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| journal or publication title | Annals of Nuclear Medicine |
| volume | 23 |
| number | 4 |
| page range | 373-381 |
| year | 2009-06-01 |
| URL | http://hdl.handle.net/2297/17578 |

doi: 10.1007/s12149-009-0248-2

# Prognostic value of myocardial perfusion and ventricular function in a Japanese multicenter cohort study (J-ACCESS): The first-year total events and hard events.

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Ann Nucl Med. 2009 Apr 14. [Epub ahead of print]

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## ABSTRACT

*Objective* To determine the prognostic value of myocardial ischemia, function and coronary risk factors on total and hard cardiac events using myocardial perfusion imaging in a Japanese population.

*Methods* A prospective cohort study was performed in 117 Japanese hospitals, each with a nuclear cardiology facility. A total of 4,031 patients with suspected or confirmed ischemic heart disease were registered. The patients were followed up for a year to investigate total and hard events, and those who had any events were followed up for 3 years to evaluate subsequent hard events. A stress-rest gated myocardial perfusion study was performed with $^{99m}$Tc-tetrofosmin using gated single-photon-emission computed tomography (SPECT) and analyzed by semi-quantitative scores.

*Results* During the one-year follow-up period, 263 (6.5%) patients had total events comprising all-cause death, non-fatal myocardial infarction (MI), heart failure, unstable angina, angina pectoris and coronary revascularization. Cardiac death occurred in 23 patients (0.6%) and non-fatal MI in 11 (0.3%). Among patients with ejection fraction (EF) of <45% and a summed difference score (SDS) of ≥2, 18.7% (2.4% for cardiac death and 0.6% for non-fatal MI) experienced total events compared with 3.9% (0.3% for cardiac death and 0.2% for non-fatal MI; p <0.0001) of those with EF ≥45% and SDS <2. Multivariate analysis identified EF, SDS, age, history of revascularization and diabetes as significant predictors of all events, while the significant predictors were age and EF for hard events. When the patients who had heart failure in the first year were followed up, 9 of 41 (22.0%) experienced cardiac death in the subsequent three-year follow-up period.

*Conclusion* Myocardial ischemia defined by SDS and ventricular function were the main predictors of total events despite the relatively low incidence of hard events in this Japanese population. In patients with cardiac events in a year, closer attention should be paid to subsequent hard events particularly in patients with heart failure.

**Key Words**: Myocardial perfusion imaging, gated SPECT, prognosis, multi-center study, cardiac events

## INTRODUCTION

Nuclear cardiology tests have been applied to patients with suspected and proven coronary artery diseases for optimal diagnosis and prognostic evaluation. Risk stratification in patients with a clinical risk of a subsequent cardiac event has been considered an important objective of nuclear cardiology. [1] The possibility of a different role of nuclear cardiology for risk evaluation among the Japanese population has been discussed because such a population has a relatively low disease prevalence and mortality, milder ischemic events, and different aspects of underlying risks for coronary artery diseases.[2-4]

We therefore performed a multi-center cohort study to establish a database called the Japanese Assessment of Cardiac Events and Survival Study by quantitative gated single-photon emission computed tomography (SPECT) (J-ACCESS) involving 117 hospitals and 4,629 patients who were consecutively registered for follow-up.[5, 6] Therefore, the study reflected average nuclear cardiology practice in Japan. According to the initial summary of hard cardiac events during the 3-year follow-up period (n=4,031), hard events occurred in 2.4% of the patients; namely, cardiac death (1.4%) and non-fatal myocardial infarction (MI) (1.0%). The annualized cardiac event rate after normal myocardial perfusion SPECT was 0.5% for hard events and 0.8% if severe heart failure requiring hospitalization was included. Although left ventricular (LV) volumes and ejection fraction (EF) were important factors for predicting cardiac events in addition to semi-quantitative summed stress score, stress-induced ischemia (summed difference score) was not the primary predictor of hard events.

In the present study, we postulated that induced ischemia detected by myocardial perfusion SPECT was related to the rate of total events, including unstable angina, heart failure, coronary intervention and bypass grafting. The present study analyzes the Japanese large-scale SPECT database with specific focus on the relationship of total and hard events over a one-year period to determine the role of nuclear cardiology in a Japanese population. Subsequent hard events by the third year following the initial cardiac events were also investigated.

## PATIENTS AND METHODS

### Subjects

The principal design of the J-ACCESS study is described elsewhere.[5] The registration period was between October 1, 2001 and March 31, 2002. The patients underwent stress and rest myocardial perfusion SPECT using electrocardiographically gated $^{99m}$Tc-tetrofosmin SPECT. The inclusion criteria included patients ≥ 20 years of age who were undergoing stress-rest gated SPECT due to suspected or known ischemic heart diseases. A total of 4,629 consecutive patients were registered at 117 hospitals. Since 223 patients (4.8%) were lost to follow-up, the prognostic data were derived from a follow-up of 4,406 of the patients (95.2%). Early revascularization within 60 days of the SPECT study was excluded from the analysis, [7] and 4,031 patients were analyzed for first-year events in the present study. Patients with onset of MI or unstable angina pectoris within 3 months, valvular heart disease, idiopathic cardiomyopathy, severe arrhythmia, heart failure with class III or higher New York Heart Association (NYHA) classification, and severe hepatic or renal disorders were excluded.

### Myocardial perfusion imaging

Most of the hospitals (99%) used a one-day protocol for stress and rest SPECT studies. The standard dose of $^{99m}$Tc-tetrofosmin was administered, with mean doses of 305 and 709 MBq for the first and second studies, respectively. Only a few hospitals (1%) used a 2-day protocol. Either an exercise (69%) or pharmacological stress (31%) protocol was used, with dipyridamole or adenosine triphosphate used in the latter . All institutions used multi-detector SPECT systems. Patients were examined by gated SPECT at least under a resting condition. The SPECT image acquisition conditions are described elsewhere in detail.[8]

### Quantitative and visual analysis of SPECT data

Quantitative gated SPECT data were analyzed at all hospitals using QGS software (Cedars Sinai Medical Center, CA, USA) and standard automated

processing methods with manual modification if necessary. The parameters of EF (%), end-diastolic volume (EDV, mL) and end-systolic volume (ESV, mL) were calculated at each institute. Visual scoring used the validated 20-segment model, and defects were scored from 0 to 4 in individual segments as 0, normal; 1, mildly reduced; 2, moderately reduced; 3, severely reduced and 4, absent.[9] The summed stress score (SSS) and the summed rest score (SRS) were calculated. The summed difference score (SDS) was defined as the difference between the SSS and the SRS, and was indicated as the amount of stress-induced ischemia. The severity of myocardial perfusion defects for the prognostic model was categorized into normal (0 - 3), mild (4 - 8), moderate (9 -13) and severely (> 13) abnormal SSS.

Reproducibility of quantification

The precision of the QGS parameters or preference-based variability among institutions was excellent, with the standard deviation of EF being < 3.6% and the coefficient of variation of EDV being < 9.3%.[10] All images were scored at the 117 participating hospitals. It was necessary to provide support to hospital staff in interpretation and quantification of typical SPECT images. We also compared the segmental scores between participating hospitals and the Image Evaluation Committee using a sample group of 81 studies. The agreement of summed scores was good (kappa, 0.85).

Patient follow-up and definition of cardiac events

Physicians at each hospital investigated the types of cardiac events 1 year after registration based on medical records. We used one-year analysis in this study, because we considered the practical importance of predicting every type of event at an early year. Indeterminate medical records were confirmed by written questionnaires and by direct telephone interview. Hard cardiac events were defined as cardiac death and non-fatal MI. Total events were defined in addition to hard events as death from non-cardiac causes, unstable angina, newly diagnosed angina pectoris, heart failure, coronary intervention and coronary bypass grafting. The description of angina symptom preceded to PCI and CABG was classified into the events of PCI

and CABG, respectively. The end point of follow-up was any of the initial events listed above. Patients with at least one event within the previous year were followed up to identify subsequent hard events in the second and third year. The number of hard events included in the above total events was analyzed for comparison.

### Ethics approval

The institutional review board at each of the involved hospitals approved the J-ACCESS protocols, and written informed consent was obtained from all patients who participated in the study.

### Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD). We applied the Wilcoxon rank sum test to compare results from patients with and without cardiac events, and the $\chi^2$ test to categorical data. The independent variables in the univariate Cox proportional hazard model included age, gender, cardiac risk factors (chest pain, body mass index, hypertension, dyslipidemia, diabetes mellitus, smoking history, family history of coronary artery disease, prior MI and revascularization), summed scores, QGS parameters of EF and volumes. The multivariate Cox proportional hazard model was applied using a forward stepwise method. Statistical significance was defined as $P < 0.05$.

## RESULTS

### Patient characteristics

Table 1 shows the demographics of the patients. The average age was 65.9 ±10.1 years. A history of MI and diabetes each was identified in ~30% of the patients, and dyslipidemia was evident in ~50% of them. The EF determined by QGS was 62%±14%, and EDV was 85±36 mL.

### Cardiac events

A total of 263 patients (6.5%) experienced cardiac events within one year, of which 23 (0.6%) were cardiac death and 11 (0.3 %) were non-fatal MI. Figure 1

shows that the incidences of diabetes, a history of myocardial infarction and hypertension were higher in the event group. The frequency of dyslipidemia and smoking did not significantly differ between the groups.

The initial events and subsequent events during the first year are listed in Table 2. The diagnosis of angina pectoris without additional cardiac events in the first year (n=22) was confirmed by coronary angiography (n=16) and history of coronary revascularization (n=4). In the remaining two patients, the diagnosis of angina pectoris was clinically made 192 days and 316 days after the registration, and the patients were medically treated without coronary angiography. The initial events were angina pectoris (n=23), PCI or CABG (n=135), heart failure (n=41), non-fatal MI (n=10) and all-cause death (n=54). When subsequent hard events were observed, one had non-fatal MI and six had cardiac death within a year. Figure 2 summarizes what types of hard events followed after the events of the first year. When the patients were followed up by the third year, 5 patients had cardiac death and 5 patients had non-fatal MI in the second and third years. Following the medically treated angina (n=23), 2 patients (8.7%) had non-fatal MI. Patients with PCI as the first event had repeated revascularization in a year in 11 of 114 patients (9.6%), and 5 (4.4%) had hard events by the third year, whereas after CABG (n=21), no patients had hard events during the follow-up period. Conversely, in 41 patients with non-severe (n=4) and severe heart failure (n=37), cardiac death occurred in 9 patients (22.0%). Average EF, EDV, SSS, SDS of the heart failure patients without cardiac death (n=32) were 42±16% and 136±65ml, 21±16 and 2±4, respectively; whereas those with cardiac death (n=9) were 40±15% and 150±93 ml, 14±16 and 2±4, respectively (p=n. s. for all). Significant coronary stenosis or subsequent revascularization were observed in 2 of 9 patients with cardiac death (22.2%) and 14 of 32 patients without cardiac death (43.4%) (p=n. s.).

Patients with total events were older and comprised a higher ratio of males than those without total events (Table 3). During the follow-up, patients with cardiac events had higher SSS ($p < 0.0001$) and SDS ($p < 0.0001$) than those without events. The EF was lower ($p < 0.0001$) and ESV was higher ($p < 0.0001$) in the group with cardiac events in comparison to that without cardiac events.

Table 4 summarizes the effects of EF, ESV, SSS and SDS on cardiac events. Event rates were 3-fold higher among patients with EF < 45% than those with EF ≥ 45% (15.6% vs. 5.5%, p < 0.0001). The ratio of hard event rates included in total events was 0.6% and 2.6% in patients with EF ≥ 45% and < 45%, respectively. The incidence of total event rates was also higher among male and female patients with ESV ≥60 mL and ≥40 mL, respectively (p < 0.0001), using cutoff values for Japanese.[8] Patients with higher SSS and SDS had higher total event rates (p < 0.0001), in which SDS was significant for total events. The total event rates proportionally increased according to the increase in SSS categories (p < 0.0001) (Figure 3). The occurrence of hard events was <0.6% for patients with SSS ≤ 8, and >1.5% for SSS ≥ 9 (p = 0.0027).

When cardiac event rates were analyzed with a threshold of SSS = 9 (a threshold value between slight and moderate severity) and with the presence of diabetes, the event rate was highest (12.5%) for diabetic patients with SSS ≥ 9, but decreased for non-diabetic patients with SSS ≥ 9 (9.0%), diabetic patients with SSS < 9 (6.4%) and non-diabetic patients with SSS < 9 (4.1%) (p < 0.0001, Figure 4A). The hard event rates were lower but were decreased in this order (p<0.0001). When analyzed with the threshold of SDS = 2 and EF = 45%, total event rates of patients with SDS≥2 and EF <45% were 4.8-fold higher than those with SDS<2 and EF≥45% (p<0.0001). In patients with EF ≥ 45%, event rates were higher among those with SDS ≥ 2 than those with SDS < 2 (p = 0.0001, Figure 4B). The $\chi^2$ test for trend was significant for both total (p<0.0001) and hard (p=0.0003) event rates.

Univariate and multivariate Cox regression analyses

Risk factors and SPECT parameters analyzed for predicting cardiac events with a univariate Cox regression model revealed that significant variables included a history of MI (Hazard ratio, 1.706, p < 0.0001), diabetes (1.586, p = 0.0003), hypertension (1.308, p = 0.0337), age (1.028, p < 0.0001) and body mass index (BMI) (0.956, p = 0.0219). All values of SSS, SRS, SDS, EF, EDV and ESV were significant and included hazard ratios of 1.030, 1.024, 1.078, 0.965, 1.008 and 1.010, respectively (p < 0.0001 for all). Table 5 summarizes the principal independent

variables that were finally accepted by a multivariate model. Variables of EF, SDS, age, history of revascularization and diabetes were significant predictors in the order of $\chi^2$ values for total events. On the other hand, age and EF were significant predictors for hard events.

Incremental values of clinical factors and ischemia

Global $\chi^2$ values were calculated by a Cox proportional hazard model using combinations of age, diabetes, history of revascularization, SDS and ESV (Figure 5). The global $\chi^2$ values by adding parameters in this order were 15.5, 26.8, 51.8, 93.5 and 148.0, respectively. Adding SDS to the combination of age, diabetes and history of revascularization yielded 1.8-fold $\chi^2$ values in the prediction of total events.

## DISCUSSION

The J-ACCESS investigation is the first large-scale prognostic study using myocardial perfusion SPECT data from an Asian population. We previously summarized prognostic values of myocardial perfusion gated SPECT for predicting hard events and found that the frequency of hard events was significantly lower in a Japanese population than in populations focused on in US studies.[6] When total events were analyzed in the present study, stress-induced ischemia was a significant predictor of future events. The main conclusion of this study was that the hard event rate was significantly affected by baseline LV function, whereas total events were determined by both induced ischemia and ventricular function. Diabetes was one of the most important predictors for cardiac events in Japan, for both total and hard events. The importance of intensive care following the first year's events should be emphasized.

The evidence level of nuclear studies in the Japanese population has remained limited, and significant predictors of cardiac events differ among studies. One Japanese study examined cardiac events in elderly patients using quantitative gated SPECT.[11] Of 18 total cardiac events among 175 registered patients, only 2

cardiac deaths and 1 non-fatal MI occurred during 3.4 years of follow-up. Another investigation of mid-term follow-up (average period of 26.9 months) in a hospital included a $^{201}Tl/^{99m}Tc$ dual nuclide study of 1988 patients.[12] The annual event rates of cardiac death were 0.1% and 2.9% for SSS 0 - 3 and > 13, respectively, and non-fatal MI and unstable angina occurred in 0.9% and 2.4% for SSS 0 - 3 and > 13, respectively. Although these studies suggested a relatively low incidence of hard events, statistical analysis necessitated far more patients considering the low incidence of cardiac death. The first J-ACCESS report thus confirmed the low incidence of hard events from the Japanese multi-center study, and this study demonstrated an additional role of stress-induced ischemia for total events.

The prognostic value of combined myocardial perfusion and ventricular function has been studied. The LV EF provides incremental prognostic information over perfusion in predicting cardiac death, whereas stress-induced ischemia predicts acute coronary syndromes.[7, 13-15] A European study by Petix et al. found that the most powerful predictor of all cardiac events was the degree of myocardial ischemia, while adding ventricular function data yielded an incremental value for predicting hard events but not all events.[14] Although the settings differed among these studies, our data suggested a closer relationship between hard events and baseline LV function and between all events and both stress-induced ischemia and LV function in our population. Shaw et al. studied the role of resting and stress myocardial perfusion imaging, and found that rest imaging might be reflective of a patient's baseline risk, whereas stress ischemia is defined as a risk inherent in the presenting symptom burden.[16] The baseline LV function may be related to EF, ventricular volume and myocardial perfusion defect in the resting condition. The present study demonstrated that the combination of perfusion and ventricular function determined by gated SPECT helped to predict cardiac events, which is consistent with a recent Japanese prognostic study in acute coronary syndrome. [17]

Since SDS yielded significant prognostic power for predicting total events by global $\chi^2$ analysis, the incremental value of myocardial ischemia over clinical background factors and ventricular function was demonstrated. The insignificant effect of SDS on hard events in the initial J-ACCESS summary was not anticipated,

but it might be explained partly by the consecutive patient registry in multiple centers. Although the registration was performed in patients suspected of having ischemic heart disease, the relatively low-risk profile of Japanese patients for coronary artery disease and selection biases between Japan and Western countries might also be related.

The total-event analysis showed that diabetes and history of revascularization were important predictors. Additional predictors of gender, hypertension and prior MI were identified by univariate analysis. Hayes et al. reported similar univariate predictors from total events, including age, gender, hypertension, diabetes, history of MI and revascularization, adenosine stress and SSS.[18] Elhendy et al. examined predictors of cardiac events after revascularization using $^{99m}$Tc tetrofosmin.[19] They found by using the multivariate Cox model that male gender, diabetes, stress rate-pressure product and an abnormal scan were predictors of hard events, whereas male gender, diabetes and reversible defects were selected for all events. Shaw et al. emphasized the importance of metabolic syndrome and diabetes with multiple risk factors for enhancing cardiovascular risks, in which the prognosis of patients with five risk factors was particularly poor.[20] Finally, we emphasized that diabetes is one of the most important predictors in all Western and Japanese studies.[3, 9, 18-21]

The J-ACCESS investigation can be fed back to clinical practice in a Japanese population. The factor of myocardial ischemia would become an important predictor for total events. Moreover, ~10% of patients with PCI as the first event repeated revascularization in a year, and 4.4% had hard events by the third year. The event rate reflected the recent prognostic course in Japanese clinical practice and was comparable to that of the J-SAP (Japanese stable angina pectoris) study conducted since 2001.[22] In the J-SAP 1-1 report, additional PCI and/or CABG was required in 33.2% of the group of PCI-preceding therapy in the average follow-up period of 3.4 years, and overall rate of cardiac death and acute coronary syndrome was 4.7% in the same period. Intensive care would be required following the first soft events. On the other hand, since an episode of heart failure in the first year was highly associated with subsequent cardiac death (22%), strategies to maintain or improve cardiac function should be sought to reduce cardiac death. Cardiac death following the first

episode of heart failure could not be predicted by the initial ventricular function. The ischemia-related scores of SSS and SDS could not predict cardiac death either, probably because their cardiac deaths might be related to subsequent deterioration of cardiac function in addition to ischemic events. Considering the low incidence of obesity, the insignificant impact of dyslipidemia and high impact of diabetes in a Japanese population, intensive care for diabetic patients might be of prime importance for reducing cardiac events. However, since lifestyle changes in Japan in recent decades have increased the prevalence of hypercholesterolemia and diabetes, attention should be paid to future trends for coronary risk factors in Japan.[4]

One of the limitations of this study is related to the participation of 117 institutions. When only a few institutions are involved in a large-scale study, diagnostic methods, therapeutic strategies and follow-up can be controlled quite uniformly. Conversely, when >100 hospitals are involved, as was the case in the J-ACCESS study, the diagnostic and therapeutic approaches including indications for interventions cannot be made strictly consistent. The indication bias towards revascularization also is related to different approaches to patients with slight ischemia between Japan and Western countries. Second, each institution performed quantitative evaluations. To overcome inter-institutional differences, we repeatedly provided support to the participants in scoring at several workshops, and variations in QGS results were also examined to minimize the effect of preference-based differences.[10]

## CONCLUSION

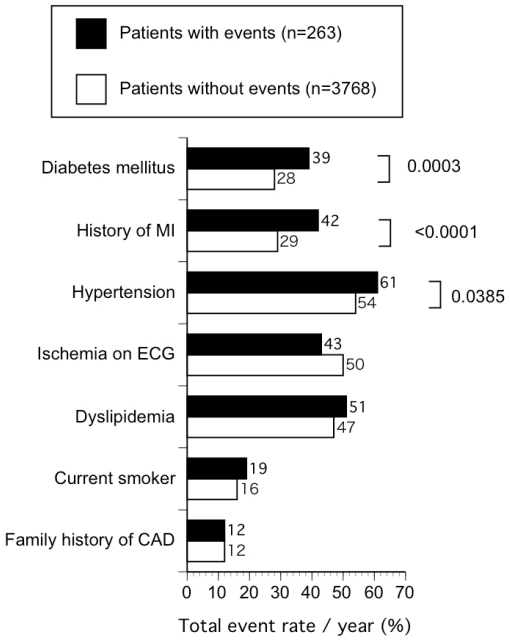
The J-ACCESS study demonstrated a relatively low incidence of hard events among Japanese, compared with American and European populations. When total and hard events were analyzed, myocardial stress-induced ischemia and ventricular function were the main predictors of total cardiac events, while baseline LV function affected the incidence of hard events. Diabetes was the most important predictor of cardiac events among coronary risk factors in this Japanese population, indicating a need for targeted efforts for its management . Careful treatment strategy should be considered after an episode of heart failure, because subsequent risk of hard events is

high.

## Acknowledgements

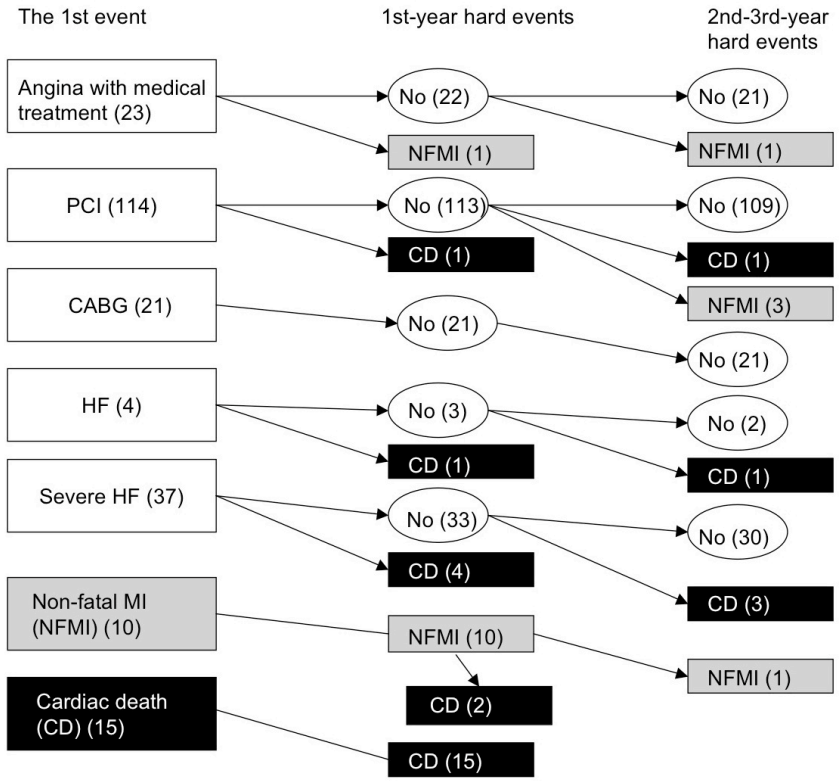
A list of participating institutions and physicians has been published elsewhere. [5] We thank a number of physicians and technologists at the participating hospitals for their cooperation with the J-ACCESS study The J-ACCESS study was supported by grants from the Japan Cardiovascular Research Foundation.

## FIGURES




### Figure 1

Incidence of associated clinical factors in patients with and without total events (black and white bars, respectively). MI, myocardial infarction; CAD, coronary artery disease




### Figure 2

The first event in a year and subsequent hard events in the second and third years. Number of patients is shown in parentheses.

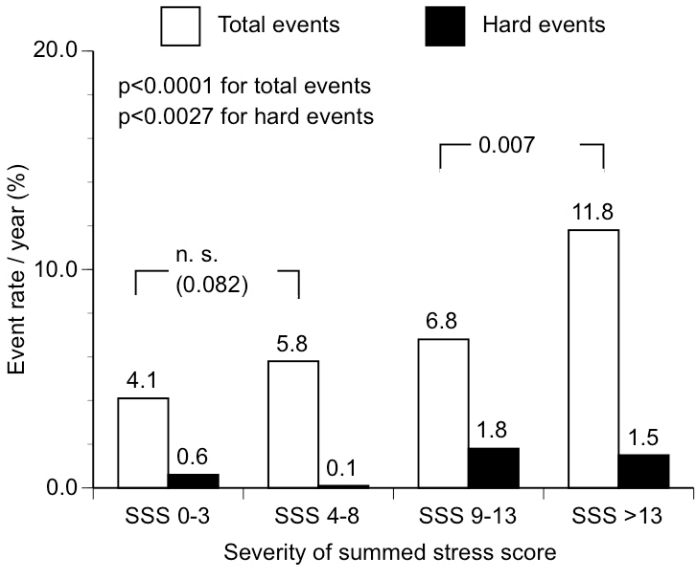



**Figure 3**

Event rates per year for SSS categories with no (0-3) mild (4 - 8), moderate (9 - 13) and severe (≥14) scores. $\chi^2$ values for trends are 136.0 ($p < 0.0001$) and 9.022 ($p=0.0027$) for the total and hard events, respectively. P values among 4 groups were based on $\chi^2$ test.

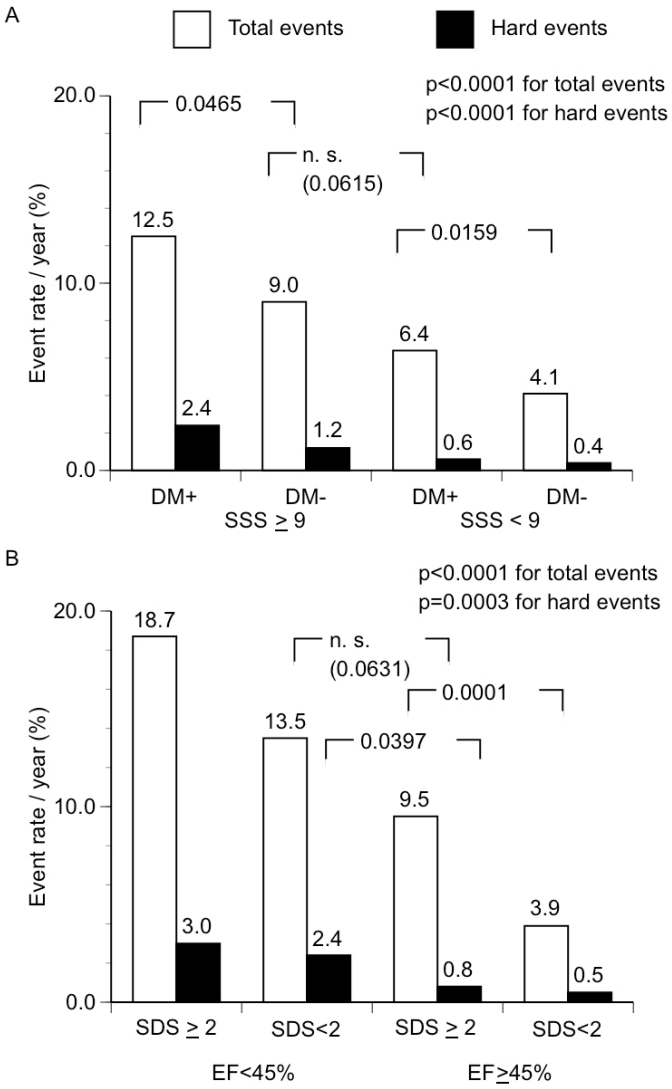



**Figure 4**

Total and hard events of cardiac death and non-fatal MI. Upper and lower panels indicate effects of diabetes and SSS, and of SDS and EF on total and hard events. Regarding diabetes and SSS, the $\chi^2$ value for the trend is 143.8 ($p < 0.0001$) and 17.1 ($p < 0.0001$) for total and hard events, respectively. Regarding EF and SDS, it is 162.1 ($p < 0.0001$) and 15.2 ($p = 0.0003$) for total and hard events, respectively. P values among 4 groups were based on $\chi^2$ test.

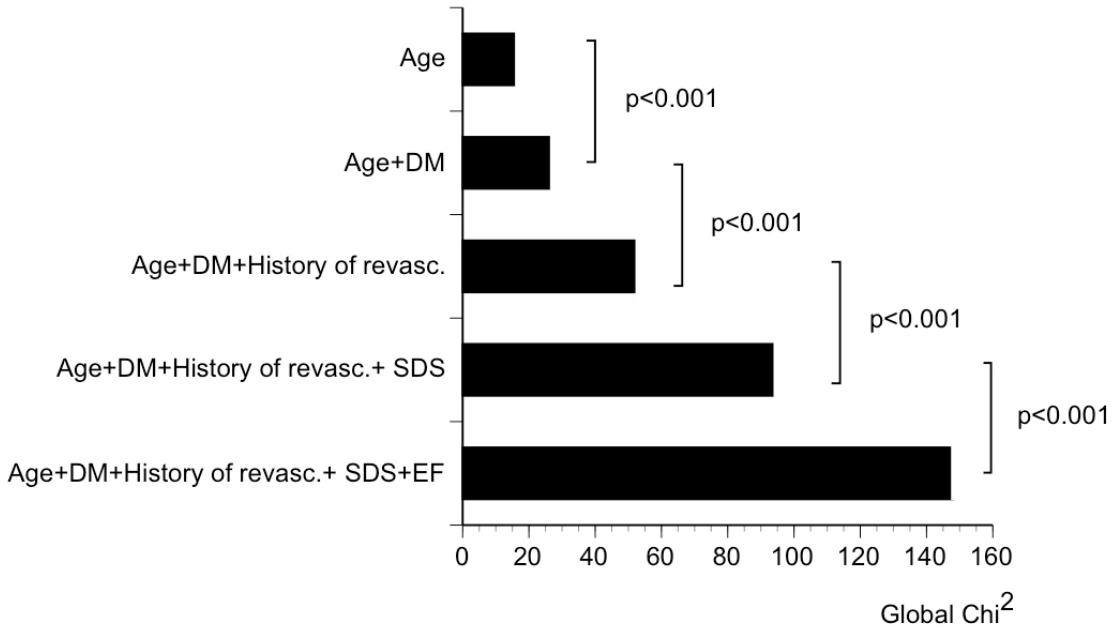



**Figure 5**

Incremental prognostic value of clinical and perfusion variables for predicting total cardiac events. Revasc., revascularization; DM, diabetes mellitus.

Table 1. Patient characteristics

| Characteristic | Mean±SD or % |
|---|---|
| Number of patients | 4031 |
| Background factors | |
| Age (years) | 65.9±10.1 |
| Male sex | 64% |
| Typical chest pain | 46% |
| BMI ($kg/m^2$) | 23.7±3.2 |
| Diabetes mellitus | 29% |
| History of MI | 29% |
| History of revascularization | 36% |
| Hypertension | 55% |
| Ischemia on ECG | 51% |
| Dyslipidemia | 47% |
| Current Smoker | 16% |
| Family history of CAD | 12% |
| Perfusion score and left ventricular function | |
| SSS | 8.7±11.2 |
| SRS | 7.3±10.6 |
| SDS | 1.4 ±3.8 |
| EF (%) | 61.9±13.6 |
| EDV (mL) | 84.7±36.0 |
| ESV (mL) | 35.8±29.0 |

Abbreviations

BMI, body mass index; MI, myocardial infarction; ECG, electrocardiogram; CAD, coronary artery disease; SSS, summed stress score; SRS, summed rest score; SDS, summed difference score; EF, ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume

Table 2. Initial event and subsequent events during the first year

| Initial event | Subsequent events | Subtotal | Total |
|---|---|---|---|
| Angina pectoris (medically treated) | | | 23 |
| | no additional events | 22 | |
| | non-fatal MI, severe HF, PCI, CABG | 1 | |
| PCI | | | 114 |
| | no additional events | 98 | |
| | re-PCI | 10 | |
| | CABG | 1 | |
| | severe HF | 4 | |
| | cardiac death | 1 | |
| CABG | | | 21 |
| | no additional events | 20 | |
| | PCI | 1 | |
| HF | | | 4 |
| | no additional events | 3 | |
| | cardiac death | 1 | |
| severe HF | | | |
| | no additional events | 26 | 37 |
| | CABG | 3 | |
| | cardiac death | 4 | |
| | PCI | 3 | |
| | severe HF | 1 | |
| Non-fatal MI | | | 10 |
| | no additional events | 1 | |
| | cardiac death | 1 | |
| | PCI | 5 | |
| | severe HF | 1 | |
| | severe HF, cardiac death | 1 | |
| | severe HF, PCI | 1 | |
| Death | | | |
| | cardiac death | 15 | 54 |
| | non-cardiac death | 39 | |
| | | | 263 |

MI, myocardial infarction; HF, heart failure; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; severe HF denotes HF requiring hospitalization for treatment.

Table 3. Background factors and SPECT results in patients with and without events

| Parameters | Total events | No events | p value |
|---|---|---|---|
| Number | 263 (6.5%) | 3768 (94.5%) | |
| Age (y) | 68.3 ±9.6 | 65.7±10.1 | <0.0001 |
| Male sex (n, %) | 188 (71%) | 2392 (63%) | 0.0109 |
| BMI (kg/m$^2$) | 23.3±3.2 | 23.7±3.2 | 0.0299 |
| SSS | 13.6±13.1 | 8.3±11.0 | <0.0001 |
| SRS | 10.7±12.2 | 7.0±10.5 | <0.0001 |
| SDS | 2.9±5.0 | 1.3±3.7 | <0.0001 |
| EF (%) | 54.9±14.9 | 62.4±13.3 | <0.0001 |
| EDV (mL) | 99.0±45.4 | 83.7±35.0 | <0.0001 |
| ESV (mL) | 49.5±38.9 | 34.9±27.9 | <0.0001 |

Abbreviations in Table 1

Table 4. Total events and hard events in a year

| | | Total event rate | | No. of hard events | | | |
|---|---|---|---|---|---|---|---|
| | N | Number (%) | p value | Cardiac death | Non-fatal MI | Total hard events | P value |
| Ejection fraction | | | | | | | |
| ≥45% | 3606 | 197 (5.5%) | | 14 (0.4%) | 9 (0.2%) | 23 (0.6%) | |
| <45% | 417 | 65 (15.6%) | <0.0001 | 9 (2.2%) | 2 (0.5%) | 11 (2.6%) | <0.0001 |
| End-systolic volume (mL) | | | | | | | |
| ≥60 (male) | 451 | 54 (12.0%) | | 4 (0.9%) | 2 (0.4%) | 6 (1.3%) | |
| <60 (male) | 2125 | 133 (6.3%) | <0.0001 | 7 (0.3%) | 7 (0.3%) | 14 (0.7%) | n. s. |
| ≥40 (female) | 137 | 25 (18.2%) | | 6 (4.4%) | 0 (0.0%) | 6 (4.4%) | |
| <40 (female) | 1310 | 50 (3.8%) | <0.0001 | 6 (0.5%) | 2 (0.2%) | 8 (0.6%) | <0.0001 |
| Summed scores | | | | | | | |
| SSS≥9 | 1372 | 140 (10.2%) | | 16 (1.2%) | 6 (0.4%) | 22 (1.6%) | |
| SSS<9 | 2659 | 123 (4.6%) | <0.0001 | 7 (0.3%) | 5 (0.2%) | 12 (0.5%) | <0.0003 |
| SDS≥2 | 1195 | 128 (10.7%) | | 9 (0.8%) | 4 (0.3%) | 13 (1.1%) | |
| SDS<2 | 2836 | 135 (4.8%) | <0.0001 | 14 (0.5%) | 7 (0.2%) | 21 (0.7%) | n. s. |

Abbreviations in Table 1

Table 5. Significant variables for cardiac events by Cox multivariate analysis

| Variables | Hazard ratio | 95% CI | Wald $\chi 2$ | p |
|---|---|---|---|---|
| Total events | | | | |
| EF | 0.969 | 0.961-0.977 | 71.0 | <0.0001 |
| SDS | 1.071 | 1.047-1.096 | 34.7 | <0.0001 |
| Age | 1.031 | 1.017-1.045 | 19.9 | <0.0001 |
| History of revascularization | 1.582 | 1.236-2.024 | 14.0 | 0.0002 |
| Diabetes mellitus | 1.315 | 1.021-1.693 | 4.5 | 0.0331 |
| Hard events | | | | |
| Age | 1.063 | 1.020-1.108 | 8.26 | 0.0041 |
| EF | 0.951 | 0.915-0.989 | 6.32 | 0.0119 |
| Diabetes mellitus | 1.836 | 0.913-3.694 | 2.90 | n.s. (0.0885) |

Abbreviations in Table 1

## References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