Myocardial Infarct Size Determined by Computed Transmission Tomography in Canine Infarcts of Various Ages and in the Presence of Coronary Reperfusion

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Thirty-one dogs underwent in vivo scanning with computed transmission tomography; 15 dogs were studied within 7 days (mean 4) after coronary occlusion, 10 dogs 21 to 25 days (mean 28) after occlusion and 6 dogs 4 days after coronary reperfusion of a 2 to 3 hour coronary ligation. Ungated scans (1 cm in depth) of the left ventricle were obtained from apex to base to determine infarct size. In all animals with documented (postmortem) infarction (n = 26), contrast medium caused delayed enhancement of the entire infarct or the periphery of the infarct. Infarct size was calculated from scans showing contrast enhancement of the infarct. Infarct size was also determined from the postmortem heart using histochemical morphometry (nitroblue tetrazolium) and then compared with infarct size derived from tomography using the outer margin of the contrast-enhanced periphery of the infarct as the border of the infarct. Infarct size calculated by the tomographic technique (excluding the animals without an infarct) correlated well with infarct size determined at autopsy (r = 0.90, p < 0.001). The tomographic estimate (18.2 ± 11.3 g) of infarct size was similar to autopsy values (18.6 ± 11.8 g, p = NS).

Thus, ungated computed transmission tomographic imaging of the heart can reliably estimate infarct size in a variety of potential clinical circumstances, particularly when the area of rim enhancement of the infarct is included within the presumed infarct region.

A substantial number of reports (1–5) have suggested that myocardial infarct size is important in assessing clinical prognosis after myocardial infarction. An approach for evaluating infarct size would aid in the evaluation of interventions designed to reduce the amount of damaged myocardium during ischemia. Both ex vivo (6–9) and in vivo (10–12) studies have shown that computed transmission tomography is a reliable technique for assessing infarct size, though the precise method for measuring infarct size has varied. Additionally, the duration of the coronary occlusion and the lack of coronary reperfusion were similar in each of the studies.

The present study was designed to define the accuracy of tomographic scans for quantitating size of infarcts of varying age and in hearts with both permanent coronary occlusion and myocardial reperfusion, thus mimicking a variety of clinical situations in which the amount of contrast medium that reaches the infarct varies. Moreover, the ability to analyze infarct size in reperfused hearts has potential immediate clinical application in assessing the importance of the time of reperfusion after the onset of ischemic symptoms during infarction in relation to possible myocardial salvage.

Methods

Experimental model. Thirty-one conditioned mongrel dogs (mean weight 28 ± 7 kg) were studied. Each animal was preanesthetized with 3 mg/kg body weight of subcutaneously administered morphine sulfate, then anesthetized with 25 mg/kg of pentobarbital given intravenously. Through a left thoracotomy, a hydraulic coronary occluder was placed around the proximal left anterior descending artery. The
occluder was fashioned from pediatric feeding (p-50) tubing placed around the artery. The catheter was burrowed subcutaneously and externalized. The wound was aseptically closed and the dogs were allowed to recover.

In 25 of the 31 dogs 2 to 3 days later, the hydraulic occluder was inflated with normal saline solution. Each dog was pretreated with subcutaneous morphine sulfate and intramuscular procainamide before coronary occlusion and was again allowed to recover. Computed transmission tomographic scanning was performed in 15 of these dogs (acute group) within 7 days of the initial occlusion (mean 4, range 1 to 7), and in 10 dogs (subacute group) within approximately 28 days (range 21 to 35) after the initial occlusion. In the remaining six dogs (reperfusion group), the occluder was inflated for 2 to 3.5 hours and then deflated; these dogs underwent imaging 3 to 4 days after the initial occlusion.

Postmortem examination. Within 2 days after the final tomographic scans were obtained, each dog was anesthetized with pentobarbital and sacrificed with intravenous potassium chloride. In the reperfusion group, the animals were sacrificed immediately on cessation of scanning to minimize the effects of reperfusion edema on infarct size estimation.

After sacrifice, each heart was removed and sectioned at 1 cm intervals from apex to base along the major axis of the left ventricle and incubated in nitroblue tetrazolium dye as described previously (13,14). The endocardial and epicardial borders of the left ventricular wall were traced onto clear film overlays. In the septal area, the right ventricular side of the septum was substituted for the epicardial border. The area of grossly visible myocardial infarct was also traced onto the film overlays.

The amount of left ventricular mass involved by the myocardial infarct was measured by planimetry from the area of the left ventricular wall previously traced on the overlays. This was accomplished with an ultrasonic digitizer interfaced with a Hewlett-Packard model 9825T desktop microprocessor and printer-plotter. Each ventricular slice was assumed to be cylindrical. Identical assumptions were made for the tomographic scans. The variability of this technique in our laboratory is ± 3.5% when the slices are retraced and redigitized. A normal noninfarcted cross section is shown in Figure 1, and several contrast-enhanced sections are shown in Figure 2.

Computed transmission tomography. Scanning protocol. All studies were performed on a Technicare 2020 whole body scanner with an individual scan time of 2 seconds. The scanner has 720 stationary detectors and a 512 × 512 image matrix. Each scan section was 1 cm thick and obtained at 120 kVp and 40 mA. Approximately 30 seconds was necessary to obtain an entire ungated tomographic series.

During the scanning procedure, each dog was preanesthetized with 2 to 5 mg/kg body weight of morphine sulfate and anesthetized with 25 mg/kg of intravenous pentobarbital. The dogs were mechanically ventilated and placed in the scanner gantry. Each animal was paralyzed with succinylcholine administered intravenously. The animal’s condition was then allowed to stabilize for 20 to 30 minutes before the administration of contrast material. Meglumine diatrizoate (Renografin-76) was administered at a rate of 6 ml/min for 5 minutes and then at 3 ml/min for 5 minutes with a Harvard infusion pump, after which time the infusion was halted. Exactly 10 minutes after the contrast infusion was stopped, ungated images, 1 cm thick, were obtained from the caudal to cranial portion of the left ventricle.

Analysis of scan and morphometric data. The canine heart tends to be oriented so that the long axis of the ventricle is parallel to the spine. Thus, cross-sectional scans approximate the postmortem sections. However, the orientation is sufficiently displaced to make the scan sections somewhat similar but not identical to the morphometric cross sections. Nonetheless, the difference in orientation should play a minor role in infarct size estimation if the technique is to be clinically useful and meaningful correlations made. Analysis of both the scan and morphometric data included the area around the aortic and mitral valve (but excluded the valve itself).

The images were printed on transparent film along with spatial calibration markers. The infarct was defined as the outer margin of the area of differential contrast enhancement between the infarcted region and normal myocardium on each individual section. In most cases, the zone measured by planimetry included a section of reduced attenuation compared with normal muscle (without contrast enhancement) and an adjacent contrast-enhanced segment. The area
Role of contrast enhancement in infarct size estimation. The present study demonstrates that in vivo quantification of myocardial infarct size is feasible in a variety of contexts.

**Discussion**

**Statistical analysis.** All data were expressed as the group mean ± standard deviation. Linear regression equations and correlations were performed with a least squares fit. Statistical comparison of infarct size by computed tomography and postmortem examination was done using a paired Student's $t$ test.

**Results**

**Analysis of infarct size.** Five of the 31 dogs that underwent left anterior descending coronary occlusion (3 in the subacute group, 1 in the acute group and 1 in the reperfusion group) had no evidence by computed tomography or postmortem examination (gross inspection and myocardial staining) of myocardial infarction. The remaining 26 dogs had evidence of infarction by both methods. Of these 26 dogs, 21 had evidence of transmural infarction and 5 had evidence of subendocardial infarction.

The individual values for infarct volume as determined by histochemical morphometric analysis are given in Figure 3. There was no significant difference in infarct size between the tomographic and postmortem estimates. The standard error of the estimate was $2.9 \pm 11.3$ versus $18.6 \pm 11.8$ g, probability $[p] = $ not significant (NS). The overall correlation coefficient for the linear relation between computed transmission tomographic infarct volume and the postmortem morphometric volume was $0.90$ ($Y = 9.6X + 26.6$, $p < 0.002$). When the time periods were separately analyzed, correlation coefficients and regression equations were similar (Table 1).

**Figure 2.** Several sections demonstrating contrast-enhanced infarcts are shown along with the region measured by planimetry (dotted lines). The arrows point to a documented left ventricular thrombus.
Table 1. Correlation of Autopsy and Computed Tomographic Infarct Sizes

<table>
<thead>
<tr>
<th>Infarct Group*</th>
<th>Correlation Coefficient</th>
<th>Regression Equation</th>
<th>SEE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute (n = 12)</td>
<td>0.92</td>
<td>101 ± 2 g</td>
<td>24 g</td>
</tr>
<tr>
<td>Subacute (n = 9)</td>
<td>0.83</td>
<td>96 ± 14 g</td>
<td>29 g</td>
</tr>
<tr>
<td>Reperfusion (n = 5)</td>
<td>0.97</td>
<td>92 ± 22 g</td>
<td>24 g</td>
</tr>
</tbody>
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*Acute = tomographic study performed within 7 days of the initial occlusion. Reperfusion = study performed after reperfusion and 3 to 4 days after the initial occlusion. SEE = standard error of the estimate. Subacute = study performed 21 to 35 days after the initial occlusion.

References


