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CHALLENGES AND OPPORTUNITIES IN NUCLEAR CARDIOLOGY FROM LATIN AMERICAN AND ASIAN PERSPECTIVES−REVIEW ARTICLE

Trends and Perspectives of Stress Myocardial Perfusion Imaging in Japan

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Abstract

Although ischemia should be evaluated before revascularization, stress myocardial perfusion imaging (MPI) is declining in Japan. On the other hand, computed tomography coronary angiography (CTCA) is increasing. Elective PCI increases in proportion to increase of CTCA. Fractional flow reserve (FFR) can also assess ischemia and identify the lesion for revascularization. FFR-guided revascularization improves prognosis, so FFR is increasingly used before PCI. However, elective PCI hardly decreases. FFR-CT can assess ischemia similar to FFR and correlated well with FFR. Therefore, the role of stress MPI as a gate keeper for CAG/PCI may be partially replaced by FFR-CT in the near future.

Keywords: Computed tomography coronary angiography, Myocardial perfusion imaging, PCI, Perspective, Trend

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Since the advantage of Fractional Flow Reserve (FFR)-guided reperfusion strategy is elucidated (1-3), major guidelines for coronary reperfusion highly recommend this strategy (4). FFR indicates severity of ischemia in each coronary branch and detects the most flow-limiting site. Therefore, target lesion can be easily identified. However, total ischemic burden (myocardium) is hardly estimated. The total ischemic myocardium is one of the most powerful predictors of prognosis in patients with coronary artery disease (CAD) (5, 6), and myocardial perfusion imaging (MPI) is the most popular modality to estimate total ischemic burden. In addition, ischemia-guided revascularization using MPI demonstrated favorable prognosis similar to the FAME studies (7).

History of MPI in Japan

^{201}Thallium (^{201}Tl) is approved by the Japanese Ministry of Health, Labor, and Welfare (JMHLW) in 1987 for diagnosis of heart disease (8). Then stress MPI using ^{201}Tl is initiated using planar imaging which was less sensitive to detect CAD compared to the single photon emission computed tomography (SPECT) because some areas overlap, such as apex and inferior wall in left anterior oblique planar projection. ^{201}Tl is an analog of potassium and requires only single injection for stress-rest protocol because of its redistribution nature. ^{201}Tl is still the most prevalent perfusion tracer in Japan probably due to its handy characteristic. ^{99m}Tc sestamibi and ^{99m}Tc tetrofosmin were approved in 1993 and 1994, respectively (8, 9). Multiple-head gamma cameras were introduced in late 1980's, and MPI studies increased as multiple-head gamma cameras prevalent because throughput and image quality were improved (10). Germano et al. developed Quantitative Gated SPECT (QGS) program using electrocardiography (ECG) gated SPECT acquisition in 1995 (11). This program makes it possible to assess myocardial perfusion and function simultaneously, which has incremental diagnostic value. Therefore, stress MPI increased further until 2002 (8). Multi-detector computed tomography was developed around 2000, and 64-row CT scanners were prevalent around 2004 in Japan. Computed tomography coronary angiography (CTCA) be-

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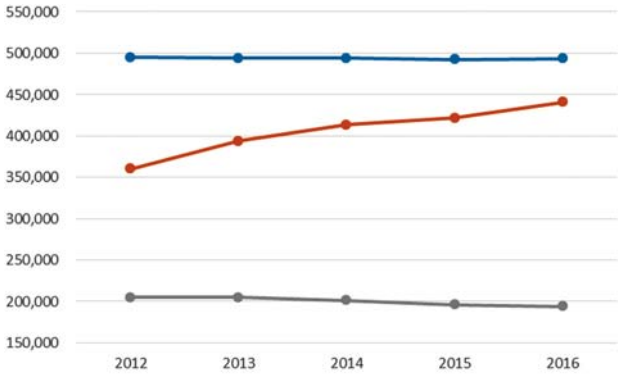

Fig. 1 Number of Invasive CAG, CCTA, and stress MPI performed in Japan 2012-2016 JROAD 2016 Survey (8)

came popular and increased year after year, while stress MPI declined (12).

Stress MPI and CTCA as a diagnostic test for CAD

Stress MPI has been used to identify the appropriate candidates for revascularization. However, after CTCA is introduced, CTCA has been increasing, meanwhile stress MPI has been declining in Japan (Fig. 1) (12). Stress MPI also declines in the United States (13, 14). Why stress MPI declines in the United States and Japan? DePuey presumed that health care (insurance) system and reimbursement issues mostly influence declining the stress MPI (13). In addition, trends in incidence of both myocardial infraction and stable angina pectoris have been declining in the United States. Besides, invasive CAG, PCI, and CABG are also declining over the past decades (14). Both CAD patients and cardiac procedures are declining in the United States. Then it is natural that stress MPI is also declining. However, situation is different in Japan. Trends in incidence of acute myocardial infarction and total PCIs are still increasing. In conjunction with this trend, CTCA has been increasing dramatically from 360,311 in 2012 to 440,525 in 2016 (22.3% increase over 6 years). In contrast, stress MRI is declining from 204,781 in 2012 to 193,675 in 2016 (5.4% decrease over 6 years) (Table 1) (12).

Initial CCTA strategy

SCOT-HEART study enrolled 4,416 patients and demonstrated that standard care plus CTCA increases certainty of diagnosis of CAD, enables targeting interventions, and might reduce the incidence of myocardial infarction, compared with standard care alone in patients with stable chest pain (15). However, larger randomized PROMISE trial enrolled 10,003 patients and demonstrated that initial CTCA strategy significantly increased invasive CAG and revascularization without any advantageous outcomes, compared with functional testing including stress MPI (16). Therefore, initial CTCA strategy is not cost-effective. However, this strategy is getting prevalent over the past decade in Japan (12) because many cardiac facilities install cardiac catheter laboratories and 64-row or above CT scanners (17,18). In addition, CTCA is less expensive and not a time-consuming test compared with stress MPI in Japan. On the other hand, stress MPI is available at relatively limited facilities and waiting time tends to be longer. These are additional possible reasons of stress MPI decreases. JROAD report demonstrates that the number of CTCA is increasing and this trend may cause the trend of elective PCI increase (Fig. 2 and 3). CTCA provides anatomic information, such as location, distribution, and severity of stenosis and plaque characteristics. Although total ischemic burden may be estimated from CTCA, this important prognostic indicator is merely estimated from CTCA. FFR is getting prevalent before elective PCI in Japan. However, not many cardiac facilities routinely utilize FFR measurement. In addition, PCI tends to be performed in case stenosis is severe on CAG even though FFR >0.8. Therefore, anatomy-based PCI is still dominant in Japan. Besides, this strategy is not cost-effective (16) and would not improve prognosis, compared with ischemia-guided strategies (1-3, 7). Appropriate Use Criteria (AUC) for elective PCI recommends assessment of ischemic myocardium before elective PCI (19). Lack of AUC for stress MPI, CCTA and elective PCI in Japan may be one of the causes of this trend. Therefore, AUC of these modalities and therapies should also be developed in Japan.

Growing utility of FFR and FFR-CT

After FAME study is introduced, it is widely recognized that FFR-guided revascularization improves prognosis (1-3), so FFR is increasingly used to assess physiological significance of stenotic lesions. In general, as FFR measurement increase, elective PCI decreases because “defer cases” would increase. However, elective PCI hardly decreases in Japan. While both stress MPI and FFR can assess ischemia, advantage of stress MPI is non-invasive nature and can assess total ischemic burden. Recently FFR-CT is introduced and can assess ischemia similar to FFR but non-invasively and correlated well with FFR (20). PLATFORM study demonstrated that CTCA and selective FFR-CT guided care was associated with equivalent outcomes and quality of life and lower cost, compared with usual care over 1-year follow-up in patients with stable chest pain and planned invasive CAG (21). In addition, FFR-CT may be able to virtually estimate total ischemic burden in the future. “ADVANCE” registry is designed prospectively to assess utility, clinical outcomes and resource utilization based on CCTA alone versus CCTA plus FFR-CT in patients with stable CAD (22). Approximately 5,000 patients will be enrolled from up to 50 sites in Europe, USA, Canada, Asia, and about 1/3 of total patients were

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Table 1 Cardiac procedures performed in Japan (2012-2016)

	2012	2013	2014	2015	2016
Stress Echo.	5,856	5,998	5,915	5,966	NA
Stress MPI	204,781	204,913	200,889	195,815	193,675
Coronary CTA	360,311	393,872	413,495	421,855	440,525
Invasive CAG	495,128	493,901	493,857	492,523	493,379
Total PCI	249,198	253,626	253,370	255,416	264,573
Stress ECG	758,747	722,022	697,863	686,185	667,251
Emergent PCI	67,207	68,749	68,254	69,867	71,799
Elective PCI	181,991	184,877	185,116	185,549	192,774
CABG	18,176	19,345	19,306	18,762	18,551

NA: not available

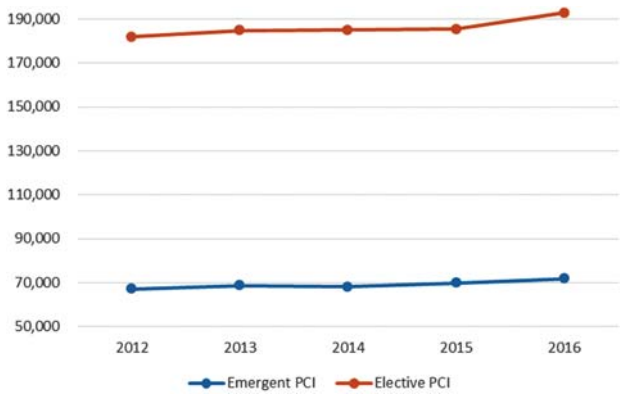

Fig. 2 Number of Emergent PCI and Elective PCI in Japan 2012-2016 JROAD 2016 Survey (8)

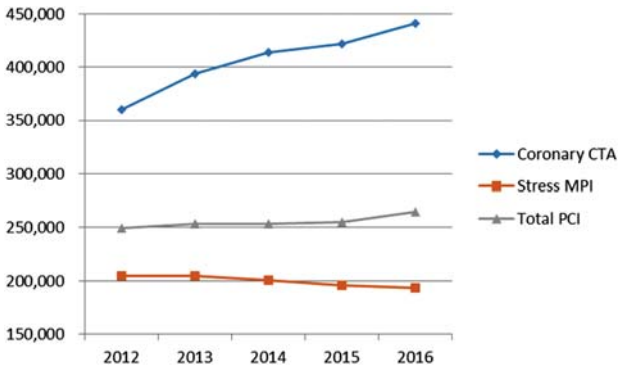

Fig. 3 Number of CCTA, Stress MPI and Total PCI in Japan 2012-2016 JROAD 2016 Survey (8)

enrolled from Japan as of Jun 2017. The results of this study may promote utility of FFR-CT before PCI, causing declining stress MPI further in the future. Although stress MPI relates more with coronary flow reserve (CFR) rather than FFR, and CFR may be more powerful parameter in predicting prognosis compared with FFR (22), FFR-CT will increasingly utilize to assess physiological significance of stenotic lesion because FFR-CT will be approved by the Japanese Ministry of Health, Labor and Welfare in the future. This direction is not favorable. Both FFR/FFR-CT and stress MPI can assess ischemia but from different point of view. Therefore, these modalities should be used as compensatory not as competitively.

Summary and perspectives

In summary, all of the CAD patients, diagnostic tests, and therapeutic procedures are declining in the United States. Therefore, it is natural that stress MPI also declines. On the other hand, incidence of myocardial infarction, the number of CCTA and elective PCI still increase in Japan, meanwhile stress MPI declines. Although FFR is increasingly utilized to assess physiological significance of stenotic lesions, anatomy-based PCI is still dominant in Japan. In the future, physiological PCI may be prevalent using FFR and FFR-CT, meanwhile stress MPI may decline further by replacing its role by FFR-CT in part.

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Conflicts of interest

None.

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