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REVIEW ARTICLE—JSNC AWARD

Clinical Value of Ischemia Evaluation with Nuclear Cardiology to Predict a Risk of Cardiovascular Events: Award from the 18th Meeting of the Japanese Society of Nuclear Cardiology

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Abstract

Nuclear cardiology is useful for risk stratification of major cardiac events (MCEs) in Japanese patients with coronary artery disease (CAD). Results of the J-ACCESS study demonstrated that the severity of the summed stress score (SSS) stratifies the risk of future MCEs. A normal SSS predicts a good prognosis and a higher SSS indicates a higher MCE risk. Investigating the association between therapeutic strategy and the risk of MCEs, we demonstrated that revascularization reduces the risk of MCEs in patients with >10% ischemia while optimal medical therapy achieves the same outcome in patients with ≤5% ischemia. We also formulated a risk equation on the basis of evidence obtained from nuclear cardiology to predict the risk of MCEs excluding severe heart failure. In order to benefit from such evidence, it is necessary that expert interpreters precisely evaluate ischemia based on images derived during nuclear cardiology studies. However, automated quantification with total perfusion deficit does not require expert interpreters. We have reported the usefulness of automated quantification with the total perfusion deficit derived from a Japanese normal database in Japanese patients with CAD. Ischemic data obtained from nuclear cardiology are extremely useful for predicting MCEs in patients with CAD. A therapeutic strategy guided by the ischemic data facilitates good medical management with an associated improved prognosis.

Keywords: Automated quantification, Cardiac event risk stratification, Myocardial perfusion SPECT, Risk score
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Myocardial perfusion single-photon emission computed tomography (SPECT) is useful for evaluating ischemia and predicting major cardiac events (MCEs) in Japanese patients with coronary artery disease (CAD). The severity of the summed stress score (SSS) stratifies the risk of future MCEs. Results of a multicenter prospective Japanese Assessment of Cardiac Events and Survival Study in patients with ischemic heart disease (J-ACCESS) demonstrated that a normal SSS is predictive of a good prognosis and a higher SSS indicates a higher risk of MCEs (1). Evaluation of ischemia with SPECT is regarded as the gold standard in the Japanese Circulation Society guideline for nuclear cardiology based on the results of a series of J-ACCESS studies including a subsequent J-ACCESS II in asymptomatic patients with diabetes mellitus (DM) (2), J-ACCESS III in patients with chronic kidney disease (CKD) (3), and many sub-studies. This article summarizes the usefulness of data on ischemia evaluated with SPECT for predicting MCEs on the basis of results obtained from our studies.

Therapeutic strategies and future cardiac events in patients with stable CAD

Hachamovitch et al. reported that early revascularization improved prognoses in patients with ≥10% ischemia detected

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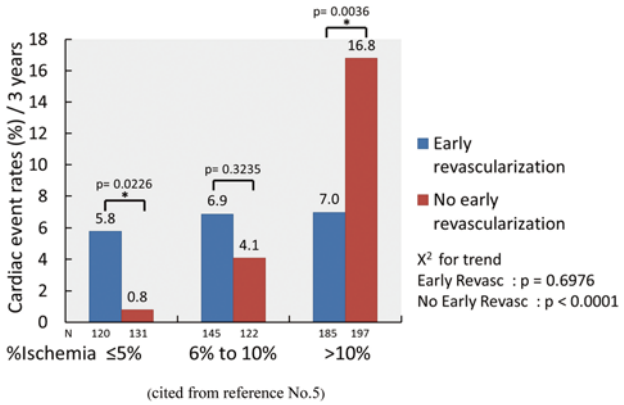

(cited from reference No.5)

Fig. 1 Cardiac event rates during the three-year follow-up between propensity score-matched patients with ≤5%, 6% to 10%, and >10% ischemic myocardium (cited from reference No.5)

with SPECT while medical treatment was effective in patients with <10% ischemia (4). Since there was no such evidence for Japanese patients, we investigated the correlation between therapeutic strategies and prognoses in Japanese patients with stable CAD to determine whether early revascularization affects the incidence of MCEs excluding severe heart failure. In propensity score-matched patients, the prognosis in the early-revascularization group was similar to that in the no-early-revascularization group. Of those, however, patients with >10% ischemia had a better prognosis and lower MCE rates in the early-revascularization group than in the no-early-revascularization group. In contrast, patients with ≤5% ischemia had a better prognosis and lower MCE rates in the no-early-revascularization group than in the early-revascularization group (Fig. 1). According to the above, we concluded that early revascularization may possibly lead to MCEs due to the procedure but may be an effective therapeutic strategy leading to an improved prognosis in patients with moderate to severe ischemia (5). Regarding patients with 6% to 10% ischemia, there was no significant difference in the MCE rate between the early-revascularization and no-early-revascularization groups during the three-year follow-up. In such patients with borderline ischemia, risk-stratification with non-invasive fractional flow reserve, which is a physiological ischemic variable derived from coronary computed tomographic angiography, could be used to help determine a therapeutic strategy and could be predictive of prognoses in combination with SPECT. Fig. 2 illustrates typical polar maps obtained in CAD patients with >10% ischemia who had either a good or poor prognosis. The polar maps shown in Fig. 2 (a) were obtained from a 55-year-old male patient with typical angina. His SPECT image showed ischemia in the anteroseptal to apical area. The SSS, summed rest score (SRS), and summed difference score (SDS) were 18, 0, and 18 respectively. He underwent CAG, which showed 75% stenosis in the proximal region of the left anterior descending artery (LAD) and 75% stenosis in the middle region of the left circumflex artery (LCX). He underwent PCI for the stenosis in the LAD. Thereafter, he experienced no cardiac events. The polar maps shown in Fig. 2 (b) was obtained from a 77-year-old female patient with shortness of breath. Her SPECT image showed ischemia in the inferolateral area. The SSS, SRS, and SDS were 16, 2, and 14 respectively. CAG showed 90% stenosis in the proximal region of the LAD, 100% stenosis in the proximal region of the LCX, and 75% stenosis in the proximal region and distal region of the right coronary artery. She rejected coronary artery bypass grafting recommended as a therapeutic strategy and opted instead to receive medical treatment. Eventually, she experienced cardiac death.

Risk stratification of MCEs in patients with CKD

Patients with CKD are at high risk of MCEs even if they do not have symptoms. We have reported on the prediction of MCEs using baseline estimated glomerular filtration rate (eGFR) and SSS in patients at all stages of CKD including those on hemodialysis (6). The incidence of MCEs over one year increased in proportion to the progression of CKD. In addition, baseline eGFR, reduction in eGFR measured after one-year follow-up, and SSS were significant independent predictors of cardiac death and combination of cut-off values, i.e. 10 for reduction in eGFR and 9 for SSS, stratified the risk of cardiac death in patients with CKD (7).

Prediction of MCEs with a risk score

The Heart Risk Table based on nuclear cardiology is a useful tool for estimating the incidence of MCEs, including severe heart failure, in Japanese patients with CAD (8). We conducted a large-scale retrospective prognostic study to come up with a formula that would provide risk scores for MCEs excluding heart failure over a three-year period (9). The results showed that the factors predicting MCEs were clearly different from those predicting only cardiac death (Table 1). Age, SSS, and eGFR were common factors predicting MCEs including cardiac death. In addition to these, presence of DM was a predictor of MCEs and stress left ventricular ejection fraction was a predictor of cardiac death. Consequently, we formulated the following two different risk equations: MCE risk (%/3 years)＝1/{1＋Exp[-(-3.176＋0.018 × age＋0.602 × diabetes-0.022 × eGFR＋0.051 × SSS)]} × 100 and cardiac death risk (%/3 years)=1/{1+Exp[-(-2.602+0.031 × age-0.031 × eGFR+0.038 × SSS-0.029 × stress ejection fraction)]} × 100. MCE risks estimated using the equation were consistent with the actual incidence of MCEs showed by Kaplan-Meier analysis in patients who were not involved in the study or preparation of the risk equations (10).

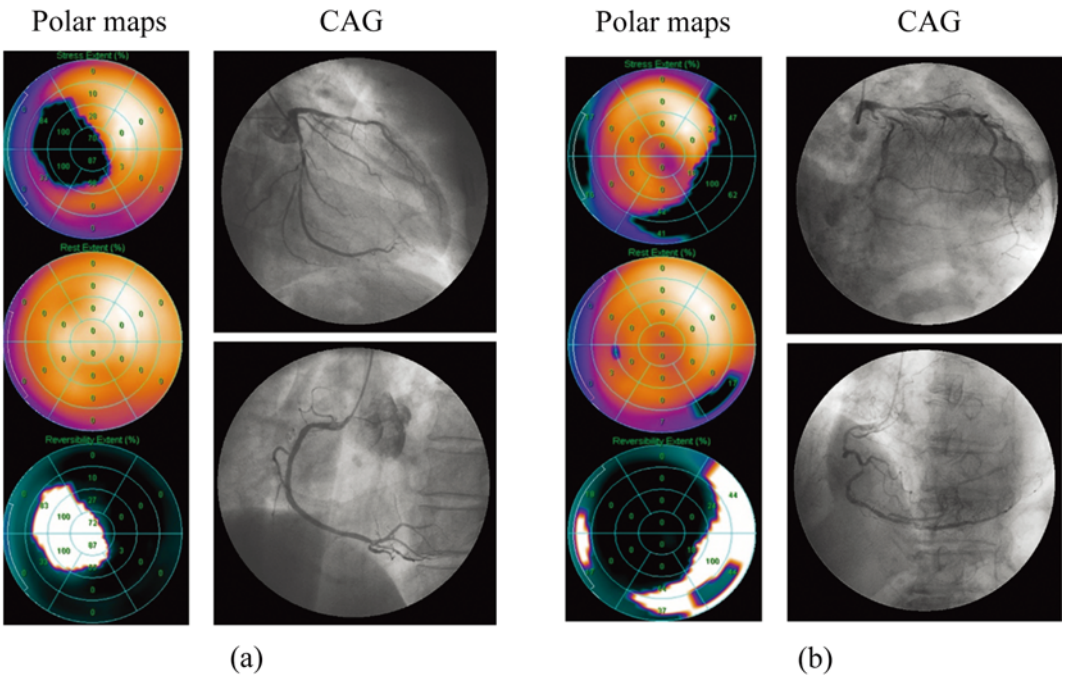

Fig. 2 Typical polar maps and coronary angiography (CAG) obtained in representative two patients with coronary artery disease having >10% ischemia

Table 1 Multivariate logistic regression analysis for risk of cardiac events

a. MCE prediction model

	Coefficient	Standard error	Odds ratio	95% CI	P value
Age	0.018	0.0090	1.0179	1.0001-1.0360	0.0490
Diabetes mellitus	0.602	0.1686	1.8271	1.3128-2.5428	0.0004
eGFR	-0.022	0.0035	0.9787	0.9719-0.9855	<0.0001
SSS	0.051	0.0070	1.0526	1.0382-1.0672	<0.0001
Constant	-3.176				

MCE: major cardiac event; CI: confidence interval; eGFR: estimated glomerular filtration rate; SSS: summed stress score.

b. Cardiac death prediction model

	Coefficient	Standard error	Odds ratio	95% CI	P value
Age	0.031	0.0132	1.0318	1.0053-1.0590	0.0185
eGFR	-0.031	0.0050	0.9698	0.9602-0.9796	<0.0001
SSS	0.038	0.0125	1.0392	1.0140-1.0649	0.0021
Stress LVEF	-0.029	0.0092	0.9710	0.9537-0.9885	0.0013
Constant	-2.602				

CI: confidence interval; eGFR: estimated glomerular filtration rate; SSS: summed stress score; LVEF: left ventricular ejection fraction.

Effective use of automated quantitative assessment index of ischemia

Total perfusion deficit (TPD) is an objective parameter automatically calculated by quantitative perfusion SPECT software with the normal database, representing both the severity and extent of a defect. The American Society of Nuclear Cardiology imaging guideline 2010 for SPECT describes automated quantification with the TPD as a useful method for assessing ischemia as well as the conventional visual quantification. However, automated quantification with the TPD had not been a method commonly used in Japan to evaluate ischemia in Japanese patients with CAD. We investigated the diagnostic value of TPD automatically derived from SPECT images through the software with the Japanese normal database and have confirmed the high diagnostic accuracy (11) and good reproducibility (12) of

automated quantification when using it in Japanese patients with CAD. The accuracy and reproducibility of automated quantification were comparable to conventional visual quantification. Automated quantification was also confirmed to be useful for prognostic risk stratification of MCEs (13).

Conclusion

The SSS and stress TPD correctly derived from SPECT images are useful for risk stratification and prediction of MCEs. The SDS and ischemic TPD are useful for determining an effective therapeutic strategy. A therapeutic strategy guided by the ischemic data facilitates good medical management with an associated improved prognosis. The risk score estimated with data obtained from SPECT can be used effectively in daily clinical practice because it is important to be able to explain benefits and risks to patients before deciding a therapeutic strategy.

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Conflict of interest

All authors declare that they have no conflict of interest.

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