RAPID COMMUNICATION

Updated Japanese Ministry of Health, Labour and Welfare Reimbursement Policy for Cardiac Positron Emission Tomography and Coronary Intervention

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Abstract

The Japanese Ministry of Health, Labour and Welfare (JMHLW) approved ^{13}N-ammonia (^{13}N-NH$_3$) for detecting coronary artery disease (CAD) and ^{18}F-fluorodeoxyglucose (^{18}F-FDG) for cardiac sarcoidosis in 2012. These 2012 PET approvals shifted cardiac PET from research PET to clinical PET in Japan. Since the 2012 approvals, the nuclear cardiology community has realized the challenges of applying ^{13}N-NH$_3$ PET in clinical practice given the limited reimbursement through the health insurance system. Similar to the case with cardiac sarcoidosis, Japanese cardiologists have put great effort into treating patients with great arteritis such as Takayasu arteritis and have also shown the diagnostic utility of ^{18}F-FDG PET/CT. Considering these issues, the Japanese Society of Nuclear Medicine (JSNM) and Japanese Circulation Society (JCS) worked together with JMHLW to update health insurance policy regarding PET. In addition, physiology-based coronary intervention has played an important role in the management of patients with CAD. Based on these recent developments and discussions with major societies, JMHLW released its updated reimbursement policy on March 5, 2018. This rapid communication will address the key issues of this policy update related to cardiovascular PET and coronary intervention.

Keywords: Approval, Japanese Ministry of Health, Labour and Welfare, Percutaneous coronary intervention, Positron emission tomography
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The initial approval of the Japanese Ministry of Health, Labour and Welfare (JMHLW) for positron emission tomography (PET) for nuclear cardiology was in 1996 for ^{15}O-labeled gas for left ventricular (LV) functional measurements. On March 5, 2012, JMHLW introduced major reimbursements for cardiac PET applications including approvals of ^{13}N-ammonia (^{13}N-NH$_3$) for myocardial perfusion imaging (MPI) and ^{18}F-fluorodeoxyglucose (FDG) for cardiac sarcoidosis testing (Table 1) (1, 2).

Increasing ^{13}N-NH$_3$ reimbursement

In the United States, the Food and Drug Administration (FDA) approved the clinical use of ^{82}Rubidium (^{82}Rb) myocardial perfusion imaging (MPI) in 1989 and gave additional ^{82}Rb approval in 2016 and ^{13}N-NH$_3$ approval in 2000. Reimbursement by the Centers for Medicare and Medicaid Services (CMS) for PET MPI began in 1995. Currently, CMS reimbursement applies to ^{82}Rb, ^{13}N-NH$_3$, and ^{18}F-FDG (3). Over a decade after the FDA approval, JMHLW approved ^{13}N-NH$_3$ PET MPI for detecting myocardial ischemia in patients with CAD in 2012 (1, 2). This approval was long awaited by the Japanese nuclear cardiology community. However, there were two major issues with or limitations to the approval of ^{13}N-NH$_3$. First, it is conditional approval. JMHLW approves ^{13}N-NH$_3$ study in cases where other diagnostic tests do not detect myocardial ischemia. The

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Table 1 Latest Japanese Ministry of Health, Labour and Welfare's approval of the use of PET or PET/CT in nuclear cardiology

Test	Indication		Reimbursement	
	Before	March 5, 2018	Before	March 5, 2018
^{15}O-labeled gas	Diagnosis of heart disease	Diagnosis of heart disease	75,000 JPY (687 USD)	75,000 JPY (687 USD)
^{18}F-fluorodeoxyglucose	Diagnosis of viability (in case of difficult to diagnose myocardial viability using myocardial SPECT	Diagnosis of viability (in case of difficult to diagnose myocardial viability using myocardial SPECT	75,000 JPY (687 USD)	75,000 JPY (687 USD)
	Detection of inflammatory myocardial regions in cardiac involvement sarcoidosis	Detection of inflammatory myocardial regions in cardiac involvement sarcoidosis	75,000 JPY (687 USD)	75,000 JPY (687 USD)
		New Indication Detection of inflammatory aortic regions or evaluating disease activity in great arteritis		For PET 75,000 JPY (687 USD) For PET/CT 86,250 JPY (790 USD) May 16, 2018
				Additional approval for another pharmaceutical company's product
^{13}N-ammonia	Diagnosis of ischemic heart disease when other tests are not able to make diagnosis	Diagnosis of ischemic heart disease when other tests are not able to make diagnosis	75,000 JPY (687 USD)	New Reimbursement 90,000 JPY (824 USD)

1 USD equals 109 JPY based on foreign exchange rate on Monday, April 30, 2018.
JPY: Japanese Yen, PET: positron emission tomography, USD: US dollar

global trend for MPI has shifted from performing single-photon emission computed tomography (SPECT) MPI first to performing PET MPI first because PET MPI has higher diagnostic accuracy and lower radiation exposure than does SPECT MPI (4).

^{13}N-NH$_3$ PET MPI

Second, in 2012 JMHLW approved a reimbursement payment of 75, 000 JPY (687 USD) for ^{13}N-NH$_3$. This reimbursement is equivalent to that for other ^{18}F-FDG PET scans for either cancer imaging or myocardial viability assessment. The standard protocol for ^{13}N-NH$_3$ includes pharmacological stress and rest imaging (5, 6). For ^{13}N-NH$_3$ PET MPI study, most Japanese PET facilities are using adenosine as a vasodilator agent, which involves an additional cost for PET MPI study (2). Although ^{13}N-NH$_3$ has a relatively short physical half-life (10 minutes), the second ^{13}N-NH$_3$ administration should be performed 40 to 50 minutes after the first tracer administration. Therefore, clinical stress and rest ^{13}N-NH$_3$ study usually requires ^{13}N-NH$_3$ to be produced twice. These factors significantly raise the cost of performing the ^{13}N-NH$_3$ PET study. Clinical oncology ^{18}F-FDG PET requires only one tracer administration at resting condition. In this regard, it may have been appropriate for JMHLW to establish a different reimbursement policy for ^{13}N-NH$_3$ PET upon initial approval. The issue of reimbursement may be one reason for the underutilization of ^{13}N-NH$_3$ PET MPI in clinical settings in Japan. The Japanese Society of Nuclear Medicine (JSNM) was concerned about the underutilization of ^{13}N-NH$_3$ PET MPI after the 2012 JMHLW approval. Therefore, the JSNM health insurance policy committee raised the issue of ^{13}N-NH$_3$ reimbursement to JMHLW and worked together with it to resolve this issue. The discussions between the JSNM committee and JMHLW continued over about 4 years and JMHLW eventually updated the ^{13}N-NH$_3$ PET reimbursement policy amount from 75, 000 JPY to 90, 000 JPY (a 20% increase) on March 5, 2018 (Table 1). We hope this update will contribute to the wide clinical use of ^{13}N-NH$_3$ PET MPI in Japan.

Currently, most facilities use hybrid PET/CT scanners. However, the current approval of ^{13}N-NH$_3$ PET MPI is for PET, and simultaneous CT study is not reimbursed. It is expected that this issue will also have to be taken into consideration with regard to the reimbursement policy.

^{18}F-FDG PET and PET/CT approval for great arteritis

Japanese cardiologists have found several significant diseases and some of them have been recognized internationally as important pathophysiological conditions. These diseases include takotsubo cardiomyopathy, cardiac sarcoidosis, cardiac Fabry disease and triglyceride deposit cardiovasculopathy. Takayasu arteritis is a disease initially reported by Japanese physician Rokushu Yamamoto in 1830. In a scientific report, Dr. Mikito Takayasu discussed the case of a 21-year-old woman whose optic fundi showed peculiar coronary anastomosis in 1905 (7). Since then, Japanese

Table 2 2018 JMHLW policy: PCI indication for stable angina in CAD

	Indication
(1)	CAG: Stenosis >90%
(2)	Angina related to coronary stenosis (without other stenotic lesions)
(3)	Inducible ischemia based on diagnostic test

CAD: coronary artery disease, CAG: coronary angiography, JMHLW: Japanese Ministry of Health, Labour and Welfare, PCI: percutaneous coronary intervention

physicians have published the characteristic of this as a pulseless disease and have investigated the pathophysiology and treatment approaches of Takayasu arteritis. Up to 90% of the patients with this disease in Japan are women, with the disease located mainly in the ascending aorta. In other countries, the percentage of men with the disease is higher than it is in Japan and the main lesions of the disease are found in the abdominal aorta (8). The current treatment for Takayasu arteritis is the use of antiplatelet drugs and anti-inflammatory therapy such as corticosteroid or immune-suppressive drugs. Since many of Takayasu's arteritis patients are relatively younger women and treatment strategies have been developed, many cardiologists are seeking accurate diagnostic approaches and markers of disease activity that can contribute to patient management. ^{18}F-FDG PET has shown diagnostic utility and value for monitoring treatment effects in Takayasu arteritis and other forms of great arteritis (9-11). In fact, EANM/SNMMI and ASNC issued a joint procedural recommendation for ^{18}F-FDG PET/CT imaging in large-vessel vasculitis in 2017 (12). Based on their evidence and Japanese evidence regarding ^{18}F-FDG PET use in Takayasu arteritis (13, 14), the Japanese Circulation Society (JCS) health care policy committee applied for reimbursement approval for ^{18}F-FDG PET/CT use in the diagnosis of Takayasu's arteritis. In its March 5, 2018, approval, JMHLW specified that the clinical use of ^{18}F-FDG PET/CT was for detecting the location and evaluating the disease activity of arteritis. Previous JMHLW approvals for cardiac PET were for PET imaging only and not for PET/CT. Notably, in the case of great arteritis, approval includes either PET or PET/CT use. These reimbursement parameters should match the current clinical practice in most PET laboratories in Japan. A detailed expert statement regarding the use of ^{18}F-FDG PET/CT in Takayasu's and other forms of arteritis is provided in this issue of *Annals of Nuclear Cardiology*.

In addition, 2 pharmaceutical companies currently supply ^{18}F- FDG in Japan. JMHLW initially approved one pharmaceutical company's ^{18}F-FDG for detecting the site of arteritis on March 5, 2018. Shortly thereafter, on May 16, 2018, JMHLW approved another company's application for use of ^{18}F-FDG in patients with great arteritis. Therefore, hospitals in Japan are able to apply ^{18}F-FDG PET/CT imaging for patients with great arteritis using both companies' products. However, JMHLW still has not approved the use of ^{18}F-FDG produced on-site in hospitals for great arteritis diagnosis.

Indication for coronary intervention in patients with stable CAD

Physiology-based percutaneous coronary intervention (PCI) based on fractional flow reserve (FFR) showed better outcomes than did anatomy-based PCI (15). ACC/ AATS/ AHA/ASE/ASNC/SCA/SCAI/STS-appropriate criteria also noted that one of the indications for PCI in stable coronary artery disease (CAD) was inducible myocardial ischemia. In this regard, inducible myocardial ischemia should be evaluated using non-invasive diagnostic tests prior to PCI. However, the JROAD survey has shown the utility of increasing anatomical diagnostic testing such as CT angiography (CTA) but reducing functional tests such as exercise ECG and MPI (16). JMHLW discussed with cardiology experts the appropriate management of stable CAD patients in terms of coronary revascularization. Based on this discussion, JMHLW initially introduced the policy of PCI indication for stable angina (Table 2). Significantly, this indication included inducible ischemia based on diagnostic testing.

Future directions

The latest JMHLW approvals of cardiac/cardiovascular PET add the diagnosis of great arteritis and increased reimbursement for ^{13}N-NH_3 PET MPI. The JSNM health care subcommittee is working continuously to improve health care policy related to nuclear cardiology. Further new indications and improvements to the policy are expected in the near future.

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Conflicts of interest

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