Assessment of the size of acute myocardial infarction II: electrocardiography and imaging methods

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The electrocardiogram gives a reasonable estimate of infarct size but the confidence limits are wide, and the estimates are unreliable in inferior wall infarction. Infarct size also can be determined from perfusion scintigraphy, assessment of left ventricular dimensions, wall motion disturbances, and other characteristics of the left ventricular wall. Nuclear magnetic resonance imaging, particularly with contrast enhancement, has the greatest potential for accuracy.

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ELECTROCARDIOGRAPHIC METHODS

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This article reviews the uses, merits, and limitations of nonbiochemical methods of assessing infarct size, including electrocardiography and various imaging methods. A companion article deals similarly with biochemical methods.

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ELECTROCARDIOGRAPHIC METHODS

The ECG is universally available to diagnose myocardial infarction. It is relatively inexpensive, causes no harm to the patient, and its recording methods and nomenclature have been internationally standardized from its earliest days.

The potential of the ECG to assess the size of myocardial infarction has been studied extensively over the last decade. For example, Selvester and associates introduced a QRS scoring system to determine infarct size based upon computer simulations of human heart activation. Wagner and co-workers simplified this 32-point scoring system to a 29-point system, in which all 37 criteria relate to duration of initial Q or R wave and R/Q or R/S ratios.

These scoring systems have been validated by comparing the results to peak level or cumulative release of cardiac enzymes, autopsy results, radionuclide studies, and angiography findings. Although these validation studies have produced somewhat contradictory results, the conclusion appears justified that the QRS scoring allows a reasonable estimation of infarct size in anterior infarction with marked discrepancies in...
individual cases. The ECG is of questionable reliability in determining the size of inferior infarction.

Following myocardial infarction, it is common for the ECG to revert gradually to normal and for pathological Q waves to disappear. Therefore, the ECG to be used for infarct sizing should be obtained as soon as the QRS complex stabilizes following the acute event—usually after 1 to 2 weeks.

Some ECG abnormalities, particularly conduction disturbances and multiple infarctions, may render the QRS complex unsuitable for infarct sizing. Furthermore, some acute infarctions do not produce pathological Q waves or other significant changes of the QRS complex. In these cases the only remaining ECG parameter is the initial repolarization disturbance. Aldrich and associates observed a good correlation between initial repolarization disturbance and subsequent QRS score, while Br and colleagues found that a high sum of ST elevations in the acute stage of myocardial infarction correlated significantly with infarct size.

In contrast, Hogg and co-workers found, in patients who underwent thrombolytic treatment, that the initial ST elevations did not allow prediction of infarct size by QRS score.

Selwyn and associates, studying time-varying changes of ST and QRS in patients with inferior infarction using a 72-point precordial ECG map, concluded that there is no simple relationship between areas of ST elevation, loss of R amplitude and appearance of Q waves. Likewise, Norris and colleagues concluded that in patients with anterior infarction, ST elevations are not a reliable index of size or severity of infarction.

These results are generally disappointing, and have stimulated several studies that used a vectorcardiographic approach or precordial ECG mapping with up to 120 body surface ECG signals. The results of these studies are difficult to compare because of a lack of standardization. These sophisticated approaches have led to better insight into ECG phenomena but not to significantly better accuracy in assessing infarct size.

SCINTIGRAPHIC TECHNIQUES

Imaging with thallium 201

Thallium 201 is the most widely used radiotracer for myocardial perfusion imaging. The distribution of thallium 201 following intravenous administration correlates with regional blood flow. Myocardial infarction can be diagnosed by identifying a "cold spot" lesion, or area of diminished tracer uptake, in regional myocardial areas.

As early as 1976, Wackers and colleagues showed the sensitivity of planar thallium 201 imaging for detection of acute myocardial infarction when studies are performed within 24 hours of onset. The same group of investigators also demonstrated a good correlation between the thallium 201 defect size and the postmortem findings in 23 patients who died from acute myocardial infarcts. In addition, the autopsy studies showed thallium 201 scintigraphy to be unequivocally superior to ECG in localizing and sizing myocardial infarcts.

Early in the postinfarct period, a thallium perfusion defect reflects both necrotic and ischemic myocardium; it is only after resolution of peri-infarction ischemia that thallium defect size corresponds accurately with actual infarct size. The practical importance of this finding is that thallium 201 administered immediately after reperfusion with thrombolytic therapy overestimates the amount of necrotic tissue; if thallium administration is delayed until more than 48 hours after reperfusion, the estimate will be more accurate.

Serial imaging after the initial 48 hours also may help to differentiate between successful and failed thrombolysis.

SPECT imaging

Single photon emission computed tomography (SPECT) imaging has been advocated to enhance the contrast between ischemic lesions and normally perfused myocardial zones; the technique increases the sensitivity for detecting infarcted myocardial areas. In essence, SPECT provides tomographic images by reconstruction from projections.

Thallium 201 SPECT has been used to measure the mass of infarcted left ventricular myocardium as a percentage of total left ventricular mass or by applying a threshold method. Prigent and associates demonstrated in dogs an excellent correlation between SPECT defect size and the pathologic infarct size. Thallium SPECT estimates of myocardial infarct size were also found to correlate well with cumulative CK-MB release in man. Because it can quantify the volume of infarcted myocardium, the thallium-SPECT technique is more accurate than planar imaging for infarct sizing.

Delayed imaging technique

Technetium 99m labeled to hexakis-2-methoxy-2-methylpropyl-isonitrile (technetium-99m Sestamibi) is a new radiopharmaceutical that appears useful for myocardial perfusion imaging. Like thallium 201, technetium-99m Sestamibi accumulates in normal myocardium in direct proportion to blood flow; unlike thallium 201, it has a slow washout from the myocardium with minimal redistribution. Imaging can therefore be delayed for up to 6 hours and still
provide information about the distribution of myocardial perfusion at the time of administration.\(^4\)  

**Infarct-avid imaging**

Infarct-avid imaging refers to the accumulation of a radiopharmaceutical within a region of irreversibly injured myocardium. The influx of the radiopharmaceutical into the myocyte produces a “hot spot” in the infarcted area. The most commonly used infarct-avid imaging agent is technetium 99m stannous pyrophosphate, but indium 111 antimyosin has recently been used for the same purpose. Technetium 99m pyrophosphate forms a complex with the calcium deposited in damaged myocardial cells, while indium 111 antimyosin shows a specific affinity for cardiac myosin.

In experimental anterior myocardial infarcts involving more than 3 g of myocardium, the extent of technetium 99m pyrophosphate activity on planar images correlated well with anatomic infarct size.\(^4\) Ko and colleagues observed a good correlation between pyrophosphate uptake and the peak level of creatine kinase in patients with acute myocardial infarction.\(^4\) Lewis and co-workers used SPECT to measure technetium 99m pyrophosphate activity in dogs following coronary artery ligation.\(^4\) For larger infarcts an excellent correlation was observed between scintigraphic findings and anatomic infarct weight but the correlation was weaker for infarcts involving less than 10 g of myocardium.

Willerson and associates showed that SPECT imaging with technetium 99m pyrophosphate can accurately measure infarct size in patients with acute myocardial infarction.\(^4\)\(^5\) Hashimoto and colleagues showed that early positive acute technetium 99m pyrophosphate imaging with SPECT is a reliable and safe way to document early reperfusion and an effective way to size and localize the infarct as early as 8 hours after its onset.\(^4\)\(^5\)

SPECT imaging with indium 111 antimyosin to measure acute infarct size correlates well with left ventricular ejection fraction, peak CK-MB and thallium defect size, as shown by Antunes and associates.\(^5\) Their values were in the same range as reported with SPECT pyrophosphate.

The sensitivities of SPECT imaging methods are high, but their specificities are low because myocardial radioisotope accumulation occurs in several different disease processes. For example, positive images with technetium 99m pyrophosphate have been observed in patients with ventricular aneurysm, myocardial trauma, and after radiation therapy. Also, uptake of the radioisotope by bone may restrict estimation of infarct size. Myocardial uptake of labeled antimyosin has been described in patients with acute myocarditis and in allograft hearts with evidence of transplant rejection.

### POSITRON EMISSION TOMOGRAPHY

Positron emission tomography (PET) allows the study of tracers that have been incorporated into natural substrates—for example, palmitate labeled with \(^1\)C as a marker of fatty acid metabolism.\(^5\)\(^2\)\(^5\)

\(^1\)C-labeled palmitate has been used to assess infarct size in patients with acute myocardial infarction.\(^5\)\(^2\) After geometric reconstruction of the tomographic slices, regions of acute infarct were defined as those with palmitate uptake of 50% or less than maximal. The areas were planimetered and within each slice the infarct areas were summed to derive the total mass of infarcted myocardium. This value correlated closely with enzymatic infarct size derived from CK release.

Other clinical PET studies using metabolic markers showed that myocardial regions with unequivocal thallium perfusion defects may still have metabolic activity.\(^3\) The implication is that perfusion imaging may overestimate infarct size.

PET imaging may be more useful than thallium 201 imaging to quantify infarct size and differentiate viable from nonviable myocardium; but the overall clinical value of this expensive and not commonly available new technique remains unsettled.

### MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging (MRI) has emerged as a new diagnostic technique to study the extent of anatomical and functional abnormalities in patients with acute myocardial infarction. Magnetic resonance imaging is a nonionizing high-resolution tomographic technique that provides good soft-tissue contrast, sharp delineation of the myocardium, and adequate characterization of myocardial tissue (Figure 1).

The signal intensity of the images depend on both the hydrogen density and the relaxation times (T1, or longitudinal relaxation time, and T2, or transverse relaxation time) of the myocardial tissue. Image contrast increases with a higher hydrogen density, shortened T1, and lengthened T2.

Both experimental and clinical experience with MRI for direct anatomic estimation of infarct size are limited. The first studies, done in dog hearts, showed that T1 and particularly T2 were usually prolonged in disease states characterized by edematous changes that occur in regions of acute myocardial ischemia or infarction.\(^5\) Measurements of the
relative size of an acute myocardial infarction based on regional changes in T2 relaxation times in the myocardium following experimental coronary artery occlusion have correlated closely with postmortem estimates of infarct size.\(^{55}\)

Recently, Bouchard and associates demonstrated experimentally that infarct size could be assessed on the basis of T2 differences in infarcted and normal tissue.\(^{56}\) Wisenberg and associates showed in dogs that the evaluation of T1 is unsuitable for early assessment of infarct size and delineates the extent of an infarction only by day 21.\(^{57}\) This finding was corroborated in patients 3 weeks after acute myocardial infarction in whom infarct size could reliably be assessed.\(^{58}\)

Tissue relaxation parameters have limited clinical reliability in the acute phase of infarction. Regional wall thinning may have better potential as a measure of infarct size in patients with either a recent or remote infarction. White and associates\(^{59}\) recently estimated the size of acute infarction by the extent of regional left ventricular wall thinning as observed on magnetic resonance images. Relative infarction size was calculated from the cumulative volume of regionally thinned left ventricular wall and the total myocardial volume of the left ventricle. The resulting values for relative infarct showed a good inverse correlation with left ventricular ejection fraction determined by either radionuclide angiography or biplanar contrast angiography.

Despite the ability to use the relaxation parameters T1 and T2 to generate images of varying contrast, it is far from easy to detect abnormalities in tissue physiology in the early stage of myocardial ischemia. Therefore, paramagnetic contrast agents have been developed. One of these agents, gadolinium (Gd)-DTPA, can be safely used for contrast imaging in patients with acute myocardial infarction. Gd-DTPA shortens both T1 and T2 relaxation times in irreversibly damaged myocardial tissue. The effect on T1 relaxation time is predominant, and therefore T1 weighted images will show enhanced signal intensity in acutely infarcted myocardium after administration of Gd-DTPA.

Nishimura and co-workers recently compared measurement of infarct size by MRI and Gd-DTPA with indium-111 antimyosin imaging.\(^{60}\) The T1 shortening associated with Gd-DTPA significantly enhanced contrast in the infarcted area, with precise expression of infarct size.\(^{60}\)
We determined infarct size by nuclear magnetic resonance imaging and Gd-DTPA (0.2 mmol/kg IV) in 20 patients who received streptokinase for acute myocardial infarction.\(^6\) Nine slices (10 mm thick, 2 mm gap) perpendicular to the long axis of the left ventricle were obtained; for every slice the area with enhanced signal intensity (>mean + 2 standard deviations) was considered to be infarcted. These areas were summed for all slices and infarct size was calculated and expressed as a percentage of the total left ventricular volume. Infarct size proved to be significantly smaller in patients in whom reperfusion was achieved as compared to patients without reperfusion (8% (SD, 5%) vs 15% (SD, 4%).

**ANGIOGRAPHIC METHODS AND ECHOCARDIOGRAPHY**

Radionuclide angiography, contrast angiography, and echocardiography all provide the same type of information—left ventricular dimensions and wall movements. Of these three methods, contrast angiography gives the highest definition of detail, but the other two methods have the advantage of being noninvasive and applicable in difficult settings such as the coronary care unit.

Recently the importance of “remodeling” of left ventricular geometry after myocardial infarction has been emphasized. Following myocardial infarction, changes in left ventricular dimensions and wall movements occur gradually over prolonged periods. Therefore, data obtained at one point in time can provide only limited information about infarct size. However, the results of correlation studies are better than might be expected. Morrison and colleagues reported a good correlation between radionuclide angiographic estimates of infarct size and release of CK-MB.\(^6\)

In a randomized study to investigate the effects of thrombolytic therapy, we found that the alpha-HBDH—determined reduction of infarct size in the treated group correlated with significantly improved left ventricular ejection fraction measured by radionuclide angiography.\(^6\) In the same study, follow-up contrast angiograms in 266 patients showed a satisfactory correlation between enzymatic infarct size, left ventricular volumes, and volume-derived function parameters.\(^6\)

Another large study of thrombolysis found similar correlations\(^6\), and Anderson and colleagues found improved radionuclide ejection fraction in patients who underwent successful thrombolysis.\(^8\) These data support studies which show that left ventricular volume and wall movements are major indicators of survival in patients who have sustained acute myocardial infarctions.\(^8\)

In contrast, Jaarsma and co-workers found little correlation between enzymatic infarct size and echocardiographic findings.\(^8\) However, these investigators used only peak CK-MB values obtained at 6-hour intervals which makes their enzymatic data unreliable.

In addition to the classical parameters, such as systolic and diastolic left ventricular volumes and wall movements, other measures have been used to enhance echocardiographic accuracy. These include total wall motion score,\(^10\) expansion and thinning ratio,\(^7\) endocardial surface mapping,\(^7\) and regional hyperkinesia.\(^6\)

Despite the promise of these methods, we have insufficient data to determine their value with regard to infarct sizing. A combination of diagnostic methods, as was attempted by Grande and colleagues,\(^5\) may eventually lead to an optimal estimation of infarct size and location.

**REFERENCES**


