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EDITORIAL

Technetium-99m-Sestamibi: Another Window on Myocardial Viability?

The ability to assess myocardial viability following ischemic injury has been the central quest of many imaging modalities, including nuclear, ultrasound, magnetic resonance, and angiographic techniques. In this issue, Freeman et al. have offered further evidence to support the concept that the new myocardial perfusion tracer technetium-99m- (^{99m}Tc) sestamibi reflects not only blood flow but also cell viability is particularly welcome and exciting (*1*).

Of the currently available imaging modalities, the ultimate gold standard of the presence of viable but ischemic myocardium is the return of myocardial function following revascularization (*2*) or evidence of persistent glucose metabolism in an area of ischemia on positron emission tomography (PET) (*3*). Unfortunately, the former is only valid in retrospect, while the latter is not available in the usual clinical settings. The myocardial perfusion agents used for SPECT imaging are much less ideal for this purpose. It has been well known that the traditional stress and redistribution thallium scans may underestimate the extent of viable myocardium due to inadequate redistribution on the standard 4-hr delay studies (*4,5*). The ability to obtain a 24-hr delayed scan (*5*) or to reinject a second dose of thallium prior to the redistribution study can improve the detection significantly (*6*). The potential of imaging myocardial perfusion while obtaining information on myocardial viability using ^{99m}Tc-sestamibi opens an entirely new prospect in the study of myocardial viability.

In this study, Freeman et al. by using an occlusion/reperfusion swine model, administered ^{99m}Tc-sestamibi prior to or during coronary occlusion or at 30 min following reperfusion. The authors have found that if sestamibi was given during coronary occlusion, there was a significant reduction of myocardial sestamibi activity in both the ischemic and infarcted hypoperfused zones. On the other hand, if sestamibi was given during reperfusion, it demonstrated a relatively normal activity in the ischemic zone, while there was a marked reduction in activity in the infarct zone. This suggested that myocardial cell viability was indeed important for the uptake and retention of the isotope. Furthermore, if sestamibi was given prior to occlusion, there was also decreased sestamibi activity in the infarct zone subsequent to reperfusion. This can be interpreted as faster clearance of the

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sestamibi in the infarct zone due to the inability of the myocytes to retain this tracer. Visual scans confirmed these observations from in vitro studies.

This study also agrees with other investigators' experience. Verani et al. in a canine model of occlusion and reperfusion demonstrated that sestamibi during reperfusion can outline the infarct zone accurately when compared with pathologic techniques (*7*). Furthermore, Sinusas et al. demonstrated that the reperfused stunned myocardium demonstrated less sestamibi activity in proportion to regional blood flow as determined by microspheres (*8*). Both of these studies can be interpreted in light of the current study to indicate that the diminished activity in myocardial infarction regions reflects both decreased flow and compromised cell viability. A further study by Beanlands et al., from our laboratory using a perfused heart model in a non-flow limited myocardial injury model, indicated that sestamibi uptake is directly proportional to the degree of cellular viability (*9*).

In light of this new confirmatory evidence, sestamibi is not only an excellent perfusion tracer but also reflects myocardial viability. Only perfused viable myocardium will take up the tracer fully. In a hypoperfused situation, the flow will be proportional to blood flow; in a viability compromised situation, the uptake will be proportional to viability. On a single myocardial scan, if there is normal sestamibi uptake, one may confidently conclude that there is both normal perfusion as well as cell viability. Under situations of changing blood flow such as comparing stress with rest scans, the viable myocardium will show a difference in sestamibi activity between the scans proportional to the perfusion change. On the other hand, non-viable myocardium will not demonstrate this change as the tracer uptake is cell-function limited.

During coronary reperfusion therapy, similar conclusions can be drawn. If a scan shows normal sestamibi uptake following reperfusion, it suggests that there has been restoration of blood flow as well as preservation of viable myocardium. On the other hand, if there has been no change on serial scans with respect to a large defect, then most likely there was no restoration of blood flow. In contrast, if there were changes in the border area surrounding a central residual defect, then this indicates the presence of reperfusion with a mixture of stunned myocardium surrounding an area of infarction.

We have thus reached another crossroad in nuclear cardiology where newly available imaging tools may provide information previously difficult to ascertain. The ability to use sestamibi to detect viable myocardium will have to be challenged by comparison with the gold standards of PET imaging as well as studies in patients before and after revascularization. The comparable merits with double-dose thallium scans will have to wait until the results of larger clinical trials are available. However, the quest to accurately identify viable myocardium is now another step closer.

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