Correlation of Radionuclide Estimates of Myocardial Infarction Size and Release of Creatine Kinase-MB in Man

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SUMMARY  Creatine kinase-MB isoenzyme release (CK-MB-g-Eq) was correlated with left ventricular (LV) radionuclide gated blood pool wall motion estimates of percent abnormally contracting regions (%ACR), ejection fraction (EF) and quantitative thallium-201 (Tl-201) LV perfusion scintigraphy (Tl-201 perfusion index) during evolving myocardial infarction (MI). Of the 35 patients, 14 had no evidence of either prior MI or right ventricular (RV) MI, and the CK-MB-g-Eq showed reasonable correlation with %ACR (r = 0.72; SEE = 18.28), with EF (r = −0.78; SEE = 0.07) and with the Tl-201 perfusion index (r = 0.65; SEE = 7.93).

In the six patients with prior MI there was no significant correlation between CK-MB-g-Eq and %ACR, EF or Tl-201 perfusion index.

Eight other patients had a RVEF that was less than one-half of the LVEF, as well as regional RV wall motion abnormalities, suggesting a combination of LV and RV necrosis. In these patients, there was no significant correlation between CK-MB-g-Eq and %ACR, LVEF or Tl-201 perfusion index.

In seven patients with two peaks to their CK-MB release curve, before CK-MB returned to baseline, CK-MB-g-Eq was associated with early %ACR (r = 0.71; SEE = 21.06), EF (r = −0.81; SEE = 0.14) and with the early Tl-201 perfusion index (r = 0.78; SEE = 6.46), suggesting either that small extensions are beyond the resolution of the radionuclide assessment techniques used in this study or that these patients represent a variant CK-MB release pattern unassociated with extension.

These independent radionuclide and enzymatic data suggest that radionuclide techniques may be a reliable clinical method for assessing the extent of LV necrosis during MI. However, limitations may exist in certain cases when either concurrent RV necrosis or prior MI are present.

PHARMACOLOGIC INTERVENTIONS that alter the biochemical environment of ischemic myocardial zones may alter ultimate myocardial infarct size. Abundant experimental evidence in animal models indicates that this is so.

Recent interest in methods to reduce the extent of myocardial necrosis in man during acute myocardial infarction has emphasized the importance of accurate techniques to assess the magnitude of completed myocardial infarct size. Sobel et al. proposed a mathematical model whereby estimates of myocardial infarct size may be obtained from serial analysis of serum creatine kinase (CK)-MB isoenzyme during evolving myocardial infarction. Reasonable quantitative relationships between CK-MB isoenzyme accumulated release and angiographic estimates of infarct size obtained at a mean of 33 days after myocardial infarction have been reported. Bleifeld et al. showed that in humans who died after acute myocardial infarction, CK infarct size correlated closely with morphologic infarct size determined at postmortem examination. Although some controversy exists as to the validity of CK infarct sizing when the mathematical model is extrapolated to patients with acute myocardial infarction, most CK-MB data suggest this enzymatic system has at least qualitative validity in man.

Other acute phase independent descriptors of myocardial infarct size are needed in addition to enzymatic estimates. There is evidence that gated blood pool wall motion and thallium-201 are useful for describing left ventricular performance and infarct size during acute myocardial infarction. In this report we describe radionuclide assessment of left ventricular infarct size and left ventricular function in patients in the acute phase of myocardial infarction and their correlation with the release of the CK-MB isoenzyme during myocardial infarction.

Methods

Clinical Studies

The study population was composed of all patients admitted to the coronary care unit of North Shore University Hospital from November 1978 through

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Supported by the American Heart Association, Nassau Chapter; USPHS grant 1 S08 RR09128-01A, GRS Biomedical Research Development Program, NIH; the Herman Goldman Foundation; the Samuel Dorsky Research Fund; and the Board of Trustees Research Fund, North Shore University Hospital.

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June 1979 who met the following criteria: (1) acute transmural myocardial infarction diagnosed by rise and fall of CK-MB serum isoenzyme and serial electrocardiographic abnormalities with the development of Q-waves > 0.04 second; (2) admission within 6 hours of the episode of most severe chest pain; (3) no evidence of significant hypertensive or valvular heart disease; (4) no evidence of cardiac arrest or cardiogenic shock; and (5) availability of data from radionuclide ventriculography, thallium-201 left ventricular perfusion imaging and quantitative serum CK-MB isoenzyme curves.

Enzymatic Assessment of Infarct Size

A percutaneous polyethylene catheter was positioned in an antecubital vein to allow for serial sampling of blood every 2–6 hours for CK determination. Venous blood samples were collected in tubes containing sodium EDTA, centrifuged immediately at 10,000 rpm for 10 minutes at 4°C, and the sera were frozen at −70°C. Studies showed that CK-MB isoenzyme activity remained stable for as long as 1 month under these conditions. CK-MB isoenzyme activity was separated from sera by DEAE-Sephadex column chromatography using minicolumns (Roche Diagnostics). Total serum CK activity was determined according to Rosalki, as was CK-MM and CK-MB isoenzyme activity of the column eluates. The coefficient of variation of replicate assays for CK-MB was 4.0%. Completed infarct size was calculated from all available serial CK-MB data by use of the mathematical model described by Sobel et al. The enzyme clearance rate (kd) for each patient was estimated from a computerized mathematical inspection of CK-MB vs time plot when myocardial enzyme release was zero. These individual kd values were then used to calculate infarct size.

Quantitative Radionuclide Angiography

Multiple-gated blood pool acquisition imaging was accomplished with a mobile Anger scintillation camera (Searle Radiographics Inc.) interfaced with a PDP 11/34 computer with a 48k memory (Digital Equipment Corp.). Red blood cells were tagged in vivo with 20 mCi of technetium-99m pertechnetate (Union Carbide) by the method of Pavel et al. Wall motion studies were performed with the patient in the 45° left anterior oblique position with the ventricular septum in vertical alignment on the video display of the computer. Wall motion algorithms were modifications of those described by Green et al. and Maddox et al. An independent observer using an irregular region of interest algorithm identified the left ventricle. An automated computer macro algorithm was then used to seek out the region of interest's greatest vertical and horizontal dimensions and to construct the associated rectangle by which it would be circumscribed. The circumscribing rectangle was divided into eight segments. This grid was then superimposed on the region of interest and any portions of the rectangle were erased if they ran over the latter's perimeter (fig. 1). Three rectangular background areas were computer-defined and placed at the lateral, septal and apical sides of the region of interest; background subtraction from adjacent regions was accomplished by computer algorithms as described by Maddox et al. For each study, a global ejection fraction value as well as ejection fractions for each of the eight regions were generated from global and regional time-activity curves. Using similar computer algorithms, gated regional wall motion analysis of the right ventricle was also performed. Thirty-three studies in 11 patients were analyzed for intraobserver variation. The coefficient of variation of replicate left ventricular ejection fractions was 4.0% (range 2.0–6.0%) for each of the left ventricular regions. The coefficient of variation of replicate right ventricular ejection fractions was 5.0%. Interobserver variation was assessed in 24 studies from eight patients. The coefficient of variation between analyses by the two observers was 5.0% for left ventricular ejection fractions and ranged from 2.0–8.0% for each of the left ventricular regions. The coefficient of variation for right ventricular ejection fractions was 6.0%.

To determine the validity of regional ejection fraction in assessing segmental ventricular performance, data from 18 patients with a history of remote prior myocardial infarction who underwent contrast ventriculography followed by a radionuclide wall motion study were compared. Each right anterior oblique contrast ventriculographic study was analyzed using a computerized system (Electronics for Medicine VVF).

Figure 1. Modified left anterior oblique view of the end-diastolic image with the left ventricular perimeter circled and divided into eight regions by the vertical and horizontal lines. Automatic computer-defined background-subtracted areas are identified by the three rectangles. Numbering of the left ventricular regions starts in region 1, the upper area to the left of the vertical line, and moves counterclockwise to region 8.
With stop-frame techniques, outlines of diastolic and systolic images were traced from projected cineangiograms with a light-pen digitizer by an independent observer. The left ventricular ejection fraction was calculated using a single-plane, area-length method and regression equations described by Kennedy et al.\textsuperscript{21} Computerized segmental wall motion analysis was performed as follows: the long axis of each ventricular outline (systole and diastole) was divided into four equidistant sections, defining three points on the long axis. Chords were drawn perpendicular to the axis through these points, dividing the ventricle into eight segments. The area of each ventricular segment defined by the chords was computed together with chord shortening and an ejection fraction was derived for each segment (fig. 2). Regional radionuclide-derived ejection fractions were anatomically summed and compared with corresponding angiographically determined segmental wall motion in the anteroseptal, apical and inferoposterior regions. When 54 anatomic regions (three per patient) were analyzed, reasonable correlations were obtained between segmental wall motion analysis of contrast ventriculograms and regional radionuclide wall motion (table 1).

In patients with acute myocardial infarction, the percentage of abnormally contracting regions (%ACR) was calculated from the eight regions of the radionuclide left ventriculogram. In 22 patients with a history of angina and without prior myocardial infarction who were pain-free at the time of sequential radionuclide regional wall motion assessment, 1 standard deviation of the mean ejection fraction for any given region of the left ventricle never fell below 0.40 (table 2). Hence, in patients with acute myocardial infarction, any left ventricular region with an ejection fraction below 0.40 was scored as abnormal.

**Left Ventricular Perfusion**

Thallium-201 scintigraphy was performed 30 minutes after the i.v. injection of 1.8–2.4 mCi of Tl-201 (New England Nuclear). Analog images were obtained by the scintillation camera and digitized by the computer. Images were collected in the zoom mode and presented on a color video scope (Conrac) for data analysis. A low-energy, high-resolution, converging-hole collimator was used on the camera. Anterior, left anterior oblique at 15° and 45° and left lateral projections were obtained with 500,000 counts per view in a 128 × 128 matrix. The perfusion scintigrams were enhanced with a nine-point computer smoothing technique before data analysis. With algorithms, the perimeter of the myocardial image was circumscribed in a regular region and all matrix cells outside of this region were changed to zero counts. The minimum count within the regular region circumscribing the left ventricle was considered as background and then subtracted from each cell in the matrix.

Seven equal, square regions were drawn to fit the left ventricle on each projection (fig. 3). On each projection, the region with the highest count density was used as a relative index of normal to compare with the other six regions. Counts in each region were subtracted from the region with highest count density and percent perfusion in each region was determined. The percent regional perfusion score was calculated as

\[
\text{A (highest) - B (another region) \times 100} / \text{A}
\]

Deficits greater than 20.5% in perfusion were considered abnormal. A mean value of all abnormal per-

**Table 1. Anatomic Left Ventricular Regions and Relationships of Contrast and Radionuclide Wall Motion**

<table>
<thead>
<tr>
<th>Anatomic region</th>
<th>Radionuclide regions included</th>
<th>Cine segments included</th>
<th>Radionuclide EF vs cine EF</th>
<th>r</th>
<th>SEE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global</td>
<td>1-8</td>
<td>A1-A8</td>
<td>0.88</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>Anteroseptal</td>
<td>2,3</td>
<td>A2,A3</td>
<td>0.77</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>Apical</td>
<td>4,5</td>
<td>A4,A5</td>
<td>0.76</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Inferoposterior</td>
<td>6,7</td>
<td>A6,A7</td>
<td>0.70</td>
<td>0.10</td>
<td></td>
</tr>
</tbody>
</table>

See also figures 1 and 2. Abbreviations: Cine = x-ray contrast cineangiography; EF = left ventricular ejection fraction.

**Table 2. Regional Radionuclide Left Ventricular Ejection Fractions in 22 Patients with a History of Angina and Without Prior Myocardial Infarction**

<table>
<thead>
<tr>
<th>Region</th>
<th>EF (mean ± sd)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.66 ± 0.10</td>
<td>0.51–0.80</td>
</tr>
<tr>
<td>2</td>
<td>0.51 ± 0.07</td>
<td>0.41–0.63</td>
</tr>
<tr>
<td>3</td>
<td>0.54 ± 0.06</td>
<td>0.43–0.58</td>
</tr>
<tr>
<td>4</td>
<td>0.61 ± 0.05</td>
<td>0.44–0.68</td>
</tr>
<tr>
<td>5</td>
<td>0.66 ± 0.06</td>
<td>0.60–0.72</td>
</tr>
<tr>
<td>6</td>
<td>0.60 ± 0.05</td>
<td>0.52–0.70</td>
</tr>
<tr>
<td>7</td>
<td>0.58 ± 0.05</td>
<td>0.52–0.68</td>
</tr>
<tr>
<td>8</td>
<td>0.67 ± 0.10</td>
<td>0.50–0.80</td>
</tr>
</tbody>
</table>
cent regional perfusion scores from the four views was determined and this value was considered the percent abnormal perfusion.

Scintigrams were also scored as to the number of abnormal regions (X) in all views obtained:

\[
\text{Percent abnormal area} = \frac{X}{28} \times 100
\]

Using percent abnormal perfusion and percent abnormal area, a left ventricular thallium-201 perfusion index was calculated.

In 12 patients with healed prior myocardial infarction, the reproducibility of the computer-generated thallium-201 perfusion index was assessed. The coefficient of variation of replicate thallium-201 perfusion indexes, obtained 3 or more days apart in each patient, was 3.0%. These studies were also analyzed for intraobserver variation. The difference between original and second analysis ranged from 1–4%. Interobserver variation was studied in 12 studies from four patients. The difference between analyses by the two observers ranged from 2–5%.

Statistics

Linear correlations were found by the method of least-squares analysis. A two-tailed \( t \) test was used to test the null hypothesis that no difference existed between groups of nonpaired data. The test for equality of dependent coefficients was performed according to Williams.\(^{22}\) Data are expressed as mean \( \pm \) SD.

Results

Clinical and Radionuclide Angiographic Data

Thirty-five patients (table 3) admitted during the study interval satisfied the study criteria. Of these, six had a history of documented myocardial infarction, and seven had abnormal CK-MB isoenzyme release curves that contained two distinct CK-MB isoenzyme peaks (fig. 4). Eight of the 22 remaining patients with ECG evidence of diaphragmatic wall myocardial infarction had a right ventricular ejection fraction that was less than one-half of the left ventricular ejection fraction. These eight patients also had segmental right ventricular wall motion abnormalities and, therefore, were presumed to have had a right ventricular component to their myocardial infarction. The remaining 14 patients were felt to have sustained myocardial infarctions that involved only the left ventricle.

Radionuclide Ejection Fraction and Regional Wall Motion vs Enzymatic Estimates of Infarct Size

Patients without right ventricular infarction, prior myocardial infarction or two peaks to their serum CK-MB isoenzyme curve showed a reasonable correlation between global ejection fraction and CK-MB-g-Eq \((r = -0.78; \text{SEE} = 0.07; \text{fig. 5})\). In these same patients there was an acceptable correlation between left ventricular %ACR and enzymic infarct size \((r = 0.72; \text{SEE} = 18.28; \text{fig. 6})\). The least-squares regression equation predicted a CK-MB-g-Eq infarct size of 156 \( \pm \) 15 at 100% ACR. This is in close agree-

![Figure 3. Thallium-201 left ventricular perfusion scintigram, 45° left anterior oblique projection. Seven computer-generated squares are fit to each view.](image-url)
### Table 3. Clinical, Electrocardiographic, Enzymatic and Radionuclide Data

<table>
<thead>
<tr>
<th>Pt.</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Location of MI</th>
<th>MI class</th>
<th>Δ ti</th>
<th>CK-MB-g-Eq</th>
<th>LVEF</th>
<th>%ACR</th>
<th>TI-201 perfusion index</th>
<th>RVEF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Left ventricular infarction group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>55</td>
<td>M</td>
<td>PDMI</td>
<td>I</td>
<td>6004</td>
<td>13.6</td>
<td>59</td>
<td>12.5</td>
<td>8.0</td>
<td>32</td>
</tr>
<tr>
<td>2</td>
<td>48</td>
<td>F</td>
<td>DMI</td>
<td>I</td>
<td>3123</td>
<td>19.8</td>
<td>46</td>
<td>25</td>
<td>10.2</td>
<td>43</td>
</tr>
<tr>
<td>3</td>
<td>51</td>
<td>M</td>
<td>DMI</td>
<td>I</td>
<td>42</td>
<td>20.2</td>
<td>51</td>
<td>25</td>
<td>11.5</td>
<td>35</td>
</tr>
<tr>
<td>4</td>
<td>56</td>
<td>M</td>
<td>AMI</td>
<td>I</td>
<td>1749</td>
<td>28.0</td>
<td>47</td>
<td>37.5</td>
<td>33.0</td>
<td>28</td>
</tr>
<tr>
<td>5</td>
<td>69</td>
<td>M</td>
<td>ASMI</td>
<td>II</td>
<td>5628</td>
<td>38.7</td>
<td>31</td>
<td>75</td>
<td>23.0</td>
<td>60</td>
</tr>
<tr>
<td>6</td>
<td>55</td>
<td>M</td>
<td>DMI</td>
<td>II</td>
<td>42</td>
<td>39.2</td>
<td>51</td>
<td>12.5</td>
<td>10.9</td>
<td>35</td>
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<tr>
<td>7</td>
<td>39</td>
<td>M</td>
<td>PDMI</td>
<td>I</td>
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<td>42.6</td>
<td>43</td>
<td>50</td>
<td>20.8</td>
<td>22</td>
</tr>
<tr>
<td>8</td>
<td>64</td>
<td>M</td>
<td>DMI</td>
<td>I</td>
<td>594</td>
<td>48.2</td>
<td>31</td>
<td>62.5</td>
<td>18.1</td>
<td>29</td>
</tr>
<tr>
<td>9</td>
<td>51</td>
<td>F</td>
<td>AMI</td>
<td>II</td>
<td>941</td>
<td>50.5</td>
<td>31</td>
<td>75</td>
<td>32.5</td>
<td>36</td>
</tr>
<tr>
<td>10</td>
<td>59</td>
<td>M</td>
<td>PLMI</td>
<td>II</td>
<td>2560</td>
<td>59.1</td>
<td>32</td>
<td>62.5</td>
<td>27.2</td>
<td>46</td>
</tr>
<tr>
<td>17</td>
<td>71</td>
<td>M</td>
<td>AMI</td>
<td>I</td>
<td>1248</td>
<td>85.2</td>
<td>30</td>
<td>50</td>
<td>22.9</td>
<td>50</td>
</tr>
<tr>
<td>12</td>
<td>64</td>
<td>M</td>
<td>ASMI</td>
<td>II</td>
<td>642</td>
<td>86.4</td>
<td>32</td>
<td>50</td>
<td>39.2</td>
<td>23</td>
</tr>
<tr>
<td>13</td>
<td>59</td>
<td>F</td>
<td>AMI</td>
<td>II</td>
<td>7643</td>
<td>89.0</td>
<td>28</td>
<td>62.5</td>
<td>28.3</td>
<td>33</td>
</tr>
<tr>
<td>14</td>
<td>41</td>
<td>M</td>
<td>ALMI</td>
<td>II</td>
<td>53</td>
<td>151.6</td>
<td>24</td>
<td>100</td>
<td>34.1</td>
<td>39</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td>55.9</td>
<td></td>
<td></td>
<td></td>
<td>2170.0</td>
<td>55.2</td>
<td>38.3</td>
<td>50.0</td>
<td>22.8</td>
<td>36.5</td>
</tr>
<tr>
<td><strong>SD</strong></td>
<td>±9.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **Prior myocardial infarction group** | | | | | | | | | | | |
| 15 | 62 | M | ASMI | I | 1601 | 15.2 | 30 | 83 | 11.4 | 56 |
| 16 | 74 | M | ADMI | I | 781 | 72.1 | 31 | 50 | 5.9 | 20 |
| 17 | 62 | M | DMI | I | 76 | 45.3 | 31 | 75 | 31.1 | 33 |
| 18 | 49 | M | AMI | I | 1772 | 29.8 | 24 | 75 | 27.2 | 48 |
| 19 | 59 | M | DMI | I | 2185 | 14.3 | 36 | 50 | 32.9 | 44 |
| 20 | 53 | M | PMI | I | 2093 | 55.3 | 34 | 50 | 21.7 | 41 |
| **Mean** | 59.8 | | | | 1394.3 | 38.7 | 31.0 | 63.8 | 21.7 | 40.3 |
| **SD** | ±8.7 | | | | | | | | | |

| **Right ventricular infarction group** | | | | | | | | | | | |
| 21 | 68 | M | PDMI | I | 646 | 76.8 | 26 | 87.5 | 30.9 | 9 |
| 22 | 61 | M | PDMI | I | 253 | 31.3 | 34 | 75 | 31.3 | 17 |
| 23 | 50 | F | DMI | I | 346 | 113.9 | 49 | 25 | 9.8 | 23 |
| 24 | 36 | M | DMI | I | 537 | 60.5 | 46 | 25 | 19.2 | 13 |
| 25 | 52 | M | DMI | I | 4664 | 21.1 | 72 | 12.5 | 9.2 | 25 |
| 26 | 50 | F | PDMI | I | 120 | 50.5 | 73 | 0 | 10.5 | 33 |
| 27 | 58 | M | PDMI | II | 391 | 82.0 | 63 | 25 | 19.2 | 19 |
| 28 | 69 | M | PDMI | I | 3733 | 38.2 | 46 | 25 | 8.8 | 19 |
| **Mean** | 55.5 | | | | 1586.3 | 59.0 | 51.1 | 34.4 | 17.4 | 19.8 |
| **SD** | ±10.9 | | | | | | | | | |

| **Abnormal CK-MB release group** | | | | | | | | | | | |
| 29 | 76 | F | AMI | II | 178 | 49.3 | 25 | 62.5 | 37.0 | 25 |
| 30 | 53 | M | DMI | I | 104 | 44.1 | 52 | 25 | 17.37 | 32 |
| 31 | 82 | M | ASMI | II | 115 | 75.5 | 16 | 87.5 | 35.8 | 22 |
| 32 | 67 | M | ASMI | II | 246 | 20.4 | 67 | 33.3 | 17.3 | 58 |
| 33 | 56 | M | DMI | I | 2840 | 29.4 | 67 | 12.5 | 13.0 | 20 |
| 34 | 58 | M | AMI | II | 380 | 60.7 | 38 | 50 | 27.9 | 39 |
| 35 | 51 | M | AMI | I | 213 | 42.5 | 23 | 75 | 25.3 | 33 |
| **Mean** | 63.3 | | | | 609.2 | 46.0 | 41.1 | 49.4 | 24.8 | 34.6 |
| **SD** | ±12.0 | | | | | | | | | |

**Abbreviations:** MI class = acute classification; Δt = time elapsed (min) between rise of serum CK-MB from baseline and radionuclide studies; CK-MB-g-Eq = CK-MB-gram-equivalent infarct size; LV = left ventricular; RV = right ventricular; EF = ejection fraction; %ACR = percentage abnormally contracting regions; MI = myocardial infarction; PDMI = posteroinferior; DMI = inferior; AMI = anterior; ASMI = anteroseptal; PLMI = posterolateral; ALMI = anterolateral; ADMI = anteroinferior; DLMI = inferolateral.
ment with a reported mean weight of the left ventricle in one pathologic series of 151 g,28 and in another of 156 g.24

Prior Myocardial Infarction

In the six patients with prior myocardial infarction, there was no correlation between enzymatic infarct size and ejection fraction \( (r = -0.03; \text{fig. 5}). \) Similarly, no correlation was found between enzymatic infarct size and \%ACR \( (r = -0.25; \text{fig. 6}). \) In several cases, ejection fraction was disproportionately low and \%ACR disproportionately high compared with enzymatic infarct size, probably a consequence of myocardial dysfunction due at least in part to prior infarction.

Combined Right and Left Ventricular Infarction

A right ventricular component to the myocardial infarction was assumed to be present if, on right ventricular gated blood pool scanning, the right ventricular global ejection fraction was less than one-half of the left ventricular ejection fraction, and regional wall motion of the right ventricle demonstrated segmental disease.

In the eight patients with a potential right ventricular component to their acute myocardial infarction, there was no significant correlation between enzymatic infarct size and left ventricular ejection fraction \( (r = -0.19; \text{fig. 5}). \) or enzymatic infarct size and left ventricular \%ACR \( (r = 0.06; \text{fig. 6}). \) Analysis of these eight patients, none of whom had prior myocardial infarction, indicated in certain patients an...
enzymatic infarct size markedly disproportionate to %ACR. This finding would be compatible with CK-MB isoenzyme release from other than left ventricular sources in these patients.

Abnormal CK-MB Release Curves

In the seven patients with two discrete CK-MB peaks and with neither evidence of prior myocardial infarction nor right ventricular involvement in the acute myocardial infarction, there was a reasonable correlation between enzymatic infarct size and ejection fraction ($r = -0.81; \text{SEE} = 0.14; p < 0.05$) and enzymatic infarct size and %ACR ($r = 0.71; \text{SEE} = 21.06; p = 0.05$).

Left Ventricular Thallium-201 Perfusion
Scintigrams vs Radionuclide Wall Motion and Enzymatic Infarct Size

Left Ventricular Infarction

Patients without right ventricular infarction, prior myocardial infarction or two peaks to their serum CK-MB isoenzyme curve showed an acceptable correlation between ejection fraction and thallium-201 perfusion index ($r = -0.71; \text{SEE} = 0.08$; fig. 7). The intercept of the least-squares regression line on the ordinate predicted an ejection fraction of $0.56 \pm 0.03$ for a noninfarcted ventricle (zero Tl-201 perfusion index), in close agreement with a mean ejection fraction of $0.58 \pm 0.11$, which was obtained in 22 patients with a history of angina but who were pain-free at the time of radionuclide ventriculography and who had normal thallium-201 perfusion indexes. In patients with left ventricular infarction there was an association between the thallium-201 perfusion index and enzymatic infarct size ($r = 0.65; \text{SEE} = 7.93$) and thallium-201 perfusion index and %ACR ($r = 0.70; \text{SEE} = 18.82$; fig. 8).

Prior Myocardial Infarction

In patients with prior myocardial infarction there was no significant correlation between the thallium-201 perfusion index and ejection fraction ($r = 0.12$) or the thallium-201 perfusion index and %ACR ($r = 0.36$). These latter findings may be related to scar formation in the area of previously infarcted myocardium and/or because determinants of ejection fraction other than infarct size per se, such as preload and afterload, may be altered in this subset. As expected in these patients, the thallium-201 perfusion index did not correlate with enzymatic infarct size ($r = 0.43$).

Combined Right and Left Ventricular Infarction

In these eight patients a reasonable correlation was found between the thallium-201 perfusion index and left ventricular ejection fraction ($r = -0.73; \text{SEE} = 0.13$; fig. 7) and the thallium-201 perfusion in-
dex and %ACR ($r = 0.90$; SEE = 14.34). However, no significant correlation was found between the thallium-201 perfusion index and enzymatic estimate of infarct size ($r = 0.02$).

**Abnormal CK-MB Release Curves**

In the seven patients with two CK-MB peaks, an acceptable correlation was found between thallium-201 perfusion index and ejection fraction ($r = -0.90$; SEE = 0.10), thallium-201 perfusion index and %ACR ($r = 0.86$; SEE = 15.20) and thallium-201 perfusion index and enzymatic infarct size ($r = 0.78$; SEE = 6.46).

**Discussion**

This study provides documentation of the usefulness and limitations of radionuclide techniques (gated blood pool scanning and thallium-201 myocardial scintigraphy) in estimating the extent of acute necrosis in patients with myocardial infarction.

**Enzymatic Infarct Size and Myocardial Morphology**

One of the more useful techniques for assessing the magnitude of experimental ischemic injury has been the measurement of myocardial CK determined by myocardial biopsy specimens taken from various zones of infarction.25 Depletion of CK has been correlated with both epicardial electrograms determined shortly after the onset of myocardial ischemia and with subsequent histologic appearance, usually determined 24 hours after the onset of myocardial infarction.26

Although there is, as yet, no "gold standard" for quantitating infarct size in living patients, enzymatic estimates of infarct size in studies from several centers have correlated with biochemical and morphologic analyses of the myocardium in experimental animals,1, 3, 27 morbidity, mortality,2, 14, 28 contrast angiographic assessment of infarct size6 and histochemical assessment of necrosis in patients.6 Estimates have been improved by quantifying the CK-MB isoenzyme.4, 29

Although Roe and Starmer7 reported several theoretical problems with the mathematical model for infarct size based upon CK analysis, extensive data by Sobel and associates14 in experimental animals and in man indicate that serum CK systems have at least qualitative validity in assessing the magnitude of myocardial destruction. A study by Bleifeld et al.6 correlated total CK curves with pathologically determined infarct size in a small group of patients ($r = 0.93$). Rogers et al.4 correlated CK-MB data with infarct size determined by contrast left ventricular angiography at a mean of 33 days after myocardial infarction ($r = 0.88$). Thus, the majority of data, including the present study, indicate that the CK-MB system has at least qualitative validity.

Despite the limitations of enzymatic estimates of infarct size, our data showed a surprisingly reasonable correlation between %ACR and CK-MB infarct size (fig. 6) in patients without prior myocardial infarction or right ventricular infarction ($r = 0.72$; SEE = 18.28). In addition, in the same patients the thallium-201 perfusion index correlated with the left ventricular %ACR ($r = 0.70$; SEE = 18.82; fig. 8).

**Myocardial Function and Enzymatic Infarct Size**

During the acute phase of myocardial infarction, radionuclide left ventriculography provides the means to assess left ventricular performance through quantitation of systolic ejection phase indexes, such as left ventricular ejection fraction.

CK-MB infarct size correlated inversely with left ventricular ejection fraction in patients with neither right ventricular infarction nor prior myocardial infarction ($r = -0.78$; SEE = 0.07; n = 14). This finding is in agreement with the study by Rogers et al.5 that showed a similar inverse correlation ($r = -0.78$) between enzymatic infarct size and ejection fraction determined by contrast ventriculography in a series of patients in whom prior myocardial infarction and right ventricular dysfunction were excluded. Our study shows that patients with prior myocardial infarction tend to have disproportionately lower ejection fractions compared with enzymatic infarct size, probably explained by the cumulative insult to the left ventricle. Conversely, patients with a presumed right ventricular component to their infarction tend to have disproportionately high enzymatic infarct size compared with left ventricular ejection fraction, suggesting damage to tissue outside of the left ventricle, probably the right ventricle.

**Myocardial Perfusion and Enzymatic Infarct Size**

Myocardial perfusion imaging with radioactive tracers offers a noninvasive method for detecting myocardial infarction and transient myocardial ischemia. The initial distribution of thallium-201 has been shown to reflect regional myocardial perfusion.30

Our data show that the thallium-201 perfusion index was associated with enzymatic infarct size ($r = 0.65$; SEE = 7.93) in patients without prior myocardial infarction or presumed right ventricular infarction. This finding is in agreement with the study by Wackers et al.11 that shows a reasonable correlation ($r = 0.72$) between postmortem infarct size and infarct area determined scintigraphically with thallium-201. In addition, certain animal studies have demonstrated a linear relationship between thallium-201 distribution and both regional myocardial blood flow and CK depletion.31

In our study in patients with neither prior myocardial infarction nor presumed right ventricular infarction the thallium-201 perfusion index was associated with %ACR ($r = 0.70$; SEE = 18.82; n = 14). This finding is in agreement with the study by Niess et al.12 in which an acceptable correlation was found between contrast ventriculographic quantitation of left ventricular asynergy and thallium-201 defects ($r = 0.80$). Although our study demonstrated a reasonable correlation between the thallium-201 perfusion index and regional wall motion assessment of infarct size, some
contributions to the thallium-201 perfusion index might have represented hypoperfused, ischemic noninfarcted zones, and, conversely, subendocardial necrosis might not have been represented as clear-cut thallium-201 defects. Similarly, radionuclide regional wall motion abnormalities might have over- or under-estimated myocardial necrosis. For example, several patients had disproportionately large %ACR for their respective thallium-201 perfusion indexes (fig. 8). In these patients it could be postulated that asynergic, although perfused, myocardium accounted for abnormally contracting regions, but failed to demonstrate a defect in thallium-201 uptake. In addition, a certain percentage of abnormally contracting regions may be caused by myocardial ischemia and hence would not correlate with CK-MB release, but might still correlate with the thallium-201 perfusion index. Another problem that influences the accuracy of comparing thallium-201 defects with radionuclide wall motion abnormalities is that the thallium-201 technique detects abnormalities in tangential, geometrically dependent projections. Conversely, the regional wall motion technique uses radioactive count changes in the blood pool and hence is not dependent upon geometry. With both techniques, the measurement of abnormalities is perhaps influenced, to different degrees, by adjacent normal myocardium which may "overlie" nonperfused or asynergic regions.

Right Ventricular Infarction

In the eight patients with presumed right ventricular infarction, enzymatic infarct size was not associated with left ventricular ejection fraction (r = 0.19) or with the thallium-201 perfusion index (r = 0.02). However, in this group a reasonable correlation was found between the thallium-201 perfusion index and left ventricular %ACR (r = 0.90; see = 14.34). This finding most likely reflects the high incidence of septal involvement in right ventricular infarction.32

Abnormal CK-MB Release Curves

In the present study we did not assess the rate of spontaneous extension of myocardial infarction. Seven patients displayed a second discrete peak in their CK-MB release curve before the CK-MB curve had returned to baseline (fig. 4). Some studies have evaluated total serum CK or CK-MB and ECG changes for 2–3 weeks after infarction, attempting to define extension as a second discrete event, after CK returns to baseline, rather than as an initial variability in the pattern of CK release.33,34 However, in the present study CK sampling was discontinued when serum CK returned to baseline. Mathey et al.34 used the term "infarct extension" to define a group of patients who showed continued total CK release for 24–72 hours after their infarcts and estimated that the immediate extension rate was 62%. However, pathologic studies have suggested a much lower extension rate of 17%.35 A recent experimental study by Cobb et al.36 suggests in the canine model that early alterations in CK-MB appearance is a function of both the severity of the ischemia and subsequent changes in blood flow to the regions containing infarcted myocardium (infarct extension).

In our seven patients with abnormal CK-MB release curves, radionuclide studies were performed in all but one patient during the initial, rapid-release phase of the CK-MB curve (fig. 4). A reasonable correlation was obtained in these patients between enzymatic infarct size vs left ventricular %ACR (r = 0.71; see = 21.06) and enzymatic infarct size vs the thallium-201 perfusion index (r = 0.78; see = 6.46). In these patients, the second CK-MB peak occurred 6–28 hours after the radionuclide studies. The CK-MB isoenzyme curves in the other 28 patients in the present study displayed a single peak 11–16 hours after onset of chest pain. These data suggest three possibilities:

(1) Extension had already occurred at the time of radionuclide assessment, so %ACR and the thallium-201 perfusion index marked both the initial myocardial insult and subsequent extension. Altered blood flow secondary to extension may have altered CK-MB release in certain patients and hence delayed the time of CK-MB to second peak.

(2) Extension occurred after radionuclide assessment, but the magnitude of extension was not sufficient to alter the relationship of %ACR or the thallium-201 perfusion index to enzymatic infarct size.

(3) The appearance of a second CK-MB peak, before the return of the enzyme to baseline, represents a variant CK-MB release pattern not associated with extension. The ability of regional wall motion and thallium-201 myocardial scintigraphy to recognize relatively small extensions of myocardial infarction will have to be studied in patients in whom extension has been documented by other means. The use of thallium-201 to detect extension probably cannot be tested reliably without three-dimensional quantitative myocardial scintigraphy.

Myocardial Infarction: Left Ventricular and Left Ventricular with a Right Ventricular Component

When the data from our 14 patients with left ventricular infarction and our eight patients with a presumed right ventricular component were analyzed, a poor association was found for enzymatic infarct size vs ejection fraction (r = −0.43; see = 0.13) and thallium-201 perfusion index (r = 0.43; see = 9.23). However, a reasonable correlation was found for the thallium-201 perfusion index and left ventricular ejection fraction (r = −0.72; see = 0.10). These findings are in agreement with a report by Sharpe et al.87 In that study of 26 patients with transmural infarction, 15 of whom had inferior infarction, technetium-99m pyrophosphate myocardial imaging was associated with gated blood pool assessment of left ventricular ejection fraction, but was not associated with CK-MB release, nor did enzyme estimates of infarct size correlate with left ventricular ejection fraction. Recent
Radionuclide studies have indicated right ventricular involvement occurs in 37.5–50% of patients with acute inferior wall infarction. 38,39 Hence, it is reasonable to assume that at least some of the 15 patients with inferior infarction described by Sharpe et al. had a right ventricular component to their infarction.

Correlations between the enzymatic infarct size and independent radionuclide data in patients with neither prior infarction nor presumed right ventricular infarction allow certain conclusions to be drawn about these descriptors of infarct size. First, %ACR yields a stronger correlation with enzymatic infarct size than the thallium-201 perfusion index; however, the difference in correlation between the two methods did not reach statistical significance in the present series. Second, in patients with a presumed right ventricular infarction, radionuclide assessment of the left ventricle does not correlate with enzymatic assessment, indicating that radionuclide descriptors of both the right and left ventricle must be used. Such descriptors might include technetium-99m pyrophosphate hot-spot imaging of the right ventricle. 38, 39 In addition, CK-MB release kinetics for the right ventricle would have to be examined because published data have been obtained primarily from left ventricular models. 1, 8, 27

Reliability of Radionuclide Infarct Sizing

This study included a small, select population of coronary care unit patients who survived their acute myocardial infarction. Nevertheless, the findings are important and suggest, in a selected subset of these patients, a correlation and interrelationship between enzymatic and radionuclide assessments of left ventricular necrosis. However, the enzymatic and thallium-201 techniques may be of limited value in quantitating the magnitude of left ventricular necrosis and right ventricular necrosis. Therefore, if CK-MB and thallium-201 are to be used to assess left ventricular compromise in patients with acute myocardial necrosis, acute right ventricular infarction and prior left ventricular infarction must either be excluded or concurrently quantitated by other independent descriptors.

Acknowledgment

The authors acknowledge the nurses and medical house officers in the Coronary Care/Medical Intensive Care complex at North Shore University Hospital who generously provided time in order to make these studies possible, and Helen Basile for her secretarial assistance.

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Circulation. 1980;62:277-287
doi: 10.1161/01.CIR.62.2.277

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/62/2/277.citation

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