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A Comparison of Thallium-201 Spect and F-18 Deoxyglucose Positron Emission Tomography in Assessing Myocardial Viability

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Abstract

Assessment of myocardial viability prior to revascularization procedures is an important clinical consideration for improved functional recovery of regional left ventricular dysfunction. In chronic coronary artery disease, impaired left ventricular function, at least in part, is due to ischemic or hibernating myocardium rather than just myocardial fibrosis. Functional recovery of the left ventricular dysfunction is dependent on a timely revascularization of the ischemic and/or hibernating myocardium. The assessment of myocardial viability by regional ventricular function measurements by various other modalities is imprecise. Myocardial viability in chronic ischemia, hibernating, or stunned myocardium can be assessed by Thallium-201 single photon emission tomography (SPECT) in a majority of the cases. The positron emission tomography (PET) F-18 Deoxyglucose (FDG) imaging is considered to be an accurate marker for differentiating hibernating, but viable, myocardium from infarction in a subset of patients not resolved with thallium-201 imaging. In our experience, overall sensitivity for Thallium-201 SPECT imaging for viability was 60% with a negative predictive value of 69.9% and accuracy greater than 79%.

Key words: Myocardial viability, thallium, fluorodeoxyglucose, PET, SPECT.

We reviewed 34 Thallium-201 (TL-201) SPECT records (96 segments) of patients who had fixed myocardial perfusion deficits and who had subsequently undergone FDG-PET imaging for the detection of myocardial viability in fixed perfusion deficits noted on TL-201 SPECT images. An accurate distinction between viable and scarred or infarcted myocardium has important clinical implications, particularly in patients who are being considered for coronary revascularization.

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Materials and Methods

The patients were 36 to 73 years old and had angiographically proven chronic multivessel coronary artery disease and left ventricular dysfunction. The patients were selected on the basis of at least one irreversible thallium perfusion deficit on exercise/redistribution reinjection thallium scintigraphy.[2] Subsequently, they had a FDG-PET scan for the detection of myocardial viability in order to plan appropriate intervention, such as surgical revascularization versus medical therapy.

All patients underwent exercise Thallium-201 SPECT

scintigraphy following approximately 3-millicurie (mCi) of TL-201 injected at attainable peak heart rate. Immediate postexercise images were obtained in SPECT configuration. The patients received an additional 1 mCi of TL-201, and then, about 4 hours later, delayed redistribution and equilibrium images were obtained in the same SPECT configuration. Images were reconstructed in coronal, sagittal, and transverse tomographic planes.

The FDG-PET myocardial viability study was performed in a carbohydrate loading state, following either oral administration of approximately 50 grams of glucose or IV administration of a glucose, insulin, and potassium infusion. The blood glucose and potassium levels were monitored frequently. Three position rectilinear scanning was used to position the patient in the PET scanner. A transmission scan was acquired for attenuation correction. An emission scan was obtained 40 minutes following the 8-10 mCi FDG injection. Images were reconstructed in sagittal, coronal, and transaxial tomographic planes. A semiquantitative analysis of the images was also performed.[3]

Results

Ninety-six myocardial segments with fixed perfusion deficits on TL-201 SPECT were reviewed. In our study, 31% of the severe fixed thallium segmental defects were viable by PET-FDG. Viability was defined as those segments taking up greater than 50% of peak FDG. Fifty of the 96 fixed defects were viable by Thallium-201 SPECT i.e., took up greater than 50% of the peak thallium activity. This yields a sensitivity of 60% for thallium predicting viability. The negative predictive value of thallium for determining myocardial necrosis was 69.9%; accuracy was greater than 79%.

Results
n=96 myocardial segments

	Nonviable	Viable
Thallium-201 SPECT	66	30
FDG-PET	46	50

Discussion

Thallium-201 SPECT imaging remains a useful and economical first line imaging modality for the evaluation of myocardial viability. The F-18 Deoxyglucose PET, however, remains the gold standard, and is crucial in a subset of patient population, which showed persistent perfusion deficits on TL-201 imaging.[1,8] Other criteria such as extent and severity of fixed perfusion deficit in terms of relative percent uptake have to be determined to establish some objectivity in selecting patients for PET imaging.

The differentiation of viable from scarred or necrotic myocardium with coronary artery disease is an issue of increasing clinical relevance for myocardial revascularization. Coronary artery patency and preserved regional contractile function were previously used to identify viable myocardium.[9] Recent clinical advances and research has shown that these two criteria are imprecise for an accurate diagnosis of myocardial viability.[11]

Hibernating myocardium (chronic hypoperfusion) and stunned myocardium (acute coronary syndrome with reperfusion) may pose a diagnostic dilemma with conventional TL-201 or Tc-99m Sestamibi perfusion imaging. Positron emission tomography with 18-FDG has provided a better insight and understanding for evaluating viability on the basis of myocardial cellular integrity and metabolic activity.[6]

A current approach for identifying myocardial viability can be classified in two broad categories of assessment of regional function by nonisotopic methods and assessment of perfusion, membrane integrity, and metabolism by scintigraphic methods.

The nonisotopic assessment of regional function include:

1. Two-dimensional echocardiography
2. Contrast angiography
3. Fast-cine computed tomography
4. Magnetic resonance imaging
5. Dobutamine infusion echocardiography

The isotopic assessment of perfusion and metabolism include:

1. Delayed resting thallium imaging
2. Thallium reinjection technique
3. Tc-99m labeled myocardial perfusion and functional imaging[12]
4. Measurement of coronary blood flow with N-13 ammonia, Rb-82, and O-15 water using positron emission tomography
5. Measurement of cellular metabolism with F-18 deoxyglucose

Stress/rest thallium scintigraphy

Thallium-201 scintiography has been widely used for well over two decades for the detection and characterization of ischemic heart disease. It is valuable to differentiate reversible ischemic myocardium from irreversible myocardial scarring; however, the use of TL-201 alone in identifying viable myocardium is limited. The F-18 deoxyglucose PET imaging has been a gold standard for the evaluation of cellular metabolism and viability.

Thallium-201, a potassium analog, is a cyclotron-produced radioisotope. It is a good agent for assessing perfusion and sarcolemmal integrity, hence myocardial viability. The uptake of TL-201 by the myocardial cell is active and dependent on regional blood flow and sarcolemmal integrity and, therefore, can distinguish viable from scarred myocardium with greater precision than regional anatomy or functional status evaluated angiographically. Regional TL-201 activity on redistribution images acquired early (3-4 hours) and on delayed (8-72 hours) equilibrium thallium imaging are fairly good discriminators for assessing viable myocardium from scarred tissue.

Exercise-induced thallium perfusion deficits that redistribute on delayed images are an accurate indicator of vi-

able myocardium. An initial perfusion deficit that doesn't reperfuse on delayed imaging may represent a severely ischemic or hibernating, but viable or admixture of, scar and/or viable myocardium. The irreversible thallium defect on stress/redistribution imaging underestimates viable myocardium in up to two thirds of the fixed perfusion defects. A 24-hour delayed imaging or reinjection of TL-201 has shown to improve the detection of possible reversibility.[6]

F-18 fluorodeoxyglucose, a positron emitter, is an established marker and gold standard for detecting myocardial viability. It can demonstrate preserved metabolic activity and cellular integrity in hypoperfused regions of the myocardium. Fatty acids are the major fuel for producing high energy phosphate in normal myocardium. The breakdown of fatty acids via beta oxidation in mitochondria is very sensitive to hypoxia. During ischemia, myocytes compensate for loss of oxidative potential by shifting towards greater utilization of glucose to generate high energy phosphates. The amount of energy produced via glycolysis may be insufficient to sustain mechanical work but is usually adequate to maintain cell viability.

For the preservation of myocardium at risk, an adequate flow of blood is necessary to deliver glucose to the myocytes to be used as substrate and to remove metabolites from the glycolytic pathways. A severe reduction in blood flow results in the accumulation of end products of the glycolytic pathway, causing inhibition of glycolytic enzymes, cell membrane disruption, and cell death.

Fluorodeoxyglucose, a glucose analogue, is a marker of regional exogenous glucose utilization in areas of reduced blood flow. Fluorodeoxyglucose tracks transmembranous transport and phosphorylation of glucose i.e., FDG -> FDG-6-phosphate through hexokinase pathway; however, it doesn't enter glycolysis or glycogen synthesis. Consequently, there is an enhanced uptake of F-18 FDG in the tissue. Fluorodeoxyglucose is only slowly metabolized; therefore, factors that enhance anaerobic glycolysis will increase the accumulation of FDG in the tissue. This increased FDG uptake in hypoperfused regions provides an excellent metabolic signal for myocardial viability.

Conclusion

Differentiation of viable from nonviable myocardium is of paramount clinical importance. In patients with chronic coronary artery disease, impaired left ventricular function arises, at least in part, from regions of ischemic or hibernating myocardium rather than just myocardial fibrosis. In such cases, ventricular dysfunction may improve considerably after revascularization.

The assessment of myocardial viability on the basis of regional ventricular function measurements obtained by other methods such as contrast ventriculography, coronary angiography, or echocardiography is often imprecise. Myocardial viability in chronic ischemia, hibernating, or stunned myocardium can be detected by TL-201 SPECT and FDG-PET. The FDG-PET is considered the gold standard for assessing myocardial viability.

It is well documented that between 25% to 50% of the irreversible perfusion defects on conventional thallium-201 stress/redistribution imaging will manifest normal thallium uptake and improved regional wall motion after revascularization. Various protocols are in use to improve sensitivity of thallium imaging.[5,7]

Delayed 24 to 72 hours thallium imaging and reinjection techniques further improve the detection of viability in about 50% of the irreversible perfusion defects seen at 3 to 4 hours conventional thallium redistribution imaging.[4,6]

The metabolic imaging using positron emission tomography has emerged a promising tool for identifying viable myocardium. The demonstration of increased FDG uptake by PET in regions with impaired function and reduced blood flow has been shown to be an accurate marker for the differentiation of hibernating, but viable, myocardium from scarred tissue.[10]

Positron emission tomography is superior to conventional single photon emission tomography using TL-201, but it is expensive, requires complex cyclotron technology, and is not readily available. Conversely, thallium is widely available for clinical use and provides a less expensive alternative to PET in majority of patients. A review of recent literature suggests that thallium reinjection and late redistribution imaging may provide cost effective information for assessing myocardial viability in a majority of the patients, except for a subset of patients who showed persistent perfusion deficits even after undergoing thallium reinjection and late redistribution imaging.

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