Are All Myocardial Infarctions Alike?

When is a physiologic abnormality clinically important? This question is frequently asked as more and more sensitive diagnostic tools become available to us. Technetium pyrophosphate (Tc-PPI) scanning to diagnose myocardial infarction (MI) in patients after coronary artery bypass surgery is an example of a sensitive test that has been examined extensively.1-3 Such studies have raised several important questions. What exactly constitutes a myocardial infarction? How is MI best diagnosed? Does a MI diagnosed only by a very sensitive technique have a different clinical importance from a MI diagnosed by less sensitive means?

Previous studies have used a variety of tests to determine if a perioperative myocardial infarction occurred. Using different criteria, these studies have concluded that the incidence of myocardial infarction following coronary artery bypass surgery varies widely, as pointed out by Cheng et al.4 Each test used to establish the diagnosis of MI appears to be less than ideal. For example, although the appearance of new Q waves on postoperative electrocardiograms is quite specific for MI, it is relatively insensitive. Prospective studies have suggested that the false-negative rate is over 40%.5 The clinical importance of new Q waves on the postoperative ECG, however, is great. This test identifies a subgroup of patients with a decreased survival. In a study comparing 77 patients who developed new Q waves perioperatively to 1790 patients who did not, 5-year survival was 76% in patients with a perioperative MI compared with 90% in those with no infarction.7 Serial serum enzyme concentrations, usually peak values of creatine kinase-MB, increase the sensitivity of MI diagnosis, but require the establishment of an arbitrary lower limit of normal to avoid an unacceptably high incidence of false-positive results. The variable increase of serum creatine kinase-MB activity following cardiac surgery also complicates interpretation of this test.8

In this issue of ANESTHESIOLOGY, Cheng et al. used technetium pyrophosphate scanning to assess the incidence of myocardial infarction after coronary artery bypass surgery.6

Technetium-99m pyrophosphate (Tc-PPI) is an infarct-avid compound that has been widely used to detect myocardial infarction in patients following coronary artery bypass surgery. This agent is concentrated both in areas of irreversible and reversible severe tissue damage. Uptake has been correlated with infarct size in animals models9 and creatine kinase-MB release in patients.5,10 However, some reperfused areas, while severely damaged but viable, may also concentrate Tc-PPI.11 This may mean that some scans overestimate the degree of myocardial damage. So while a positive Tc-PPI scan may be highly suggestive of a MI, i.e., highly sensitive, the technique lacks absolute specificity. Technical factors involved in the imaging process, such as separating subendocardial activity from residual blood pool activity during planar imaging, may reduce the specificity of this test further. To achieve a high sensitivity and specificity, investigators often combine the results of several different tests, diagnosing an MI only if two or more of the selected tests are positive.3,4

These technical problems of Tc-PPI imaging are ameliorated by using tomographic imaging techniques12 (single-photon emission computed tomography, SPECT),
such as performed in the study of Cheng et al.\textsuperscript{6} This technique appears to be extremely sensitive and is capable of determining location and size of infarcts.\textsuperscript{15} What is the clinical significance of a perioperative MI diagnosed by Tc-PPI SPECT alone? In the study by Cheng et al., seven of 28 patients had a positive scan.\textsuperscript{6} Those patients with ST-segment changes suggestive of myocardial ischemia in the prebypass period were more likely to have a positive scan postoperatively than those whose electrocardiogram did not reflect changes consistent with ischemia. While electrocardiographic and hemodynamic data were only recorded intermittently, it appears that ischemic electrocardiographic changes occurred despite careful hemodynamic monitoring and aggressive pharmacologic intervention. This suggests that other anatomic and physiologic factors not under the usual control of the anesthesiologist may contribute to the development of intraoperative myocardial ischemia and result in myocardial damage postoperatively. This is consistent with a growing body of literature.\textsuperscript{14-16} It is for this reason that this study is important.

Despite the positive scan, these patients did quite well. Only one of the patients with a positive scan suffered a Q wave infarction. No patient in either group died and the postoperative left ventricular ejection fraction was not affected by the presence of the myocardial infarction.

The patients reported on in this study of Cheng et al. are in fact a subset of a larger study performed at Toronto Western Hospital.\textsuperscript{5} The larger study used imaging techniques identical to those of Cheng et al. to examine 58 patients before and after elective coronary artery bypass surgery. The study examined the relationship of clinical characteristics, preoperative coronary angiography and Tc-PPI SPECT scans, and postoperative creatine kinase and creatine kinase-MB determinations to the results of postoperative Tc-PPI SPECT scans and clinical outcome. Twelve of the 58 patients (21%) had a positive Tc-PPI SPECT scan postoperatively. Only two of 58 patients (of which one had a normal scan) had a Q wave infarction postoperatively. While the peak serum concentration of creatine kinase-MB was increased in those with a positive scan, the mean value was less than 45 U/l, well within the usually accepted normal values for creatine kinase-MB following coronary artery bypass surgery. Comparing those patients with positive to those with negative scans, left and right ventricular ejection fractions were not significantly different either 48 h or 6 months postoperatively. All of the 58 patients were alive 6 months postoperatively. Interestingly, the study suggested that patients with positive postoperative scans were more likely to have more severe preoperative angina, as defined by New York Heart Association class, and narrower distal grafted vessels. In addition, all positive scans were localized to myocardial segments that were either revascularized using sequential saphenous vein grafts (five patients) or perfused by significantly stenosed arteries that were considered too small to warrant bypass grafting (seven patients). It is therefore not surprising that such areas may become ischemic prior to and after bypass.

It is reasonable to assume that myocardial Tc-PPI uptake as assessed by SPECT reflects myocardial damage. It is also reasonable to question, however, whether a positive Tc-PPI SPECT scan alone following coronary artery bypass surgery is correlated with increased complications and late mortality, as implied by the report of Cheng et al., given the relatively benign postoperative course of the patients in these studies.\textsuperscript{6} A positive scan in the absence of clinical symptoms, electrocardiographic changes, and increased concentration of enzymes could represent severely damaged but viable tissue, or small areas of myocardial necrosis rather than extensive damage. Burns et al. emphasize this point in their companion study: "Whereas perioperative AMI (acute myocardial infarction) diagnosed by new Q waves and enzyme elevation impacts adversely on short- and long-term clinical outcome, increased detection of clinically less obvious and presumably smaller AMIs by SPECT does not necessarily have the same prognostic implications.\textsuperscript{15}

A rose by any other name is still a rose. A postoperative myocardial infarction, on the other hand, may be many things. By definition, a myocardial infarction implies that irreversible necrosis of myocardial cells has occurred. Sensitive tests for myocardial damage, such as Tc-PPI SPECT, are valuable to diagnose that such damage is present. But, the physiologic consequences of this damage depend upon the additional factors of size, location, and extent (transmural vs. nontransmural), and the functional status of the remaining viable tissue. Future studies will be needed to assess the significance of these additional factors.

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