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Myocardial viability assessment using nuclear imaging

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Myocardial assessment continues to be an issue in patients with coronary artery disease and left ventricular dysfunction. Nuclear imaging has long played an important role in this field. In particular, PET imaging using ^{18}F-fluorodeoxyglucose is regarded as the metabolic gold standard of tissue viability, which has been supported by a wide clinical experience. Viability assessment using SPECT techniques has gained more wide-spread clinical acceptance than PET, because it is more widely available at lower cost. Moreover, technical advances in SPECT technology such as gated-SPECT further improve the diagnostic accuracy of the test. However, other imaging techniques such as dobutamine echocardiography have recently emerged as competitors to nuclear imaging. It is also important to note that they sometimes may work in a complementary fashion to nuclear imaging, indicating that an appropriate use of these techniques may significantly improve their overall accuracy. In keeping these circumstances in mind, further efforts are necessary to further improve the diagnostic performance of nuclear imaging as a reliable viability test.

Key words: myocardial viability, PET, SPECT

DESPITE RECENT DEVELOPMENTS in therapeutic options, heart failure due to coronary artery disease (CAD) continues to be one of the leading causes of morbidity and mortality in many countries, including Japan. It is well known that left ventricular dysfunction is not necessarily an irreversible process; dysfunctional but viable myocardium has the potential to recover in function after restoration of myocardial blood flow by either coronary arterial bypass grafting (CABG) or percutaneous coronary intervention (PCI), whereas scarred tissue will not recover even after revascularization.[1] Therefore, substantial efforts have been made to differentiate such potentially reversible, and hence viable myocardium from scar. Furthermore, it has also been reported that patient selection based on the presence and extent of tissue viability identifies patients who are at low risk for serious perioperative complications associated with CABG.[2] Nuclear imaging techniques using either PET[3,4] or SPECT[5,6] have played a major role in this field. This review describes the basic physiology of dysfunctional but viable myocardium, and the current applications of scintigraphic approaches for the noninvasive characterization of viable and scarred myocardium.

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Pathophysiology Underlying Reversible Dysfunction

It is known that chronically dysfunctional but viable myocardium may represent hibernation, repetitive stunning, or both. Hibernating myocardium, which was first described by Rahimtoola,[7] represents impaired contractile function coupled with reduced myocardial blood flow at rest that would recover after restoration of flow. Stunning, on the other hand, represents impaired contractile function that persists after an ischemic episode despite restoration of blood flow.[8] The differentiation of these situations is complicated because they may often coexist in the clinical setting. Furthermore, several clinical studies[9,10] have shown that myocardial blood flow in hibernating myocardium is, in fact, not reduced and is often within the normal or near normal range, suggesting that repetitive stunning rather than hibernation plays a major role in such chronically dysfunctional but viable myocardium. Prior studies by Bax et al.[11] and Haas et al.[12] have suggested that stunned myocardium is likely to show early

Table 1 PET tracers used for assessing myocardial viability

	Mechanism	Imaging procedure	Index of viability
^{18}F-FDG	Glucose utilization	Static/Dynamic	Relative uptake
^{11}C-Acetate	Oxidative metabolism	Dynamic	Clearance rate (K_{mono})
^{13}N-Ammonia	Flow/Metabolic trapping	Dynamic/Static	Flow/Retention
^{15}O-Water	Flow/Diffusion	Dynamic	Flow/Perfusable tissue index
^{82}Rb	Flow/Membrane integrity	Dynamic	Flow/Clearance rate

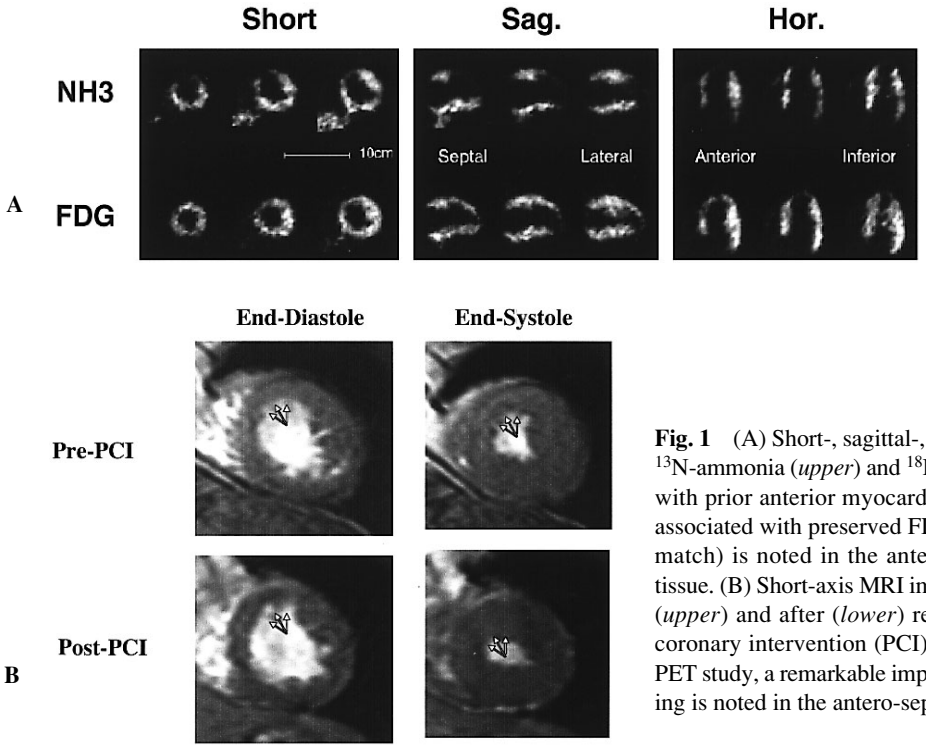

Fig. 1 (A) Short-, sagittal-, and horizontal-axis tomograms of ^{13}N-ammonia (*upper*) and ^{18}F-FDG (*lower*) PET from a patient with prior anterior myocardial infarction. Reduced perfusion associated with preserved FDG uptake (flow-metabolism mismatch) is noted in the antero-septal wall, indicating viable tissue. (B) Short-axis MRI images from the same patient before (*upper*) and after (*lower*) revascularization by percutaneous coronary intervention (PCI). As expected from the results of PET study, a remarkable improvement in regional wall thickening is noted in the antero-septal wall.

functional recovery after revascularization, whereas hibernating myocardium may take a longer time period to recover. It is also noteworthy that contractile reserve to dobutamine infusion is more common in normally perfused (stunned) myocardium than in hypoperfused yet viable (hibernating) myocardium.[13] Additionally, the timing of revascularization after the onset of hibernation may also be an issue, because progressive cellular degeneration in hibernating myocardium may reduce the chance for complete structural and functional recovery after restoration of blood flow.[14] Thus, much work still needs to be done for more comprehensive understanding of dysfunctional but viable myocardium.

What Is the Gold Standard for Viability Studies?

The choice of gold standard or reference technique for viability is an issue in most published studies. There have been many endpoints proposed for viability tests, including metabolic activity measured by ^{18}F-fluorodeoxyglucose (FDG) PET,[15] histological examination of biopsied tissue,[16] regional or global functional recovery,[3,17–20] symptom improvement,[21,22] and improved survival.[23,24] From a pathophysiological view point, biological signals by PET or histological examinations should certainly provide important insights into viability at the cellular or molecular level. Regional or global functional recovery after restoration of blood flow is also relevant because this is directly associated with the definition of stunned or hibernating myocardium. From a clinical standpoint, on the other hand, improved survival and symptoms associated with revascularization would be the optimal endpoint of viability tests, because this is the main goal of revascularization procedures. However, such prognostic information is not always available, because some patients may drop out during the follow-up period usually for years. Furthermore, the magnitude of improvement in symptoms may sometimes be difficult to measure in an objective manner. Perhaps, the global improvement of left ventricular function after revascularization is the best alternative, because this is easy to measure and, is likely to be associated with improved prognosis.[22]

PET

The clinical utility of PET imaging to identify viable tissue was first described by Tillisch et al. in the middle 1980's.[3] PET has several technical advantages over SPECT such as higher counting sensitivity, higher spatial resolution, and routine use of attenuation correction. Until now, there have been a number of PET studies, most of which used ^{18}F-FDG as a metabolic marker of viability, in the literature,[2–4,17,19,23,25] and thus PET serves as a metabolic gold standard for tissue viability. As summarized in Table 1, there are several PET tracers that can be used for assessing viability.

Metabolic Imaging

^{18}F-FDG

Free fatty acids, glucose, and lactate are the major energy sources for the heart.[26–28] Fatty acids play a major role in the metabolism of the normoxic heart, whereas glucose becomes the major substrate for the myocardium under ischemic conditions.[29–31] Therefore, PET imaging using metabolic tracers such as ^{18}F-FDG enables detection of metabolic changes at the cellular level associated with ischemia. As demonstrated in Figure 1, the preserved or increased glucose utilization, and hence ^{18}F-FDG uptake in hypoperfused and dysfunctional myocardium (flow-metabolism mismatch) is regarded as a metabolic marker of cell survival and viability, whereas concordant reduction in both blood flow and ^{18}F-FDG uptake is indicative of scar. Thus, ^{18}F-FDG PET provides a biological signal on cellular viability, and is considered to be one of the most accurate noninvasive techniques to identify viable tissue, as supported by a number of studies using PET.[2–4,17,19,23,25] From a prognostic viewpoint, it is important to note that the surgical revascularization of hibernating myocardium leads to a decreased mortality rate compared with medical treatment, whereas revascularization of irreversibly injured myocardium does not prevent further decline in function.[23,25]

In clinical practice, ^{18}F-FDG PET is often combined with flow tracers such as ^{13}N-ammonia to assess myocardial perfusion. Although ^{18}F-FDG PET imaging without flow tracer may work with reasonable sensitivity and specificity for detecting viable tissue,[32] flow/metabolism combination would provide more comprehensive information on viability and herein the differentiation of hibernation from stunning.[11,12,33]

Image interpretation is often performed visually, and relies on relative regional uptake of ^{18}F-FDG.[17] Absolute quantitation of regional myocardial glucose utilization using dynamic imaging does not appear to enhance the diagnostic accuracy of ^{18}F-FDG PET to detect viable myocardium,[34] probably because of high variability in glucose utilization rates in individual patients. Thus, relative ^{18}F-FDG uptake is clinically sufficient for this purpose.

^{11}C-Acetate

Although ^{18}F-FDG is the most established metabolic tracer for tissue viability, ^{18}F-FDG may not be suitable for use in acute myocardial infarction due to inflammatory cell accumulation in necrotic tissue, which takes up ^{18}F-FDG as does viable tissue.[35–37] Furthermore, myocardial ^{18}F-FDG uptake is influenced by multiple factors such as serum glucose, free fatty acids, and insulin levels. Acetate, on the other hand, enters the TCA cycle and its clearance rate represents cellular oxidative metabolism independent of the factors affecting ^{18}F-FDG uptake.[28] Because preserved oxidative metabolism is essential for viable cells, its clearance rate can be used as a marker of viability. Several clinical studies have demonstrated the utility of ^{11}C-acetate for assessing myocardial viability,[38–41] particularly in patients with acute myocardial infarction. Additionally, a recent study by Hata et al.[42] suggests that the use of low-dose dobutamine at the time of tracer injection further improves the delineation of reversible and irreversible dysfunction.

A potential disadvantage of ^{11}C-acetate as a viability tracer, however, is the necessity for dynamic imaging and calculation of k-mono to differentiate viable from scarred tissue. Thus, unlike ^{18}F-FDG, a simple visual interpretation of static image is not possible for this tracer. Another disadvantage is the necessity for an on-site cyclotron for production of ^{11}C, which has a relatively short physical half-life of 20 minutes. For these reasons, although the results as to the utility of this tracer as a viability marker are promising, ^{11}C-acetate has not gained wide clinical acceptance at present.

Flow Tracers

Flow measurement using PET also provides information on cellular viability.[43] In particular, unlike SPECT, absolute quantitation of myocardial blood flow is feasible using PET and tracer kinetic models.[44,45] The myocardial blood flow itself is a marker of viability because viable tissue requires a blood supply to be alive.[43] Additionally, it is of note that flow is often within the normal or near normal range in dysfunctional but viable myocardium,[9,10] suggesting that the majority of reversible dysfunction represents repetitive stunning rather than hibernation.

^{13}N-Ammonia

The suitability of ^{13}N-ammonia as a myocardial flow tracer is established in numerous studies.[44,46–52] Uptake of ^{13}N-ammonia depends on both perfusion and metabolic retention. Therefore, ^{13}N-ammonia retention in the myocardium should reflect tissue viability. This concept was tested by Kitsiou et al.[53] demonstrating that ^{13}N-ammonia retention rather than absolute myocardial blood flow was a good marker of cellular viability. Nevertheless, whether metabolic tracers such as ^{18}F-FDG are necessary for more accurate delineation of viable tissue remains to be determined by further studies.[54]

Table 2 SPECT tracers used for assessing myocardial viability

	Mechanism	Imaging procedure	Index of viability
^{201}Tl	Flow/Membrane integrity	Stress-Redistribution-Reinjection Rest-Redistribution	Defect reversibility/Relative uptake
^{99m}Tc-Sestamibi	Flow/Mitochondrial membrane integrity	Stress-Rest/Rest	Defect reversibility/Relative uptake
^{99m}Tc-Tetrofosmin	Flow/Mitochondrial membrane integrity	Stress-Rest/Rest	Defect reversibility/Relative uptake
^{123}I-BMIPP	Fatty Acid uptake	Rest	Reduced uptake compared with flow
^{18}F-FDG	Glucose utilization	Rest	Relative uptake

^{15}O-Water

Unlike ^{13}N-ammonia, ^{15}O-water distributes into the water spaces of both the myocardium and blood. In theory, ^{15}O-water is considered to be an ideal tracer for measurement of myocardial blood flow without plateau effect at high flow rates.[45,55] However, methodological complexity related with this tracer (e.g., necessity for subtraction of blood pool activity) together with very short physical half-life may cause heterogeneity of flow measurements, as demonstrated by Nitzsche et al.[56] A unique feature of ^{15}O-water PET imaging is that the proportion of the total anatomical tissue that is capable of rapidly exchanging water (water perfusable tissue index, PTI) can be used as a marker of tissue viability.[57,58] Although much work needs to be done before its clinical utility is determined, this technique appears to provide unique information on tissue viability.

^{82}Rb

Rubidium-82 is a generator produced positron emitting tracer to measure myocardial blood flow.[59] It is actively transported into myocardium by sodium-potassium dependent transmembranous ion exchange system in a manner similar to ^{201}Tl.[60] Therefore, its cellular kinetics represent membrane integrity and hence, viability. Although this concept has not been extensively validated, a study by vom-Dahl et al.[59] showed that tissue half-lives of ^{82}Rb significantly differ between viable and scar tissue.

SPECT

Although PET imaging is an established technique to distinguish viable from scarred myocardium as described above, its limited availability and high cost pose limitations for widespread use in clinical practice. Therefore, substantial efforts have been made to develop SPECT techniques for viability assessment, which are less expensive and more widely available. As shown in Table 2, there are several single-photon emitting tracers available that can be used for assessing myocardial viability.

^{201}Tl

^{201}Tl is taken up by myocardial cells by active transport and is dependent on myocardial blood flow.[60] Therefore, myocardial ^{201}Tl uptake represents both myocardial perfusion and cellular viability. It has been shown that 3–4 hour delayed imaging after stress injection of ^{201}Tl frequently underestimates the presence of viable myocardium within persistent defects as evidenced by metabolic imaging with ^{18}F-FDG PET.[61] Modified ^{201}Tl protocols such as late redistribution imaging after stress injection[62,63] or reinjection technique[6,64] have been shown to enhance the detection of viable myocardium. In particular, reinjection imaging protocol is currently widely used for this purpose, and has been found to be equivalent to ^{18}F-FDG PET in most circumstances, although viability in some myocardium may be underestimated by ^{201}Tl as compared with ^{18}F-FDG PET.[64]

Rest-redistribution ^{201}Tl imaging is another established diagnostic protocol for the detection of such viable, but compromised, myocardium.[5] Initial distribution of ^{201}Tl is considered to reflect myocardial blood flow at rest, and redistribution ^{201}Tl imaging to reflect myocardial viability rather than mere perfusion. Thus, rest-redistribution protocol is used when the question being addressed is solely myocardial viability and not stress induced ischemia. Unlike stress ^{201}Tl, late redistribution imaging after rest injection may not be necessary for this purpose.[65] When rest-redistribution ^{201}Tl imaging is compared with reinjection imaging after stress, both protocols seem to provide equivalent results as to viability when regional ^{201}Tl activity on the final image is considered as a marker of viability.[8] However, the presence and extent of stress induced ischemia gives more relevant information than viability in the majority of CAD patients. Furthermore, a recent study[66] has shown that stress induced reversible defects, which are more commonly seen on stress imaging than on rest imaging, are highly predictive of functional recovery after revascularization. Thus, the use of stress imaging protocol is encouraged whenever possible.

Images are usually interpreted visually, but quantitation of regional tracer uptake within the dysfunctional myocardium provides more objective and accurate results as to tissue viability than visual assessment.[67]

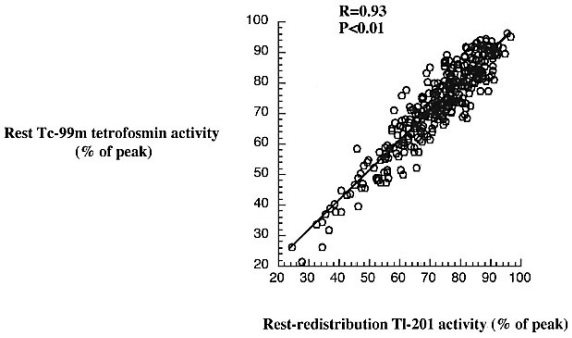

Fig. 2 Scatter plots showing correlation of quantitative regional tracer activities between rest-redistribution ^{201}Tl and rest ^{99m}Tc-tetrofosmin imaging. (From Matsunari I, Fujino S, Taki J, et al. Quantitative rest technetium-99m tetrofosmin imaging in predicting functional recovery after revascularization: comparison with rest-redistribution thallium-201. *J Am Coll Cardiol* 1997; 29: 1226–1233. Reproduced with permission of the American College of Cardiology.)

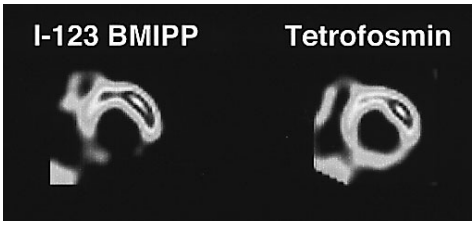

Fig. 3 ^{123}I-BMIPP (*left*) and ^{99m}Tc-tetrofosmin (*right*) images from a patient with inferior myocardial infarction. A reduced ^{123}I-BMIPP uptake less than ^{99m}Tc-tetrofosmin is noted in the inferior wall.

^{99m}Tc-Labeled Flow Tracers

Technetium-99m labeled flow tracers such as ^{99m}Tc-sestamibi and ^{99m}Tc-tetrofosmin are now widely available as alternatives to conventional ^{201}Tl. As compared with ^{201}Tl, these ^{99m}Tc-labeled agents yield higher image quality, but the diagnostic performance of these tracers for detection of CAD is offset by underestimation of flow at high flow rates.[68,69] A more important characteristic of these tracers is that, unlike ^{201}Tl, they do not show significant redistribution over time, and therefore there have been controversies regarding the use of ^{99m}Tc-labeled agents as a viability tracer.[70] In experimental studies, however, myocardial retention of both ^{99m}Tc-sestamibi and ^{99m}Tc-tetrofosmin requires cellular viability as demonstrated by Takahashi et al.[71] Perhaps due to the lack of redistribution and underestimation of flow at high flow rates, both stress-rest ^{99m}Tc-sestamibi and ^{99m}Tc-tetrofosmin underestimate defect reversibility as compared with stress-reinjection ^{201}Tl.[72,73] However, regional ^{99m}Tc-sestamibi[18] or ^{99m}Tc-tetrofosmin[20] activity closely correlates with that of ^{201}Tl as illustrated in Figure 2, indicating that quantitation of tracer uptake may be used as a marker of viability. Furthermore, Udelson et al.[18] described the utility of ^{99m}Tc-sestamibi for the prediction of functional recovery after revascularization, which was comparable to that of ^{201}Tl, in severe CAD patients. Similar results have been reported for ^{99m}Tc-tetrofosmin, a newer ^{99m}Tc-lebeled flow tracer. In a study by Matsunari et al.,[20] ^{99m}Tc-tetrofosmin uptake also predicted functional recovery as did rest injected ^{201}Tl. These data were further confirmed by subsequent studies.[74,75] Thus, quantitation of tracer uptake of ^{99m}Tc-sestamibi or ^{99m}Tc-tetrofosmin provides useful information on viability as does conventional ^{201}Tl.

^{123}I-BMIPP

^{123}I-beta-methyl iodophenyl pentadecanoic acid (BMIPP) is a fatty acid analog that is not metabolized by beta-oxidation,[76] and its clinical utility has been extensively investigated particularly in Japan and Europe. Because myocardial fatty acid uptake is easily depressed in ischemic but viable myocardium,[77] BMIPP imaging in combination with flow tracer such as ^{201}Tl or ^{99m}Tc-sestamibi can also detect potentially reversible myocardium. As demonstrated by Taki et al.[78] and others,[79,80] a discordant BMIPP uptake less than perfusion tracer uptake (Fig. 3) is considered to be a marker of functional recovery after revascularization. However, whether BMIPP imaging combined with perfusion tracer has any advantage over perfusion tracer alone for the detection of compromised but viable myocardium remains to be elucidated in a large patient cohort, although initial results are promising.[81]

^{18}F-FDG SPECT

^{18}F-FDG SPECT with ultra-high energy collimators for 511 KeV acquisition has emerged as an alternative to PET for the assessment of myocardial viability.[82] Despite the limited spatial resolution and counting sensitivity of SPECT compared to PET, several clinical studies have shown that ^{18}F-FDG SPECT offers diagnostic information similar to PET, and compares favorably with other imaging modalities, including rest-redistribution,[83] stress-reinjection ^{201}Tl imaging,[84] or low dose dobutamine echocardiography.[84] As with PET studies, metabolic activity measured by ^{18}F-FDG SPECT is interpreted in combination with flow tracer. For this purpose, a dual-isotope simultaneous acquisition (DISA) protocol with ^{18}F-FDG and ^{99m}Tc-perfusion tracer is attractive because it enables assessment of myocardial glucose utilization and perfusion in a single study[85–87] (Fig. 4). Another potential advantage of this protocol is that ECG-gating to assess left ventricular function is feasible. Thus, DISA SPECT has the potential to assess myocardial glucose utilization, perfusion, and function in a single study.

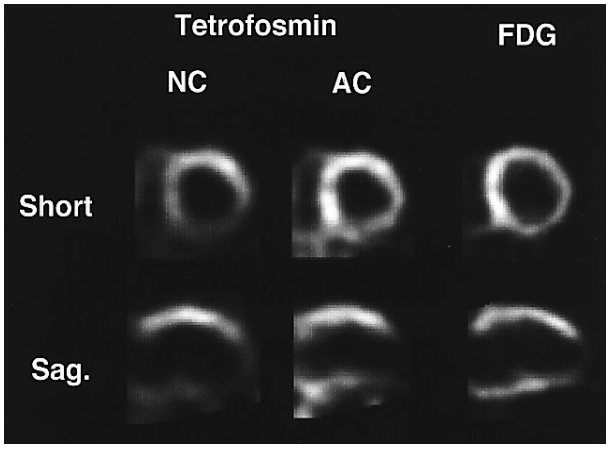

Fig. 4 The non-attenuation corrected (NC) ^{99m}Tc-tetrofosmin images (*left*), attenuation corrected (AC) ^{99m}Tc-tetrofosmin images (*center*) and positron emission tomography with ^{18}F-FDG (*right*) from a patient with 3-vessel coronary artery disease. (From Matsunari I, Böning G, Ziegler SI, et al. Attenuation-corrected ^{99m}Tc-tetrofosmin single-photon emission computed tomography in the detection of viable myocardium: comparison with positron emission tomography using ^{18}F-fluorodeoxyglucose. *J Am Coll Cardiol* 1998; 32: 927–935. Reproduced with permission of the American College of Cardiology.)

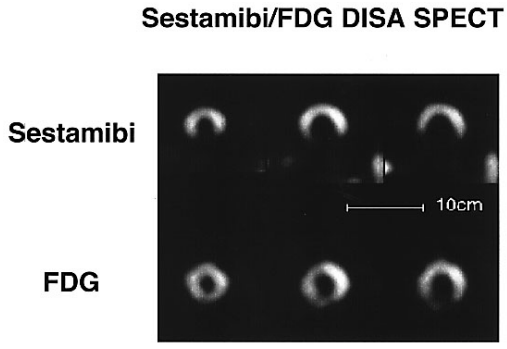

Fig. 5 ^{99m}Tc-sestamibi (*upper*) and ^{18}F-FDG SPECT (*lower*) images acquired simultaneously from a patient with inferior myocardial infarction. A reduced perfusion associated with preserved ^{18}F-FDG uptake (flow-metabolism mismatch) is noted.

Recent Methodological Developments in SPECT Viability Studies

Nitrates

The use of nitrates at the time of tracer injection reportedly enhances the diagnostic accuracy of viability tests using flow tracers, as evidenced by several studies.[88–90] In particular, Sciagra et al.[91] have found that nitrate induced changes in ^{99m}Tc-sestamibi activity are an accurate marker of potentially reversible myocardium, which was true for both regional[91] and global[92] functional recovery. Furthermore, the prognostic value of nitrate enhanced ^{99m}Tc-sestamibi imaging has been validated in another study by this group.[93] Thus, baseline-nitrate perfusion imaging appears to be an attractive approach for assessing tissue viability. One disadvantage of this protocol is the necessity for two separate injections of the tracer, relatively long time required for completion of the imaging procedure.

Attenuation Correction

It is well known that attenuation artifacts may unfavorably affect the diagnostic accuracy of cardiac SPECT imaging. In particular, patients with severe left ventricular dysfunction, in whom the extent of viable myocardium becomes an important issue for clinical decision making, are likely to have an enlarged left ventricle, and are susceptible to diaphragmatic attenuation artifacts. Therefore, the use of attenuation correction would improve the accuracy of viability tests using SPECT techniques. This hypothesis was confirmed by a recent study demonstrating that the use of attenuation correction significantly improved the detection of viable myocardium by decreasing false negatives in the inferior-septal region using ^{18}F-FDG PET as a reference technique for tissue viability,[94] although this needs to be further validated in patients undergoing revascularization.

Gated-SPECT

Recent developments in ^{99m}Tc-labeled myocardial perfusion tracers and data processing[95] have made ECG-gated SPECT imaging part of the clinical routine in nuclear imaging laboratories. Gated-SPECT may enhance the diagnostic accuracy of the viability test by increasing specificity.[96,97] In particular, dobutamine stress gated SPECT using ^{99m}Tc-labeled flow tracer provides information on both perfusion and contractile reserve in a single study as recently documented by Yoshinaga et al.,[98] who compared the accuracy of low-dose dobutamine stress gated myocardial SPECT with the accuracy of dobutamine stress echocardiography and resting perfusion SPECT for the identification of viable myocardium in patients with previous myocardial infarction. Because SPECT is more objective and reproducible than echocardiography, gated-SPECT with pharmacological intervention may become an indispensable diagnostic tool for viability testing.

Non-Nuclear Imaging Techniques

There are several non-nuclear imaging techniques that can be used for the detection of viable tissue. Each of them has its own advantages and disadvantages as compared with nuclear imaging.

Echocardiography

Contractile reserve assessed by low-dose dobutamine echocardiography is a currently well accepted marker of tissue viability.[67,99–102] When the results of dobutamine

echocardiography are compared with those of nuclear imaging, echocardiography generally has higher specificity but somewhat lower sensitivity as compared with ^{201}Tl imaging.[103]

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is another potent diagnostic tool for myocardial viability assessment. It can assess contractile reserve as does dobutamine echocardiography in a more objective manner.[15] Furthermore, delayed enhancement using contrast media seems to be a reliable marker for scar tissue as compared with ^{201}Tl imaging[104] or PET.[105] At present, however, clinical experience with MRI is limited, and therefore clinical trials especially involving patients undergoing revascularization need to be done before its utility is determined.

Sequential Strategy Using Multi-Modalities

Although one imaging technique has advantages and disadvantages over other techniques as described earlier, this can be improved by combining two or more imaging modalities. This concept was recently tested in a study by Bax et al.[106] demonstrating that the combination of ^{201}Tl and dobutamine echocardiography in a subset of patients significantly improved overall accuracy of the test, suggesting that these diagnostic techniques may work in a complementary fashion. It should be noted that the sequential strategy requires two or more diagnostic tests performed in patients, and therefore is more expensive than performing one test alone. Therefore, the question to be addressed in further studies is whether the additional costs imposed by the sequential test are offset by the improved diagnostic accuracy.[107]

CONCLUSION

Accurate assessment of myocardial viability continues to be an important issue for clinical decision making in patients with CAD and left ventricular dysfunction. Nuclear imaging using either SPECT or PET has played a major role for identification of such viable myocardium as described in this review. Recently, however, other imaging techniques such as dobutamine echocardiography have emerged as competitors to nuclear imaging. It is noteworthy that they sometimes may work in a complementary fashion to nuclear imaging, indicating that an appropriate use of these techniques may significantly improve the overall accuracy. On the other hand, reimbursement for cardiac metabolic imaging using ^{18}F-FDG PET has recently been approved by the Ministry of Health, Labour and Welfare in Japan, which would promote more wide-spread use of PET imaging in clinical practice. Thus, the circumstances surrounding nuclear imaging as a viability test are changing dynamically. Keeping these factors in mind, more efforts are necessary to further enhance the diagnostic performance of nuclear imaging as a reliable, indispensable viability test for clinical decision making.

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