# Prognostic value of myocardial metabolic imaging with BMIPP in the spectrum of coronary artery disease: A systematic review

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***Background.*** **We conducted a systematic review to summarize the current literature on the prognostic value of BMIPP imaging, fatty-acid metabolic imaging, for the prediction of cardiovascular events in coronary artery disease.**

***Methods and Results.*** **Electronic databases (including Japanese medical literature search engines) were searched by a Japanese investigator using a predefined search strategy. Eleven studies, all conducted in Japan, were included in the meta-analysis. In three studies involving 541 patients with suspected acute coronary syndrome who were excluded for acute myocardial infarction (AMI), an abnormal finding on BMIPP imaging was significantly associated with future hard events (cardiac death or non-fatal myocardial infarction). The negative predictive value of BMIPP imaging for future hard events was 98.9% (96.8-99.7%) over 3.5 years. In six studies involving 542 patients with AMI, a larger defect on BMIPP imaging was significantly associated with future hard events. The prognostic value of perfusion-metabolism mismatch compared with myocardial perfusion imaging was dependent upon the relative timing of BMIPP imaging, revascularization, and myocardial perfusion damage.**

***Conclusions.*** **BMIPP imaging is useful for the risk stratification of patients with coronary artery disease, particularly patients with acute chest pain. (J Nucl Cardiol 2010;17:61–70.)**

**Key Words: BMIPP • fatty acid imaging • myocardial viability • diagnostic and prognostic application**

## INTRODUCTION

Fatty acids are the preferred energy source of normally perfused hearts in which 60-70% of high-energy phosphate production is supplied by oxidation of fatty acids.[1] Ischemia shifts the source of myocardial energy from aerobic metabolism to anaerobic metabolism, where glucose utilization through anaerobic glycolysis becomes pivotal for energy production.[2] It has been shown that abnormalities of the metabolism of fatty acids resulting from exercise-induced ischemic events, as evidenced by imaging of fatty-acid metabolism using β-methyl-p-[123I]-iodophenyl-pentadecanoic acid (BMIPP), persist for up to 30 hours.[3] Successful imprinting of antecedent ischemia (which could not be identified with resting myocardial perfusion imaging) in BMIPP imaging is referred to as ''ischemic memory imaging.''

We have shown that BMIPP imaging has moderate sensitivity and high specificity to detect coronary artery disease (CAD) in a population with a high prevalence of CAD.[4] BMIPP, which is injected under resting conditions, is particularly useful in patients with acute chest pain if exercise or pharmacologic stress testing is contraindicated. The safety profile of BMIPP, which has been used in >500,000 patients for >10 years in Japan, is well established with no reports of clinically significant adverse effects.[5]

The Japanese Circulation Society, in guidelines for the clinical use of cardiac nuclear medicine published in 2005, stated that BMIPP imaging is useful to detect myocardial ischemia in patients presenting with acute chest pain (level of evidence: B).[5] The prognostic value of BMIPP imaging for risk stratification in CAD management has not been well defined (level of evidence: C).

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Most studies on BMIPP imaging were retrospective and based on small sample sizes. In an attempt to overcome this issue, we carried out a systematic review and meta-analysis of the literature on the prognostic value of BMIPP imaging for prediction of cardiac events in the full spectrum of CAD.

## METHODS

### Search Strategy

We initially selected the following databases: Ovid MEDLINE; Ovid MEDLINE Daily Update; Ovid MEDLINE In-Process & Other Non-Indexed Citations; Cochrane Central Register of Controlled Trials; Cochrane Database of Systematic Reviews; and the Ichushi database (Japanese medical literature search engines). These databases were searched independently and in duplicate by a Japanese investigator (YI) until March 2009 using the following medical subject headings (MeSH) and text words: BMIPP, fatty acid, and single-photon emission-computed tomography. We also searched the reference section of retrieved articles and relevant reviews.

### Study Eligibility

Articles were included if they: (1) were randomized controlled studies or longitudinal studies, (2) conducted BMIPP imaging at baseline in patients with suspected or known CAD, (3) followed up a cohort for >6 months, and (4) reported a cardiovascular event outcome. There were no exclusion criteria or language restrictions in this systematic review.

### Data Extraction

The following information was extracted from each study: references, mean age, number of patients, percentage of male patients, length of follow-up, primary outcomes, definition of abnormal BMIPP imaging, potential confounding variables, and risk estimates of cardiovascular events. The corresponding authors were contacted to obtain missing information if necessary.

### Study Quality

The quality of studies was assessed and scored as ''yes,'' ''no,'' or ''unclear'' using the following criteria: prospective follow-up of a consecutively sampled cohort, blind assessment of BMIPP imaging, blind adjudication of clinical outcomes, disclosure of withdrawals and dropouts with attrition rate, and adjustment for confounding bias.[6] The risk of bias was determined to be ''high'' if the overall number of ''yes'' scores was 0 or 1, ''intermediate'' if 2 or 3, and ''low'' if 4 or 5.

### Statistical Analysis

The primary outcomes of interest in this meta-analysis were hard cardiovascular events, defined as cardiac death or non-fatal myocardial infarction. The secondary outcomes of interest were cardiac death and overall cardiovascular events, which included soft events (defined as coronary revascularization or hospital admission for unstable angina or heart failure) in addition to hard events.

Relative risk was used as a measure of the relationship between the result of BMIPP imaging and cardiovascular outcomes. To assess for heterogeneity across studies, the Cochrane Q statistic was calculated. In addition, the $I^2$ statistic was used to quantify heterogeneity from 0% to 100%, whereby significant heterogeneity was defined >50%.[6] The DerSimonian and Laird random effect model was used to pool study results if there was significant heterogeneity; otherwise the fixed-effect model was used.[7]

Summary estimates of the adjusted relative risks, accounted for confounding factors in each study, were calculated by pooling the natural logarithms of the relative risks from individual studies, weighted by the inverse of their variances. The standard errors of the log relative risks were calculated from the reported 95% confidence interval (CI) or $P$ values. Hazard ratios were treated as relative risks, and the odds ratio was algebraically converted to relative risk using the formula described by Zhang and Yu.[8] Publication bias was examined by visual inspection for funnel plot asymmetry and the Egger's test.[6]

A priori-specified subgroup analyses were conducted according to their populations, and stratified into patients with suspected acute coronary syndrome (ACS) who were excluded for acute myocardial infarction (AMI), patients with AMI, or patients with chronic CAD who underwent elective revascularization. In addition, the following study characteristics were examined in subgroup analyses to investigate the effects on prognostic values of BMIPP imaging; number of participants, publication year, length of follow-up, and each component of quality assessment.

Perfusion-metabolism mismatch on BMIPP imaging compared with myocardial perfusion imaging (MPI) may represent a stunned or hibernating myocardium depending on the timing relative to revascularization. We therefore also conducted a meta-regression analysis to investigate the effect of the timing of BMIPP imaging on the prognostic value of perfusion-metabolism mismatch. The dependent variable was the log-transformed relative risk of a future hard event. The continuous independent covariable was the number of months between BMIPP imaging and revascularization.

Calculations were carried out using STATA (version 10) software (STATA Corporation, College Station, TX, USA). All tests were two-sided with a significance level of $P<.05$ except for meta-regression analysis in which the significance level of $P<.10$ was chosen a priori. We conformed to meta-analysis of Observational Studies in Epidemiology guidelines in the report of this systematic review.[9]

## RESULTS

### Overview of Studies

Database searches identified 541 potentially relevant citations (Figure 1). After assessment of the title

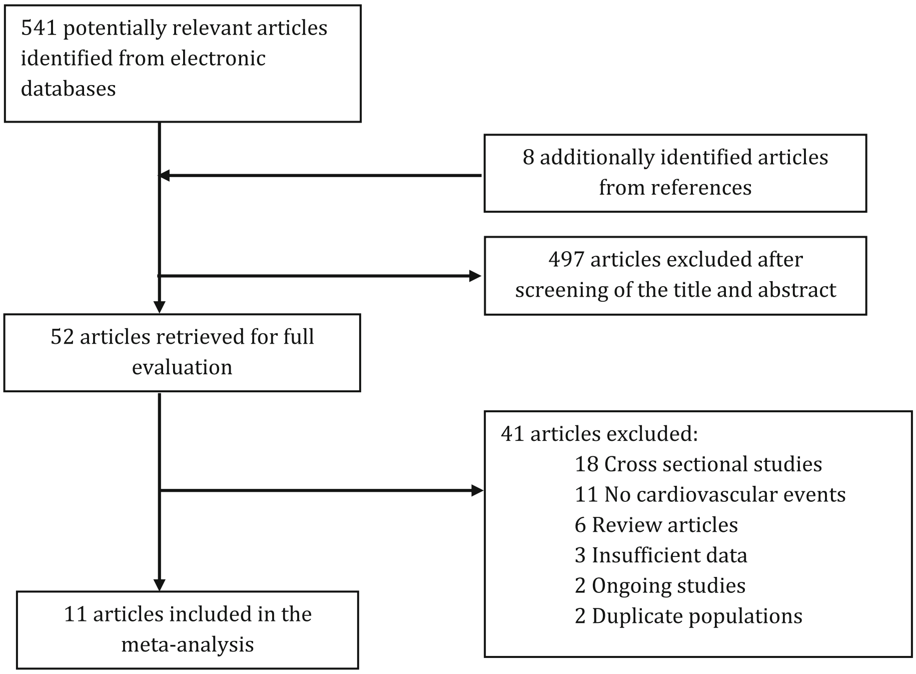

**Figure 1.** Flow diagram of the review process.

and abstract, we retrieved 52 articles for full evaluation. We then excluded 41 articles: 18 were cross-sectional studies, 11 did not report cardiovascular events, 6 were review articles, 3 did not include sufficient data for meta-analysis, 2 were ongoing studies, and 2 had duplicate study populations. The final set therefore comprised 11 studies, all of which were conducted in Japan.[10-20]

The selected studies were published between 1996 and 2008. The number of participants per study ranged from 33 to 270 for 1,315 participants across studies. The mean age of patients and the mean duration of follow-up were 63.2 years (range, 59-66 years) and 33.2 months (range, 14-48 months), respectively. BMIPP imaging was conducted under resting condition in all studies. Details of included studies are summarized in Table 1.

## Study Quality and Risk of Bias

The qualities of included studies were heterogeneous (Table 2). Three studies (27%) prospectively followed up consecutively sampled cohorts. Three studies (27%) clearly reported a blind assessment of BMIPP imaging. Two studies (18%) reported blind adjudication of clinical outcomes. Six studies (55%) adequately described subject withdrawals and dropouts. Six studies (55%) reported the number of patients lost to follow-up; the attrition value ranged from 77% to 100%. Eight studies (73%) adjusted the result for most cardiovascular risk factors by logistic regression or Cox regression. Overall, three studies (27%) were determined to have a low risk of bias, four studies (36%) an intermediate risk, and four studies (36%) a high risk.

## Statistical Pooling

Among three studies which comprised 542 patients with suspected ACS who were excluded for AMI, 13 (5%) out of 256 patients with an abnormal finding on BMIPP imaging developed hard events compared with 3 (1%) out of 286 patients with normal results. Overall, abnormal BMIPP imaging was significantly associated with future hard events (relative risk 4.07; 95% CI 1.32-12.6; $P = .015$) (Figure 2) and mildly associated with cardiac death (relative risk 3.83; 95% CI 0.91-16.1; $P = .07$). Among two studies which accounted for confounding factors, the adjusted relative risk of overall cardiovascular events was 4.51 (95% CI 2.398.51; $P < .001$).

In the same population, the negative predictive values (NPVs) of BMIPP imaging for hard events and soft events were 98.9% (96.8-99.7%) and 92.3% (88.3-95.1%) over 3.5 years, respectively. The corresponding annualized event values after negative results were 0.30% (0-2.44%) and 3.19% (1.48-6.72%) per year, respectively.

Six studies which comprised 607 patients examined the prognostic value of abnormal BMIPP imaging in patients with AMI. The definition of abnormal BMIPP imaging varied between studies: four studies used a high

**Table 1.** Characteristics of included studies

| References | Participants, n | Mean age, years | Men, % | Follow-up, months | Study outcomes | Definition of abnormal test | Confounding factors |
|---|---|---|---|---|---|---|---|
| Studies involving patients with suspected ACS who were excluded for MI | | | | | | | |
| Hatano et al[10] | 105 | 63 (10) | 59 | 14 | Cardiac death, non-fatal MI, heart failure, unstable angina, or revascularization | Segmental defect | Sex, smoking |
| Chikamori et al[11] | 270 | 62 (12) | 45 | 43 | Cardiac death, non-fatal MI, heart failure, unstable angina, or revascularization | Increased summed defect score | Previous CABG, DM |
| Matsuki et al[12] | 167 | 66 (10) | 54 | 48 | Cardiac death, non-fatal MI, heart failure, unstable angina, or revascularization | Increased summed defect score | DM, EF |
| Studies involving patients with AMI | | | | | | | |
| Fukushima et al[13] | 33 | 66 (12) | 65 | 24 | Cardiac death, non-fatal MI, heart failure, or revascularization | High summed defect score on dual Tl201/BMIPP imaging 8 (mean, 5) days after MI | EF |
| Hashimoto et al[14] | 97 | 64 (10) | 76 | 33 | Cardiac death, non-fatal MI, or heart failure | High defect score in infarcted area within 30 (median, 9) days after MI | DM, previous MI, EF |
| Nanasato et al[15] | 159 | 63 (10) | 79 | 35 | Cardiac death, non-fatal MI, heart failure, or unstable angina | High summed defect score 12.4 (mean, 8.4) days after MI | Pre-infarct angina, Ischemia time, EF, Multi-vessel disease |

**Table 1.** continued

| References | Participants, n | Mean age, years | Men, % | Follow-up, months | Study outcomes | Definition of abnormal test | Confounding factors |
|---|---|---|---|---|---|---|---|
| Nakata et al[16] | 101 | 61 (11) | 78 | 28 | Cardiac death or non-fatal MI | High summed defect score within 21 (mean, 10) days after MI | Gender, previous MI, LAD lesion |
| Nishimura et al[17] | 167 | 64 (10) | 73 | 22 | Cardiac death or heart failure | High summed defect score or mismatch score with Tl201 within 21 (mean, 7) days after MI | Age, multi-vessel disease |
| Tamaki et al[18] | 50 | 63 (10) | 86 | 23 | Cardiac death, non fatal MI, unstable angina, or revascularization | Increased number of mismatched segment with Tl201 within 6 (mean, 1.9) months after MI | Sex, anterior or Inferior MI, number of diseased vessels |
| Studies involving patients with chronic CAD who underwent elective revascularization | | | | | | | |
| Nishimura et al[19] | 90 | 65 (9) | 71 | 32 | Cardiac death | Increased mismatch scores on dual Tl201/BMIPP imaging 6 months after PCI | Age, sex, alcohol, diastolic BP, LAD lesion, LV mass index |
| Fukuzawa et al[20] | 76 | 59 (10) | 93 | 32 | Cardiac death, non-fatal MI, heart failure, or unstable angina | Increased number of mismatched segments with Tl201 imaging before revascularization | EF |

*ACS*, Acute coronary syndrome; *BP*, blood pressure; *CABG*, coronary artery bypass grafting; *CAD*, coronary artery disease; *DM*, diabetes mellitus; *EF*, ejection fraction; *LAD*, left anterior descending artery; *LV*, left ventricular; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention; and *Tl201*, thallium-201.

**Table 2.** Study quality and risk of bias of included studies

| References | Prospective vs. retrospective | Blind assessment of BMIPP imaging | Blind adjudication of clinical outcomes | Disclosure of dropouts (attrition) | Overall risk of bias |
|---|---|---|---|---|---|
| Hatano et al[10] | Retrospective | Yes | Unclear | Yes (100%) | Intermediate |
| Chikamori et al[11] | Retrospective | Yes | Yes | Yes (99%) | Low |
| Matsuki et al[12] | Prospective | Yes | Unclear | Yes (96%) | Low |
| Fukushima et al[13] | Unclear | Unclear | Unclear | Unclear | High |
| Hashimoto et al[14] | Unclear | Yes | Unclear | Unclear | Intermediate |
| Nanasato et al[15] | Unclear | Unclear | Unclear | Unclear | High |
| Nakata et al[16] | Prospective | Unclear | Unclear | Yes (93%) | Intermediate |
| Nishimura et al[17] | Unclear | Unclear | Unclear | Yes (77%) | Intermediate |
| Tamaki et al[18] | Unclear | Unclear | Unclear | Unclear | High |
| Nishimura et al[19] | Prospective | Yes | Yes | Yes (92%) | Low |
| Fukuzawa et al[20] | Unclear | Yes | Unclear | Unclear | High |

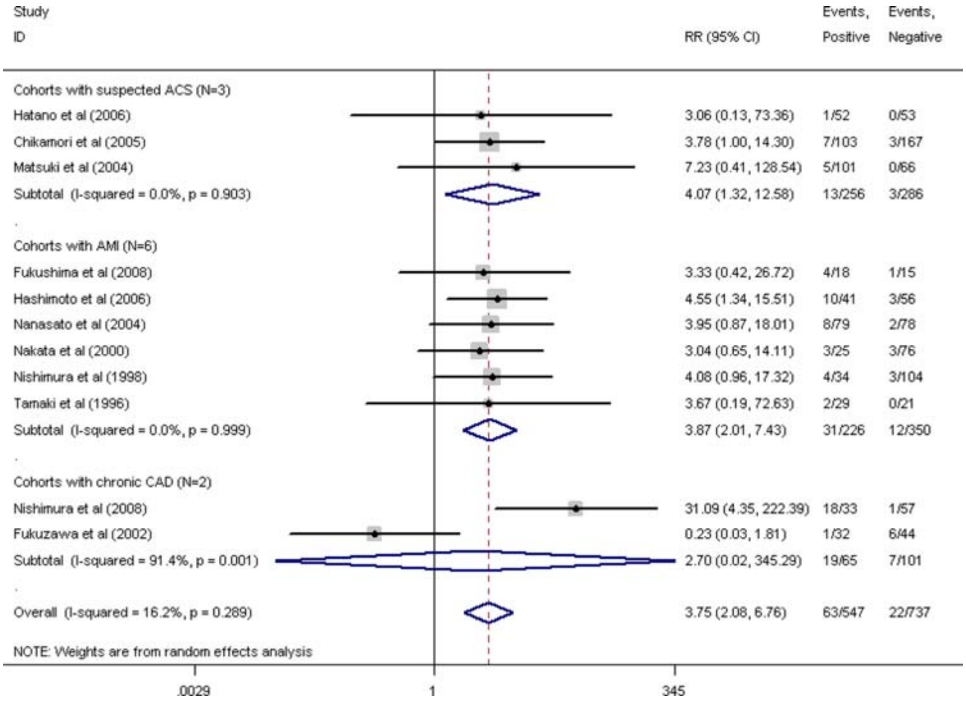

**Figure 2.** Effect of abnormal BMIPP imaging on cardiovascular hard events in the spectrum of coronary artery disease. Results were stratified according to their population. *ACS*, Acute coronary syndrome; *AMI*, acute myocardial infarction; *CAD*, coronary artery disease; and *RR*, relative risk.

summed defect score, one used a high defect score in the infarcted area, and one used an increased number of mismatched segments (Table 1). Overall, the larger defect on BMIPP imaging was significantly associated with cardiac death and hard events with a relative risk of 2.81 (95% CI 1.14-6.93, $P = .025$) and 3.87 (95% CI 2.01-7.43, $P < .001$), respectively (Figure 2). Among three cohort studies which accounted for confounding factors, the adjusted relative risk of hard events was 3.40 (95% CI 1.65-7.03; $P = .001$). This suggested that severe impairment of fatty-acid metabolism in AMI is an independent risk factor for future hard events.

Two studies included 166 patients with stable CAD who underwent elective revascularization. Both studies evaluated the prognostic value of perfusion-metabolism mismatch on BMIPP imaging compared with MPI, and showed contrasting results depending on the timing of BMIPP imaging relative to revascularization (Figure 2). Both studies were designed for different purposes: one for assessment of a viable myocardium before revascularization, and the other for assessment of a residual ischemic myocardium after revascularization.

A meta-regression analysis was conducted to investigate the effect of the timing of BMIPP imaging relative to revascularization on the prognostic value of perfusion-metabolism mismatch. Six studies, in which two included patients with chronic CAD and four included patients with AMI, reported the prognostic value of perfusion-metabolism mismatch. The log relative risk of perfusion-metabolism mismatch for future hard events was significantly associated with the timing of BMIPP imaging relative to revascularization ($P = .03$) (Figure 3). The presence of a mismatched myocardium before revascularization, which suggests a jeopardized (but viable) myocardium, is associated with fewer hard events if patients undergo successful revascularization. The later after revascularization the perfusion-metabolism mismatch (which suggests the presence of ischemia) occurs, the more hard events occur.

Subgroup analyses were conducted to examine the effects of study characteristics on the prognostic value of BMIPP imaging. We excluded two studies which involved patients with chronic CAD who underwent elective revascularization because both studies were significantly different with respect to study design and results, and therefore could affect the subgroup analysis depending on which subgroup these studies belonged to. Overall, an abnormal finding on BMIPP imaging was significantly associated with future hard events in all subgroups evaluated without significant heterogeneity ($I^2 = 0\%$ in all subgroups) (Figure 4). A funnel plot was symmetrical and Egger's test was negative for publication bias ($P = .40$).

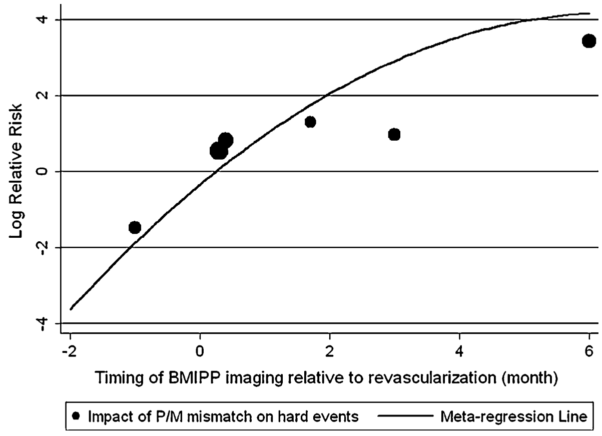

**Figure 3.** Meta-regression analysis for the association between the effect of perfusion-metabolism mismatch on future hard events and the timing of BMIPP imaging relative to revascularization. The X-axis represents the timing of BMIPP imaging relative to revascularization and the Y-axis represents the log relative risk of future hard events. The presence of a mismatched myocardium before revascularization is associated with fewer hard events, whereas the later after revascularization perfusion-metabolism mismatch is present, the more hard events occur. The size of each trial corresponds to the inverse variance of the log-transformed relative risk, and is thus related to the statistical weight of the study. *P/M*, Perfusion-metabolism mismatch.

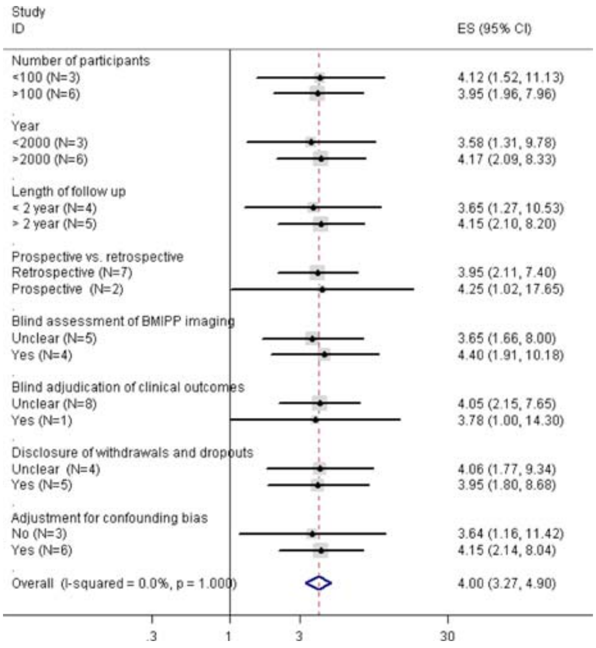

**Figure 4.** Subgroup analyses on the effect of abnormal BMIPP imaging on hard events. Results were stratified by study characteristics or each component of study qualities. There was no heterogeneity in all subgroups evaluated ($I^2 = 0\%$).

## DISCUSSION

We summarized the prognostic value of BMIPP imaging to predict future cardiovascular events over the entire spectrum of CAD. Among patients with suspected ACS excluded for MI, the presence of reduced uptake on BMIPP imaging was significantly associated with future cardiovascular events, whereas the negative test provided greater assurance with an NPV of 98.9% (95% CI; 96.8-99.7%) for hard events over 3.5 years. In patients with AMI, the presence of a large defect on BMIPP imaging was an independent risk factor for future hard events. A few cohort studies suggested that BMIPP imaging could provide prognostic information for patients with stable CAD who underwent elective revascularization.

All these results using BMIPP imaging were obtained when patients were resting; patients do not need to be ‘‘stressed’’ by exercise or pharmacological agents. Ischemic memory imaging may therefore be advantageous for risk stratification of patients presenting with acute chest pain. The meta-analysis demonstrated that negative BMIPP imaging gave 98.9% (95% CI; 96.8-99.7%) assurance that patients will not develop cardiac death or myocardial infarction over 3.5 years. Even though these results were based on small-sized studies (as suggested by the wide confidence interval), the prognostic value of BMIPP imaging in this population was comparable with MPI and exercise echocardiography, in which NPVs were 98.8% (95% CI 98.5-99.0%) over 36 months and 98.4% (95% CI 97.9-98.9%) over 33 months, respectively, in a recent meta-analysis.[21]

On the other hand, NPV of BMIPP imaging for soft events is 92.3% (88.3-95.1%) over 3.5 years, which is lower than those of MPI (NPV 96.6%; 95% CI 95.6-97.4%) or exercise echocardiography (NPV 97.4%; 95% CI 95.2-98.7%). We previously demonstrated that BMIPP imaging has higher specificity but lower sensitivity to detect CAD than MPI or stress echocardiography. This suggests that threshold of suppression of fatty acid metabolism under ischemia may be higher than the threshold of a stress-induced perfusion abnormality or wall motion abnormality, and therefore BMIPP imaging may fail to detect minor ischemic episodes. More importantly, referral bias (in which the result of BMIPP imaging affects the decision for referral to coronary angiography) is implicated for a higher rate of revascularization in studies for BMIPP imaging. Fifty-three percent of participants in one study underwent coronary angiography, which may be related to a higher chance of receiving subsequent revascularization.[11] The mean age in studies for BMIPP imaging was 64 years, much higher than those in studies for MPI or for stress echocardiography, which had a mean age of 52 years and 54 years, respectively. This suggested a difference in the baseline risk of developing soft events.

The meta-analysis also demonstrated that the presence of a larger defect on BMIPP imaging after AMI was an independent risk factor for future hard events. Such defects may represent stunned, hibernating, or irreversibly damaged myocardium, all of which can cause abnormalities in fatty-acid metabolism. Studies included in the review excluded patients with previous myocardial infarction, so defect size on BMIPP imaging after AMI should be proportional to the size of the myocardium at risk in the distribution of the culprit lesion before reperfusion therapy. It has been shown that BMIPP imaging 1 week after reperfusion is similar to Tc99m-tetrofosmin perfusion imaging during the acute phase of myocardial infarction (ischemic memory imaging).[22] This suggests that the impairment of uptake and metabolism of fatty acids after recovery of perfusion in AMI may persist for $\geq$1 week. A larger defect of BMIPP uptake after AMI suggests occlusion of the coronary artery supplying the larger territory of the myocardium, and therefore a worse prognosis.

The defect on BMIPP imaging can be further classified by identifying the specific pattern of perfusion-metabolism abnormalities compared with myocardial perfusion imaging. A mismatch pattern in which BMIPP uptake is lower than uptake of perfusion tracer suggests a stunned or hibernating myocardium, whereas a concordant reduction of both uptakes suggests a scarred myocardium. The meta-regression analysis suggested that the prognostic value of perfusion-metabolism mismatch is dependent upon the timing of BMIPP imaging relative to revascularization.

It has been shown that the presence of a mismatched pattern in a dysfunctional myocardium before revascularization is associated with fewer hard events after successful revascularization.[20] This suggests that the mismatched myocardium before revascularization represents a hibernating myocardium or a jeopardized (but viable) myocardium. Successful revascularization of such a myocardium may therefore confer survival benefit. Patients without a mismatched myocardium, suggesting the lack of a viable myocardium or a scarred myocardium, may not benefit from revascularization. The prognostic value of BMIPP imaging before revascularization has also been demonstrated in several studies: the presence of perfusion-metabolism mismatch on BMIPP imaging before revascularization is significantly associated with regional wall-motion recovery.[23,24] These evidences suggest that BMIPP imaging can differentiate a viable myocardium from an irreversibly injured, non-viable myocardium in patients with a dysfunctional myocardium. BMIPP imaging may therefore be useful for the planning of revascularization to determine which patients benefit from revascularization.

The meta-regression analysis suggested that, the later after revascularization the perfusion-metabolism mismatch occurs, the more hard events occur. This suggests that the prognostic value of the stunning or hibernation of the myocardium (both of which show perfusion-metabolism mismatch on BMIPP imaging) are quite different. In general, a mismatched pattern immediately after AMI with successful revascularization represents a stunned myocardium or transient ischemia, and carries a relatively lower risk for future hard events. The presence of a mismatched myocardium later after revascularization may represent a hibernating or chronically ischemic myocardium despite previous revascularization, and is therefore associated with more adverse outcomes. The present study therefore suggests that the clinical significance of perfusion-metabolism mismatch (stunning or hibernation) on BMIPP imaging should be considered alongside clinical history, including the timing of revascularization and myocardial perfusion damage.

The meta-regression analysis was conducted in a small number of studies in which the patient population was heterogeneous: two included patients with chronic CAD and four included patients with AMI. Among them, only one study examined the prognostic value of BMIPP imaging before revascularization. The usefulness of BMIPP imaging in the planning of revascularization or for the assessment of successful revascularization therefore had limited statistical power related to the meta-regression analysis. This phenomenon should be confirmed by large, prospective randomized controlled trials.

## LIMITATIONS

The present systematic review was limited by the small number of studies available for analysis, which made precise estimation of the prognostic value of BMIPP imaging difficult. In addition, the qualities of included studies were heterogeneous. Although subgroup analyses did not show the effect of study quality on observed results, low-quality studies (particularly retrospective studies or studies without a blind adjudication of clinical outcomes) may have biased the results in favor of showing the effectiveness of BMIPP imaging. Despite these limitations, we believe that pooling of all currently available data by using meta-analytic techniques provided the most valuable information available.

## CONCLUSION

The systematic review of current literature (mainly from Japan) suggested that an abnormal finding on BMIPP imaging was significantly associated with future cardiovascular outcomes across the spectrum of CAD. BMIPP imaging with the patient at rest is particularly useful for the risk stratification of patients with acute chest pain, with a similar NPV for future hard events as compared with myocardial perfusion imaging. A larger, prospective, randomized controlled trial is warranted to confirm these promising findings on the prognostic value of BMIPP imaging for CAD.

## Disclosure

*Dr. Bergmann has previously received grant support and served as a consultant to Molecular Insight Pharmaceuticals, Incorporated, which is involved in the manufacture of BMIPP.*

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