Radiological Physics and Technology (2008.02) 64巻2号:251～258.

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Abstract

Our aim in this study was to perform a cost-effectiveness analysis (CEA) to compare myocardial perfusion magnetic resonance imaging (p-MRI) and single photon emission computed tomography (SPECT) in the Japanese setting. The CEA of p-MRI and SPECT was performed from the payer's perspective. The subjects were outpatients who had chest pain, had no history of myocardial infarction, and showed normal or equivocal stress electrocardiogram findings. The costs of imaging techniques and treatments were assessed with use of reimbursements of medical fees from Japanese healthcare insurance for the year 2007. Clinical effectiveness was defined in terms of the percent correct diagnosis of coronary artery disease (CAD). Data from published studies provided probabilities for the CEA, including the sensitivity and specificity of each imaging modality. We evaluated the cost effectiveness ratio (CER) of p-MRI and SPECT by using a decision tree model and compared the two. The CERs for diagnosis of CAD by p-MRI and SPECT were 1,988.2 and 2,582.0 Japanese Yen (JPY), respectively. The CERs for diagnosis and treatment of CAD by p-MRI and SPECT were 7,066.1 and 7,172.2 JPY, respectively. At a pre-test likelihood of CAD of 20–70%, the CERs for diagnosis of CAD by p-MRI and SPECT were 1,476.8-3,364.3 and 2,107.3-3,957.7 JPY, respectively. For outpatients with chest pain, p-MRI had good clinical effectiveness and cost-effectiveness compared with SPECT. In the management of patients with suspected CAD, p-MRI is as useful as SPECT.

1 Introduction

For patients who have chest pain, many noninvasive tests can be used for determining whether they should undergo coronary angiography (CAG). The routine use of CAG without previous noninvasive testing is typically not advocated because of the associated risk of morbidity and death, and because of its relatively high cost [1]. In clinical practice, myocardial perfusion is usually assessed with single photon emission computed tomography (SPECT) or positron emission tomography as a noninvasive test prior to CAG. In recent years, reports about the utility of magnetic resonance myocardial perfusion imaging (p-MRI) have increased [2-4]. Recent studies have reported that p-MRI is useful for detecting coronary artery disease (CAD) [2-4], and that the diagnostic ability of p-MRI is the same as or better than that of SPECT [5]. Although p-MRI has good diagnostic ability, its cost-effectiveness has not been assessed. From a healthcare insurance viewpoint, in Japan, MRI is a more expensive method than traditional exercise electrocardiography or an echocardiogram [6,7]. To consider the availability of noninvasive tests, it is important to evaluate not only their diagnostic ability, but also their cost-effectiveness.

Our aim in this study was to perform a cost-effectiveness analysis (CEA) to compare p-MRI and SPECT in a Japanese setting.

2 Materials and Methods

2.1 Patient Population

The subjects of the CEA were adult outpatients with chest pain who had normal or equivocal stress electrocardiograms (ECGs). They were divided into the following two groups: Group 1 consisted of outpatients who underwent a p-MRI examination (p-MRI strategy); Group 2 consisted of outpatients who underwent a SPECT examination (SPECT strategy). We assumed that the target disease was angina pectoris that stemmed from arteriosclerotic coronary artery stenosis. Patients with acute myocardial infarction and vasospastic angina were excluded from the analysis.

2.2 Definition of the terms

In this study, costs were calculated from the payer's perspective. Clinical effectiveness was defined as the percentage probability of the presence of CAD being correctly diagnosed through p-MRI (SPECT) or a combination of p-MRI (SPECT) and CAG. The cost-effectiveness ratio (CER) was defined as the total cost per patient divided by the clinical effectiveness. CAD was defined as stenosis of at least 50% in the left main coronary artery or stenosis of 70% or greater in any other coronary artery, as measured by angiography. Major adverse cardiac events (MACE) were defined as fatal or nonfatal myocardial infarction, unstable angina, or sudden cardiac death.

2.3 Construction of Decision Tree Models

We constructed a decision analytic model to assess the clinical effectiveness and costs that result from different test strategies for the diagnosis of CAD. The model represents options for therapy and diagnostic testing. The tests considered in the simple decision tree models (DTMs) were p-MRI and SPECT. Figure 1 indicates the management algorithms used for the DTMs. All conditional probabilities of each outcome in the tree were calculated and obtained as a function of the variables by use of Bayesian analysis.

We assumed that patients with positive test results would undergo angiography and that the only subsequent treatment would be elective percutaneous coronary intervention

(PCI). Patients not having CAD would continue to receive follow-up examinations on an outpatient basis. We also assumed that patients with negative test results would continue to receive follow-up examinations on an outpatient basis. However, if any MACE occurred, we assumed that the patient would be admitted into the hospital and undergo emergency PCI without p-MRI or SPECT. Elective PCI and emergency PCI were assumed to be successful, excluding patient death.

2.4 Costs

The costs of imaging examinations and treatments were assessed based on the reimbursement of medical fees from Japanese healthcare insurance in 2007. The costs of imaging examinations and treatments (included hospitalization costs) were based on our institutional data (between January 2007 and December 2007: Table 1). Costs of p-MRI and SPECT were calculated based on outpatient examinations (Table 1). Costs of CAG, elective PCI, and emergency PCI were defined as median values that we randomly selected from those of 20 patients from our institutional data.

2.5 Data Sources

The pre-test likelihood of CAD for adult outpatients in Japan who had chest pain, who had no history of myocardial infarction, and who showed normal or equivocal stress electrocardiograms was estimated at 35% from previous publications [8, 9]. The sensitivity and specificity of p-MRI and SPECT for the detection of CAD were obtained from our meta-analysis data [5] (Table 2). The sensitivity and specificity of CAG were assumed to be 100%. The probability of the incidence of MACE, in the presence of normal p-MRI or SPECT, was also obtained from the literature [10-12] (Table 2). The mortality rate for CAG and other treatments was obtained from the literature [13, 14]

(Table 2). The mortality rate for p-MRI and SPECT was assumed to be 0%.

2.6 Calculation of clinical effectiveness and CER (base case)

Using the DTMs, we calculated the following values (pre-test likelihood of CAD: 35%):

1) Clinical effectiveness

2) Costs and CER for diagnosis of CAD per patient

3) Costs and CER for diagnosis and treatment of CAD per patient

4) Incremental cost effectiveness ratio (ICER) for p-MRI

2.7 Sensitivity analysis

We performed a one-way sensitivity analysis to evaluate the change in the CER for the following parameters:

1) The pre-test likelihood of CAD

2) The cost of examination

Our analyses were performed with use of Tree-Age Pro 2011 software (TreeAge Software, Williamstown, Mass). Also, our study did not require the approval of the Ethical Review Board.

3 Results

3.1 Calculation of clinical effectiveness, costs, and CER for each strategy

Table 3 indicates the clinical effectiveness and costs of each strategy when the pre-test likelihood of CAD was 35%. In Table 3, A, B, and C indicate clinical effectiveness, diagnostic cost per patient, and diagnostic and treatment cost per patient, respectively. Compared with SPECT, p-MRI reduced the diagnostic cost of CAD by 44,188 Japanese Yen (JPY) per patient. On the other hand, p-MRI increased the diagnostic and treatment cost of CAD by 17,943 JPY per patient. p-MRI exhibited greater clinical effectiveness compared with SPECT. Table 4 indicates the CER and ICER when the pre-test likelihood of CAD was 35%. p-MRI exhibited a lower CER compared with SPECT.

3.2 Sensitivity Analysis

Figures 2 and 3 indicate how the CER changes with the various pre-test likelihoods of CAD. In figures, A, B, and C indicate a clinical effectiveness, diagnostic cost per patient, and diagnostic and treatment cost per patient, respectively. p-MRI had a lower CER (B/A i.e. diagnostic cost per patient/clinical effectiveness) than did SPECT. Furthermore, there was no difference between p-MRI and SPECT in terms of their dependence on the pre-test likelihood of CAD. CER (C/A i.e. diagnostic and treatment cost per patient /clinical effectiveness) for p-MRI was approximately equivalent to that of SPECT for any pre-test likelihood of CAD. Figures 4, 5, 6, 7 indicate the changes in the CER with the various costs of examination. Compared with the base case of SPECT, the CER (B/A i.e. diagnostic cost per patient/clinical effectiveness) of p-MRI was less until the cost of p-MRI reached about 90,000 JPY, and the CER (C/A i.e. diagnostic and treatment cost per patient /clinical effectiveness) of p-MRI was less until the cost of p-MRI reached approximately 50,000 JPY.

4 Discussion

We evaluated the clinical effectiveness and cost effectiveness of two non-invasive myocardial perfusion diagnostic procedures, p-MRI and SPECT, and compared them.

p-MRI showed higher clinical effectiveness than did SPECT. For patients with any pre-test likelihood of CAD, p-MRI was a cost-effective procedure in the comparison of CER (B/A). However, in the comparison of diagnostic and treatment costs of CAD per patient, p-MRI was more expensive than SPECT. This is considered to be the case because the diagnostic ability (lesion detectability) of p-MRI is higher than that of SPECT, leading to a higher number of treatment opportunities of CAD in the CEA. Despite p-MRI's higher diagnostic and treatment costs of CAD per patient, CER (C/A) of p-MRI was approximately equivalent to that of SPECT. This is considered to be the case because treatment costs were much higher than diagnostic costs, and a difference in the cost of each diagnostic procedure did not have any influence on the CER (C/A). Also, because the clinical effectiveness of p-MRI was higher than that of SPECT, the CER (C/A) of p-MRI did not show much difference from that of SPECT.

The cost-effectiveness of SPECT has been reported in a number of clinical studies and in various patient populations [8, 9, 15-19]. Some of these studies have indicated that the use of SPECT permits a reduction in unnecessary hospitalizations and provides significant cost savings [8, 16]. Des Prez et al. indicated that, for intermediate-risk patients (pre-test likelihood of CAD $\geq$ 30%), initial investigation with SPECT is a cost-effective approach [16]. They also indicated that, for low-risk patients, a cost-effective strategy appears to be using a stress ECG, with the selective use of SPECT for those whose initial test is abnormal [16].

Our findings indicated that, if p-MRI is introduced for the same purpose as SPECT in clinical practice, good clinical effectiveness and cost-effectiveness compared to SPECT can be expected. Our findings also indicated that the clinical effectiveness of p-MRI could contribute to earlier clinical intervention in patients with CAD, compared with SPECT. In terms of the prognostic value, the MACE-free rate of p-MRI has been reported to be 0–2.3% [20-22]. If p-MRI findings are negative, the probability of incidence of MACE is considered to be as low as that for SPECT. However, p-MRI is a relatively new myocardial perfusion diagnostic technique, and findings regarding the long-term prognosis have not yet been accumulated. Therefore, we consider that investigation about the cost-effectiveness, using discounting future costs and health benefits [23], and the long-term prognosis will be required in the future.

There are several limitations to our study. First, our study was a simulation involving a great deal of assumption. Therefore, our results may not be appropriate in the different situations from our assumption. Also, as Garber et al. pointed out [24], analyses may be affected by publication bias because we used data from other publications. In order to solve this problem, we considered quoting meta-analysis results to reflect diagnostic ability, and performing a sensitivity analysis so that the technique could be applied to many different cases, although there would be some limitations.

Second, our study analysis limited the method of treatment to PCI. We also assumed all significant lesions to be a treatment objective, and that if one were found in the workup CAG, successive PCI could be performed immediately. Analysis including follow-up (notreatment), pharmacotherapy, and a coronary artery bypass graft will be required for the further assessment of cost effectiveness.

Third, we focused our analysis on a comparison between p-MRI and SPECT as non-invasive diagnostic procedures for CAD. Recently, reports about the utility of coronary computed tomographic angiography (CCTA) have increased [25-27]. In clinical practice, as with p-MRI, CCTA is a relatively new non-invasive CAD diagnostic procedure. Therefore, a cost-effectiveness comparison with CCTA will be required.

Although our study has some limitations, to our knowledge, this is the first CEA of p-MRI in outpatients who have chest pain in the Japanese setting. CEA is one of the important cornerstones of evidence-based medicine. Recently, guidelines for medical practice have been developed in Japan. To develop this, an evidence assessment is required with a comprehensive search of the literature. Research to investigate diagnostic imaging evidence, as in our study, will become increasingly important in the future. However, our study was carried out based on the medical treatment fees in the Japanese healthcare system. When the external validity of our study is considered, it will be necessary to pay attention to any differences in the cost systems in the healthcare system of each country.

5 Conclusion

From the payer's perspective, we evaluated the clinical effectiveness and cost effectiveness of two non-invasive myocardial perfusion diagnostic procedures, p-MRI and SPECT, and compared them. For outpatients with chest pain, p-MRI had good clinical effectiveness and cost-effectiveness compared with SPECT in the Japanese setting. In the management of patients with suspected CAD, p-MRI is as useful as SPECT.

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Variable	Cost (JPY)	Cost (EURO)
p-MRI	39,800	506.7
SPECT	83,000	1,056.8
CAG	426,500	5,430.4
Elective PCI	205,4400	26,157.4
Emergency PCI	239,2200	30,458.4

Table 1 Costs of imaging examinations and treatments (1 USD = 78.54 JPY: 2011.07.23)

Variable	Value	Reference Source
Pretest likelihood of CAD (%)	35	8,9
Diagnostic Ability		
Sensitivity of p-MRI	0.75	5
Specificity of p-MRI	0.89	5
Sensitivity of SPECT	0.64	5
Specificity of SPECT	0.83	5
Sensitivity of CAG	1.0	
Specificity of CAG	1.0	
Probability of incidence of MACE (%)		
p-MRI	2.3	10,11
SPECT	2.3	12
Mortality (%)		
p-MRI	0	
SPECT	0	
CAG	0.1	13
Elective PCI	0.36	14
Emergency PCI	6.1	14

Table 2 Values used in analysis

	Clinical effectiveness, A (%)	Diagnostic cost per patient, B (JPY)	Diagnostic and treatment cost per patient, C (JPY)
p-MRI	91.2	181,275	644,239
SPECT	87.3	225,463	626,296

Table 3 Clinical effectiveness and costs of each strategy (pre-test likelihood was 35 %)

p-MRI: Group 1, SPECT: Group 2

	CER (B/A)	ICER	CER (C/A)	ICER
p-MRI	1,988.2	-1,147.7	7,066.1	4,660.6
SPECT	2,582.0		7,172.2	

Table 4 CER and ICER (pre-test likelihood was 35 %)

p-MRI: Group 1, SPECT: Group 2

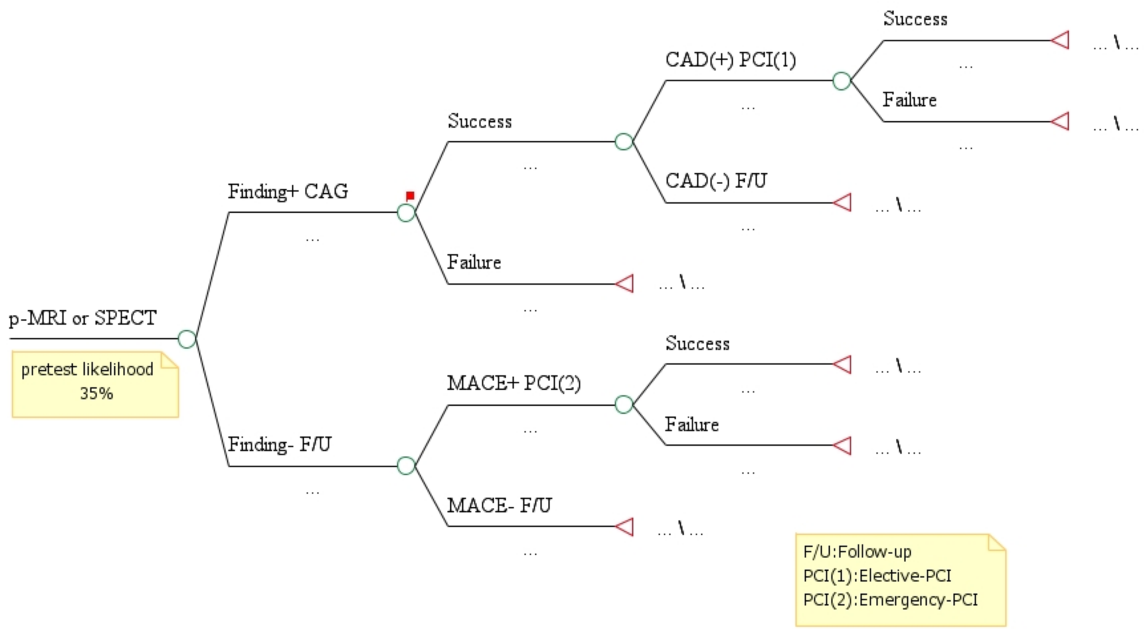

Fig. 1 Decision Tree Model

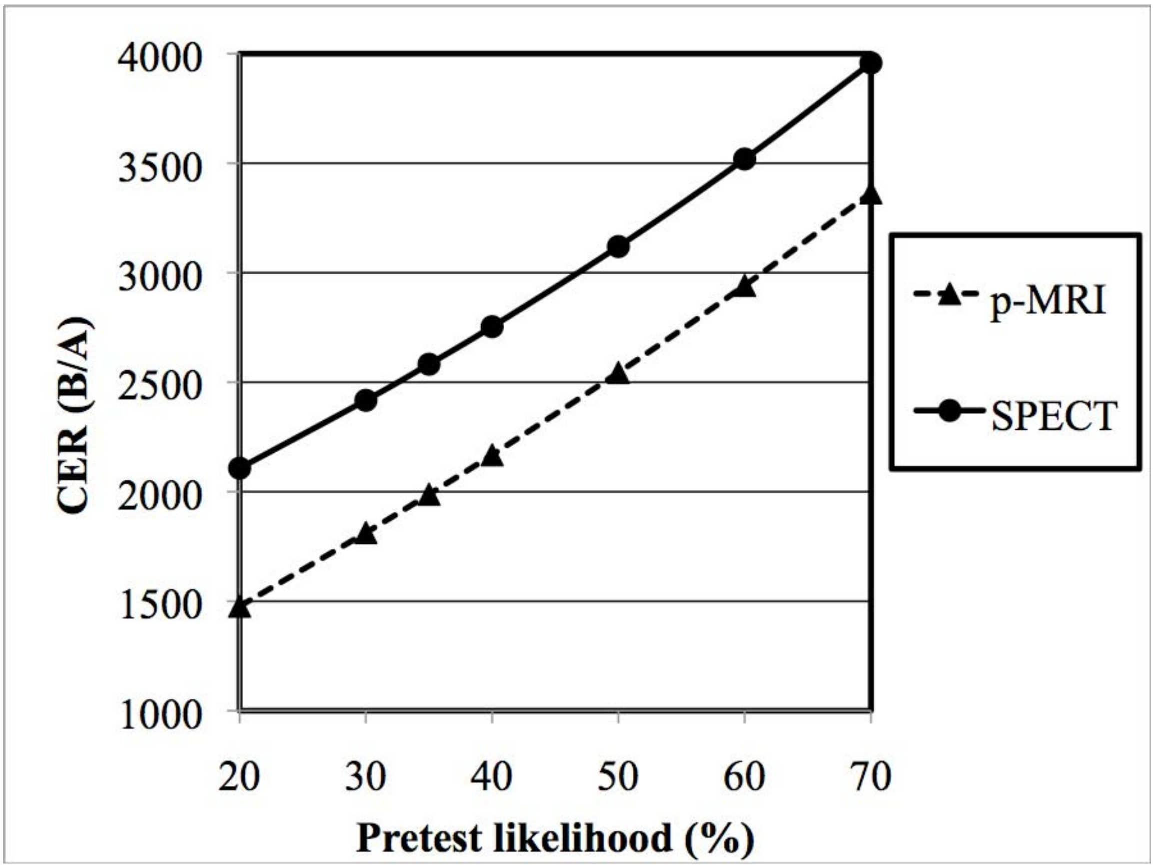

Fig. 2 Sensitivity analysis [changes of CER *(B/A)* with various pre-test likelihoods of CAD]. CER *(B/A)* means the diagnostic cost per patient divided by the clinical effectiveness

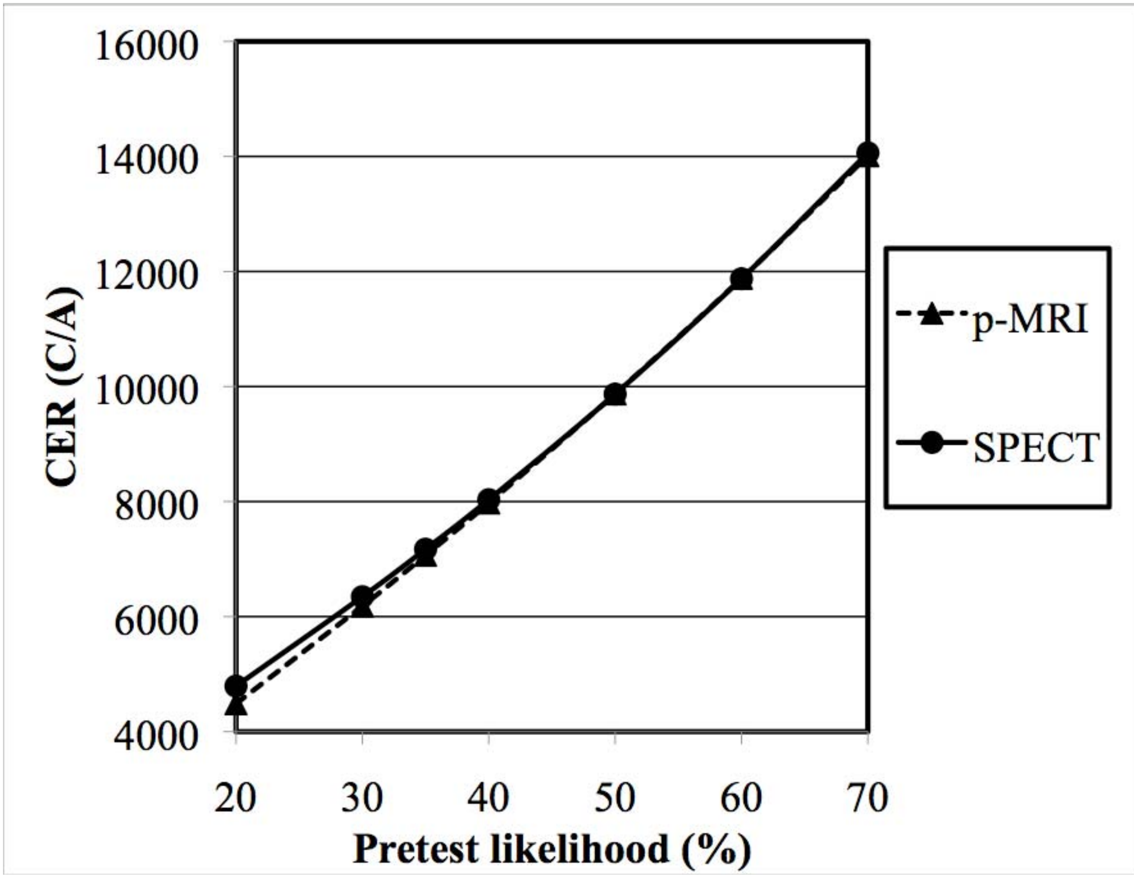

Fig. 3 Sensitivity analysis [changes of CER *(C/A)* with various pre-test likelihoods of CAD]. CER *(C/A)* means the diagnostic and treatment cost per patient divided by the clinical effectiveness

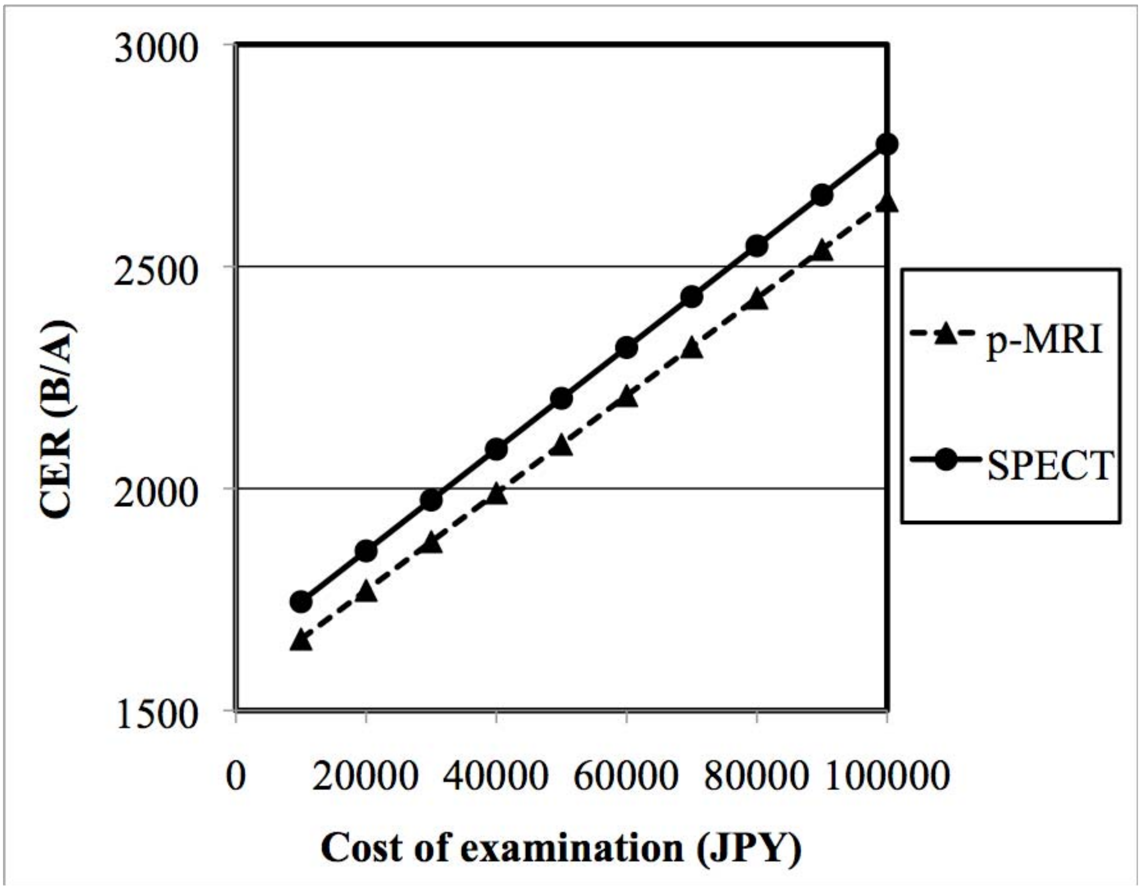

Fig. 4 Sensitivity analysis [changes of CER *(B/A)* with various costs of examination]. CER *(B/A)* means the diagnostic cost per patient divided by the clinical effectiveness

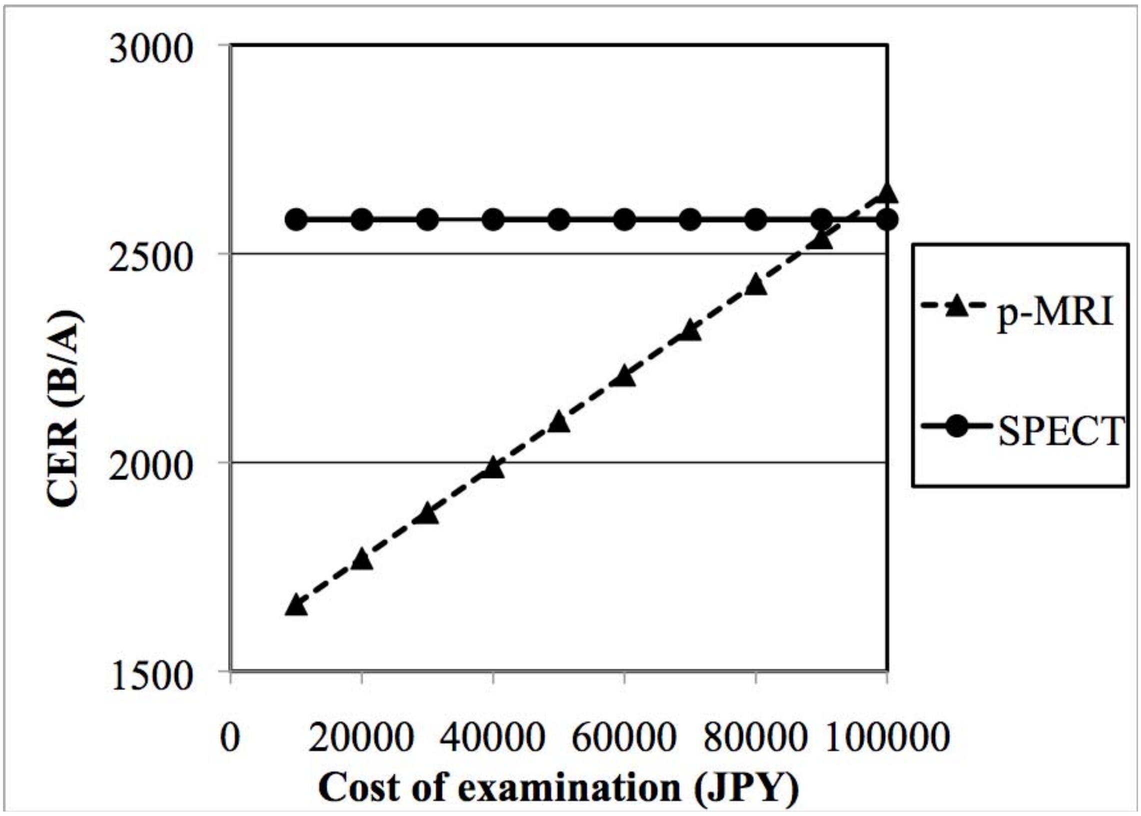

Fig. 5 Sensitivity analysis [comparison with the base case of SPECT: changes in CER *(B/A)* with various costs of examination of p-MRI]. CER *(B/A)* means the diagnostic cost per patient divided by the clinical effectiveness

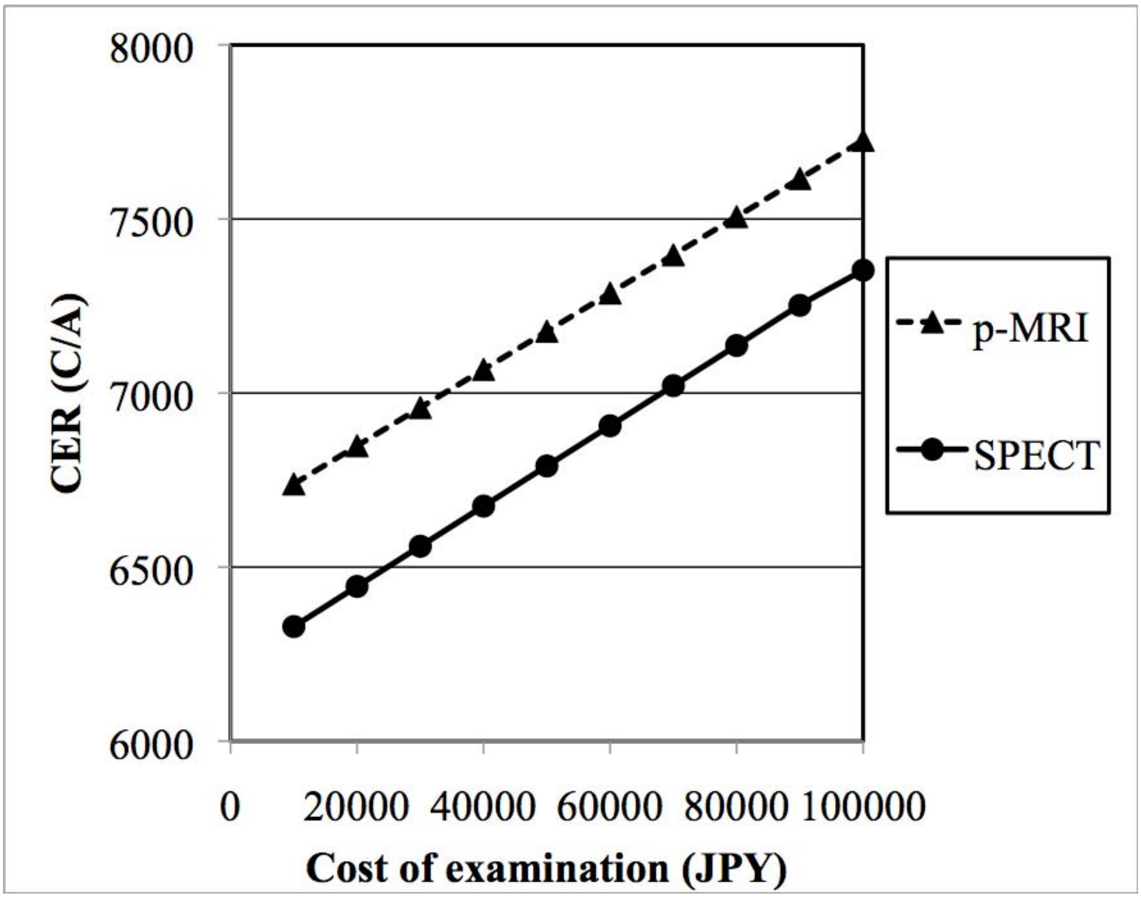

Fig. 6 Sensitivity analysis [changes in CER *(C/A)* with various costs of examination]. CER *(C/A)* means the diagnostic and treatment cost per patient divided by the clinical effectiveness

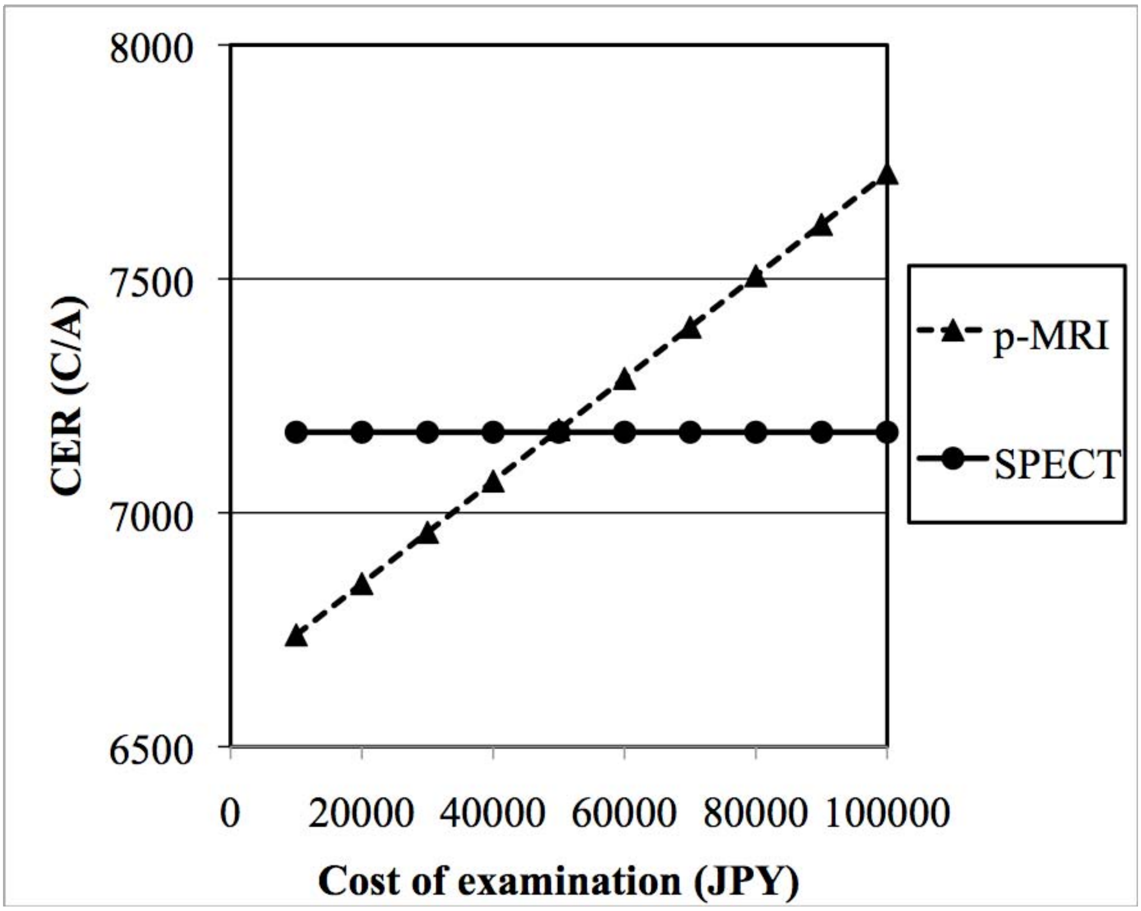

Fig. 7 Sensitivity analysis [comparison with the base case of SPECT: changes in CER *(C/A)* with various costs of examination of p-MRI]. CER *(C/A)* means the diagnostic and treatment cost per patient divided by the clinical effectiveness