EDITORIAL

Transmural Uptake of Perfusion Tracers and Infarct-Specific Tracers

Morguet et al. have preformed a well-designed, carefully executed animal study that addresses a clinically relevant topic, namely the distribution of transmural uptake of both a perfusion tracer and an infarct-specific tracer in a reperfused infarction model. This study demonstrated that uptake of both a necrosis-avid imaging agent and a perfusion tracer occur in border zones of reperfused infarctions, that in these border zones necrosis is limited primarily to the endocardium and residually viable myocardium exists in the epicardium.

The experimental protocol included open-chest LAD occlusion with early (45 min) reperfusion in a swine model. The investigators injected ^{111}In-antimyosin antibody 48 hr after the infarction and 24 hr later the chest was reopened. Technetium-99m-sestamibi was injected and 60 min later the LAD was reoccluded at the same site and fluorescein injected to label normally perfused myocardium. The animals were killed, the hearts removed and sliced. Using fluorescein and TTC staining the slices were examined macrohistologically and by fluorescence. The slices were then imaged on a camera and the macrohistochemistry, fluorescence, and scintigraphic data were correlated for each slice. Tissue samples were also counted in a well counter. From macrochemistry and fluorescence, the investigators identified three zones: normal, necrotic, and intermediate (mixed normal with islands of necrosis). The intermediate zone tended to be subepicardial at the infarct borders and corresponded on the scintigrams to uptake of both ^{111}In-AMA and ^{99m}Tc-sestamibi with counts intermediate between the normal and necrotic zones.

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Previous animal studies reporting uptake of both a myocardial necrosis-avid agent and a myocardial perfusion agent have used either ^{99m}Tc-pyrophosphate and ^{201}Tl with sequential imaging (1) or ^{111}In-AMA and ^{201}Tl with simultaneous imaging (*2*). The wide separation of the high (247 keV) photopeak of ^{111}In and the main (70 keV) photopeak of ^{201}Tl along with similar half-lives (and doses) of these two tracers make them well suited for simultaneous imaging. In the present study, which was not an in vivo imaging study, ^{99m}Tc-sestamibi was used instead of ^{201}Tl as the perfusion tracer. In two previously reported animal studies of both reperfused and nonreperfused infarctions, uptake of ^{99m}Tc-sestamibi paralleled uptake of ^{201}Tl and microspheres for ischemic and nonischemic territories and for transmural tracer distribution (*3,4*). A dose differential factor of 10 between the ^{99m}Tc-sestamibi and ^{111}In-AMA was used in the study by Morguet et al. with 24 hr elapsing between injection of ^{111}In-AMA and ^{99m}Tc-sestamibi. Using a 20% window over only the high (247 keV) photopeak of ^{111}In and a 10% window over the 140 keV photopeak of ^{99m}Tc, they recorded a total of 80–120K cts in the ^{99m}Tc window and 50–70K cts in the ^{111}In window.

In a previously reported dual-isotope (^{201}Tl and ^{111}In-AMA) tomographic imaging study in dogs in which half the animals underwent early reperfusion (2-hr occlusion) and half underwent late (no reflow) reperfusion (6-hr occlusion), infarct size was determined using a threshold method and was found to correlate with infarct size by TTC (*2*). Based on the results of the study by Morguet et al., the 2-hr reperfused infarcts should have shown uptake of both ^{111}In-AMA and ^{201}Tl in border zones and infarct sizing using a threshold technique would have overestimated infarct size by TTC. The histopathology of the early reperfused infarcts in this earlier study did in fact show islands of viable myocardium intermixed with necrosis in the early reperfused infarcts. The overall good correlation with infarct size by TTC was due to the fact that all the reperfused infarcts were smaller than the late (non) reperfused infarcts and the points for the early reperfused infarct sizes clustered at the lower part of the regression line.

Experiences with simultaneous tomographic imaging of ^{111}In-AMA and ^{201}Tl in man have been reported (*5, 6*). When the simultaneously acquired tomographic studies were interpreted qualitatively, three patterns of uptake for the two tracers were described: matches in which the thallium defect correlated in location and extent to antimyosin uptake, mismatches in which the thallium defect or defects were more extensive than areas of ^{111}In-AMA uptake, and overlap in which there was uptake of both tracers in the same myocardial wall. Matching patterns were seen more frequently in nonreperfused or Q-wave infarctions. Mismatch and overlap were seen more frequently in non-Q-wave and reperfused infarctions. A few patients with non-Q-wave infarctions have demonstrated homogenous uptake of ^{201}Tl with overlapping uptake of ^{111}In-AMA in the infarct territory. These patients presumably have necrosis localized to the subendocardial layers. To correlate scan pattern with ischemic events, patients were placed into a single category, either "match" or "mismatch" (including overlap) based on the predominant pattern. However, a combination of patterns commonly occurred in one heart. In addition, the degree of tracer overlap in this clinical study was probably underestimated because the dual-isotope tomographic

scans were analyzed qualitatively. Quantitative analysis of the thallium scans will probably reveal thallium activity overlapping ^{111}In-AMA activity in the infarct borders.

It is apparent both from the results of the study by Morguet et al. and from the clinical data that attempts to size a reperfused infarction from the extent of ^{111}In-AMA uptake alone using a threshold technique and without a perfusion tracer will lead to overestimation of infarct size. A quantitative count based method using the perfusion agent data alone would be a more reasonable approach to sizing a non-transmural infarction (*7, 8*). The data from the study by Morguet et al. also suggest that a quantitative approach to interpretation of the simultaneously acquired dual-isotope data in man would represent an important next step to refining the technique.

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