement is more effective (i.e. a subgroup for which assessment of appropriateness of applying PCI based on coronary angiography alone is difficult), reduction in the medical cost per patient by FFR measurement may increase and exceed the analysis results.

Regarding the disadvantage of deferring PCI based on FFR measurement, an increase in the probability of revascularization over a prolonged period is of concern, but the point estimation of

the probability (3.1%) of revascularization within one year after deferral of PCI and the upper limit (3.9%) of its confidence interval in the CVIT-DEFER registry study were sufficiently lower than the result of the threshold analysis (23.0%). Accordingly, even though the disadvantage of deferring PCI based on FFR measurement is considered, the robustness of the results from this analysis (FFR measurement is expected to reduce medical costs) may be high. Furthermore, to make the analysis conservative for FFR measurement, the probability of revascularization was taken into consideration only for cases in which PCI was deferred based on the FFR measurement result, but the risks leading to revascularization should be present in cases of other patterns at actual clinical sites. Thus, the medical cost reduction by FFR measurement in consideration of the probability of revascularization was underestimated, and the actual reduction may be greater.

FFR measurement is expected to reduce the medical cost by effectively correcting the visual assessment by coronary angiography and reducing inappropriate application of PCI without disadvantage. Approximately 0.23 million PCIs per year are demonstrated in Japan currently [8] and if the concept of FFR guided PCI become widespread, expected total cost reduction in Japan would be 28 billion JPY. There is therefore a significant meaning to recommend the technique in terms of the recent national budget pressure in Japan. However, there may be a patient population for whom coronary angiography alone is sufficient to evaluate treatment strategy for SCAD and if FFR measurement were demonstrated unnecessarily even for mild stenosis, the cost of FFR measurement might increase, and expected total cost reduction by FFR would disappear. Therefore, the future consideration for establishment of appropriate and effective use of FFR measurement will be important in this field.

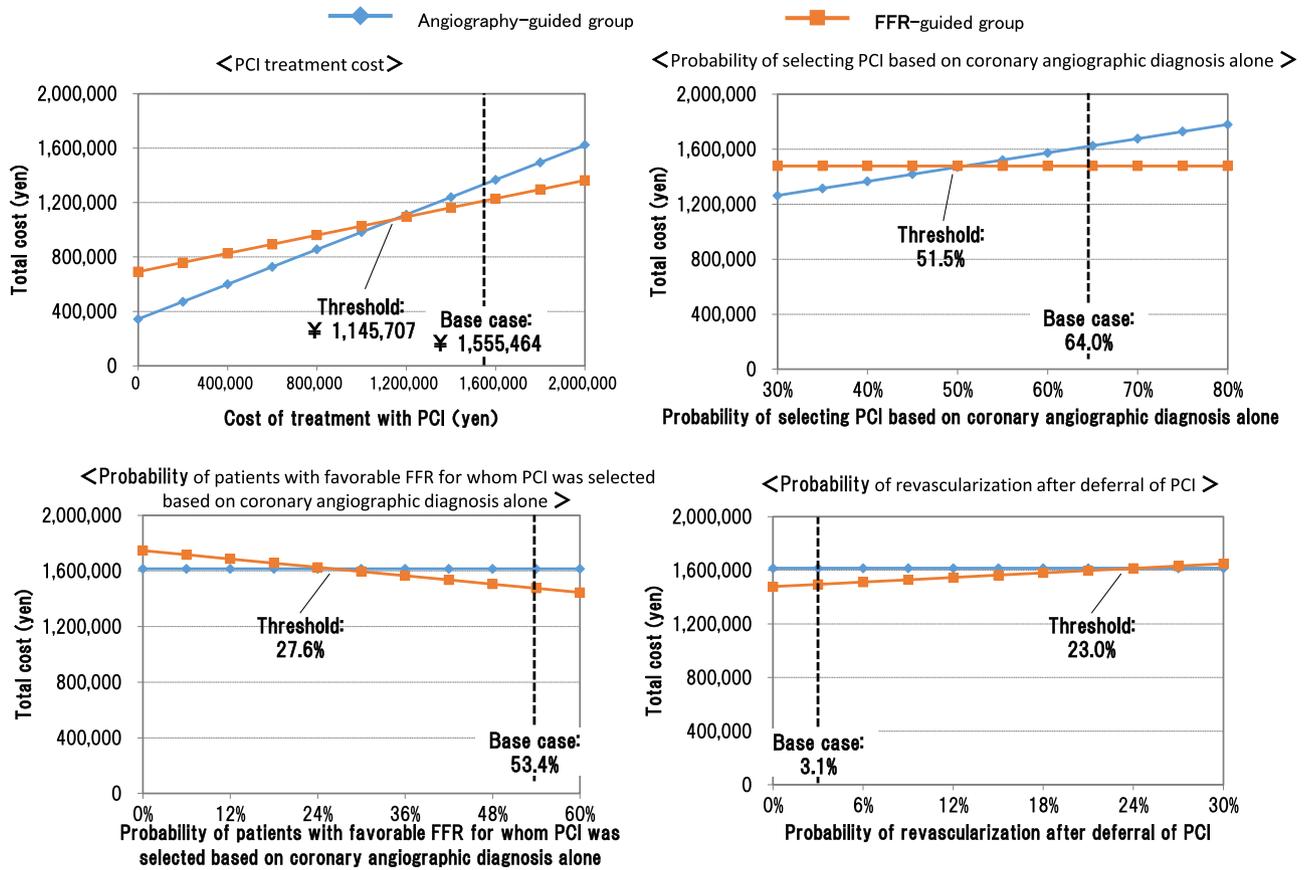


Fig. 3. Threshold analysis. The parameters with a large influence on the results of one-way sensitivity analysis and having a meaning of consideration were subjected to threshold analysis. Regarding the threshold of the parameters at which cost reduction by FFR measurement is expected, the threshold of ‘PCI treatment cost’ was 1,145,707 JPY or higher, that of ‘the probability of selecting PCI based on the coronary angiographic diagnosis alone’ was 51.5% or higher, that of ‘the probability of FFR > 0.80 in patients for whom PCI was selected based on the coronary angiographic diagnosis alone’ was 27.6% or higher, and that of ‘the probability of revascularization within one year’ was 23.0% or lower. CABG, coronary artery bypass graft; FFR, fractional flow reserve; PCI, percutaneous coronary intervention.

Limitations

There are several limitations in this analysis because it was a model analysis.

The first limitation concerns the internal validity of the analysis. As all clinical parameters were from the findings reported by the CVIT-DEFER registry study, there may have been no major problem in terms of a consistency of the patient characteristics among the clinical parameters. However, the costs of treatment with CABG, PCI, and MT in the patients allocated to each treatment pattern were calculated using the claims database of DPC hospitals in Japan. Therefore, the consistency of patient backgrounds between the patients in the CVIT-DEFER registry study and patients extracted from the claims database should be carefully interpreted. The reasons of the difference between the patient backgrounds in these two populations including prior history of PCI, unstable angina pectoris would be that this analysis was based on the claims database analysis (i.e. insufficient baseline follow-up and lack of the disease name details). However, as the age and sex distributions of the patients in these two groups were almost consistent, the possibility of large deviation in the expected costs of CABG, PCI, and MT determined by analyzing the claims database from the actual costs for the patients may be limited.

The second limitation concerns generalizability of this analysis. Generalizability of this analysis may be synonymous to that of the CVIT-DEFER registry study because the findings of the CVIT-DEFER registry study were used for analysis. As described in the report on the results of the CVIT-DEFER registry study by Nakamura et al. [9,10], it is possible that a certain selection bias remained in the patients in the CVIT-DEFER registry study. However, the results

were based on more than 3000 patients, being a large-scale population not performed before in Japan. Accordingly, the results of this analysis based on the CVIT-DEFER registry study may also be meaningful for daily practice in Japan.

Third, we did not take into account the revascularization risks concomitant with disregarded strategy. The patients who received PCI despite the negative FFR results had a 4.8% risk of revascularization. This risk was higher than in deferred patients, however, the difference was not statistically significant. We are not certain whether those disregarded judgment is constant or not. Therefore, we decided to avoid considering the revascularization risk for the patients who received PCI despite the negative FFR results in the analysis.

Fourth, this result should be confirmed in a prospective randomized cohort in future.

Conclusion

FFR measurement is expected to reduce the medical cost through effectively correcting the visual assessment by coronary angiography and reducing inappropriate application of PCI without disadvantage. These medical cost reductions by FFR measurement are robust even if the risk of revascularization after deferral of PCI based on FFR measurement is considered.

Conflict of interest

The present analysis was supported by Abbott Vascular Japan Co., Ltd. (St. Jude Medical Japan Co., Ltd.), Philips Japan, Boston

Scientific Japan, Zeon Medical Inc., Terumo Corporation, ACIST Japan, HeartFlow Japan, and Goodman.

Nobuhiro Tanaka declares consulting fees from Abbott Vascular Japan Co., Ltd. (St. Jude Medical Japan Co., Ltd.) and Boston Scientific Japan. Tatsunori Murata is an employee of CRECON Medical Assessment Inc. that received a payment from CVIT in connection with the analysis. The other authors report no conflict.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.jjcc.2018.05.018>.

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