Immediate Effect of Contrast Medium Injection on Left Ventricular Volumes and Ejection Fraction

A Study Using Metallic Epicardial Markers

DONALD L. VINE, M.D., THEODORE D. HEGG, M.D., HAROLD T. DODGE, M.D., DOUGLAS K. STEWART, M.D., AND MORRIS FRIMER, M.S.E.

SUMMARY  The immediate effect of contrast medium injection on left ventricular (LV) volume, stroke volume (SV) and ejection fraction (EF) was evaluated from postoperative LV biplane cineangiograms of 10 patients with 4–6 epicardial markers placed at the time of coronary artery surgery. After calibrating marker distances with respect to volume (r = 0.97–0.99) over one cardiac cycle for each patient, regression equations were used to compute LV volume from marker measurements for beats prior to, during and following injection.

THERE HAS BEEN CONTROVERSY concerning the immediate effects of injected contrast medium as used for ventriculography upon human left ventricular (LV) volume and ejection fraction (EF). In animals, both are significantly increased soon after the onset of injection and, accordingly, the recommendation has been made that calculations of left ventricular end-diastolic (EDV) and end-systolic (ESV) volumes be made after the period of injection to avoid the immediate volume increase which results from the added volume of the injectate. In humans, results from one study suggest that there is a significant volume increase at end-diastole by the third cycle after opacification, leading to the recommendation that films taken early in the injection period be used for physiologic information. Another study demonstrated no consistent change in EDV or EF.

For studies in man, a method has not been available for determining ventricular volumes from control beats immediately before the start of injection for comparison with volumes during and immediately following injection. Recently, we reported a method of determining spatial distances between metallic markers placed on the epicardium at the time of cardiac surgery and for calibrating these marker distances with respect to volume so that volumes and changes in volume could be derived subsequently from these measurements. The purpose of the study reported here was to evaluate the immediate effects of injection of contrast medium on EDV, ESV, SV, and EF by comparing the volumes and ejection fractions immediately before injection with those during ventricular opacification.

Methods

Patients who had had epicardial radiopaque markers placed at the time of cardiac surgery were selected for study.

End-diastolic volumes (EDV) prior to injection ranged from 93–263 ml and did not change significantly with injection. End-systolic volumes (ESV) showed a mean decrease of 7.3 ml by beat 7 following injection; this was of borderline significance. Similarly, there was no significant change of SV or EF until beat 7 when there were small but significant increases of 6.4 ml and 0.04, respectively.

The injection of moderate amounts of contrast in man does not cause significant changes in LV volume or EF through the sixth post-injection beat.

The markers consisted of four or more silver vascular clips which were attached to the epicardium at the apex and on the anterior, posterior, and free wall of the left ventricle approximately two-thirds of the distance from the apex to the base. Six to twelve months postoperatively, and with informed consent, biplane cineangiography was performed at 60 frames per second in the anteroposterior (A-P) and left lateral projections. Filming was done during held inspiration with specific instructions to avoid a Valsalva maneuver. From the biplane films, distances between markers and left ventricular chamber volumes were determined. Studies were eliminated from analysis in which the markers could not be visualized for five or more beats, beginning with the beat immediately preceding injection. Data from 15 patients, all of whom were in normal sinus rhythm, proved suitable for analysis. Despite the instructions to avoid a Valsalva maneuver, data from five subjects which were otherwise suitable for analysis were eliminated because of a progressive decrease in volume during filming consistent with a Valsalva effect. The data from the remaining 10 subjects, 4 female and 6 male, ages 46 to 62 years (mean 53), were used for this study. All were postoperative coronary bypass patients.

Ventriculography was performed with 25–70 ml (mean 50 ml) of 28.5% meglumine diatrizoate — 29.1% sodium diatrizoate (Renovist II) injected at rates of 15–36 ml/sec (mean 25 ml/sec).

The methods used for computing spatial distances between the markers and for determining chamber volumes from the marker distances have been previously described in detail. Briefly, they are as follows. From the LV cineangiograms, the three dimensional X, Y, and Z coordinates for each marker were determined from each pair of A-P and lateral biplane cine frames, beginning one heart cycle immediately before the start of injection (beat 0) and continuing for 5–7 consecutive beats. Correction factors for X-ray and projector magnification were calculated for each individual marker on each cine frame using regression equations derived from previously filmed grids.

From the corrected X, Y, and Z coordinates of all possible three-marker combinations, (A, B, C, etc.) the areas of triangles in three-dimensional space (ABC, etc.) were com-

From the Cardiovascular Research and Training Center and the Department of Medicine, University of Washington School of Medicine, Seattle, Washington.

Supported by NHLBI grants HL 13517, HL 19451, Clinical Research Center RR 37 and the American Heart Association of Washington.

Address for reprints: Harold T. Dodge, M.D., Department of Medicine, University of Washington School of Medicine, Seattle, Washington 98195.

Received March 14, 1977; revision accepted April 8, 1977.

379
There were determined injection beats. By beat each LV volume was computed for each frame of the cardiac cycle using the formula:

\[
\text{AREA} = \sqrt{S \cdot (S-AB) \cdot (S-AC) \cdot (S-BC)}
\]

Where \( S = \frac{AB + BC + AC}{2} \)

and \( AB = \sqrt{(X_A-X_B)^2 + (Y_A-Y_B)^2 + (Z_A-Z_B)^2} \).

BC and AC were similarly calculated.

Each patient’s markers were calibrated from the postoperative left ventricular cineangiogram by linear correlation of the spatial area of each triangle with the LV volume, calculated by the area-length method from each pair of biplane cine frames over one cardiac cycle in which there was ventricular opacification. The triangle formed by the three epicardial markers whose area showed the closest correlation with chamber volume was determined. These markers and the calibrating regression equations that described the above relationships were used to determine chamber volumes which were in turn used to construct a frame-by-frame plot of ventricular volumes, beginning with beat 0 and continuing through 5–7 subsequent beats. In every case, the correlation coefficient of the chosen regression equation exceeded \( r = 0.97 \). The standard error ranged from 1.6 to 7.1 ml. A typical LV volume-spatial triangle relationship is illustrated in figure 1. A derived beat-by-beat LV volume curve during contrast injection is shown in figure 2.

From the marker measurements, EDV, ESV, SV and EF were determined for beat 0 and for each of the 5–7 postinjection beats. The paired \( t \)-test was used to compare volumes and ejection fractions for each postinjection beat with those for the preinjection control beat.

Although all patients were in normal sinus rhythm before, during, and after contrast injection, five patients experienced premature contractions during the period of injection. Data from premature (PVC) and immediately postpremature contractions (p-PVC) were excluded from statistical analysis. The beat-by-beat LV volume curves during and immediately following contrast injection in a patient experiencing premature contractions is shown in figure 3. In no case was the second post-PVC beat significantly different from the control beat.

**Results**

Individual patient data are summarized in table 1. Beat-by-beat EDV, ESV, SV, and EF are illustrated in figure 4. Mean changes from control beats are illustrated for the ten patients in figure 5.

End-diastolic volumes of control beats were 93–263 ml, as shown in figure 4A. With contrast-medium injection, the changes in EDV were small and inconsistent and ranged from −10 ml to 7 ml (fig. 5A). There was no significant change in EDV through beat 7.

Control ESV were 30–131 ml (fig. 4B). Following injection, there was a gradual decrease in ESV which remained insignificantly until beat 7, when a small mean decrease of 7.3 ml approached statistical significance (\( P < 0.05 \), fig. 5A).

Pre-injection values for SV were 56–132 ml (fig. 4C). After injection there was no significant change until beat 7, when there was a small but statistically significant increase in SV of 6.4 ml (\( P < 0.02 \), fig. 5B).

The ejection fraction of control beats was 0.44–0.75 (fig. 4D). Following injection, EF remained remarkably constant and varied by 0.05 or less in all patients during the period of ventricular opacification. By beat 7, the small mean increase of 0.04 was statistically significant (\( P < 0.01 \), fig. 5B).

Slight changes in heart rate were observed in individual patients, but these were not consistent or statistically significant.

**Discussion**

Epicardial marker motion has been shown by previous studies to reflect acute ventricular volume changes induced by a variety of interventions. Its sensitivity in detecting volume changes is further illustrated in figure 3 and in an
## Table 1. Patient Data

<table>
<thead>
<tr>
<th>Patient</th>
<th>Beat no.</th>
<th>Clip derived data</th>
<th>Correlation of angio volumes vs clip area</th>
<th>Contrast used</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (bpm)</td>
<td>EDV (ml)</td>
<td>ESV (ml)</td>
<td>SV (ml)</td>
</tr>
<tr>
<td>1. E.W.</td>
<td></td>
<td>105</td>
<td>118</td>
<td>30</td>
</tr>
<tr>
<td>2. E.P.</td>
<td></td>
<td>105</td>
<td>118</td>
<td>37</td>
</tr>
<tr>
<td>3. A.T.</td>
<td></td>
<td>130</td>
<td>131</td>
<td>75</td>
</tr>
<tr>
<td>4. C.F.</td>
<td></td>
<td>81</td>
<td>186</td>
<td>96</td>
</tr>
<tr>
<td>5. C.C.</td>
<td></td>
<td>106</td>
<td>131</td>
<td>46</td>
</tr>
<tr>
<td>6. D.H.</td>
<td></td>
<td>82</td>
<td>143</td>
<td>62</td>
</tr>
<tr>
<td>7. A.D.</td>
<td></td>
<td>92</td>
<td>133</td>
<td>54</td>
</tr>
<tr>
<td>8. L.V.</td>
<td></td>
<td>105</td>
<td>113</td>
<td>55</td>
</tr>
<tr>
<td>9. M.J.</td>
<td></td>
<td>103</td>
<td>98</td>
<td>133</td>
</tr>
<tr>
<td>10. D.M.</td>
<td></td>
<td>106</td>
<td>94</td>
<td>134</td>
</tr>
</tbody>
</table>

**FIGURE 3.** Beat-by-beat LV volume curve derived from epicardial marker measurements for the patient illustrated in figure 1. Beats -1 and 0 are preinjection control beats, and beats 1, 2, and 3 are two PVCs followed by a post-PVC beat. The angiographically derived volumes for beats 3 and 4 are superimposed.
earlier study⁴ in which LV volume changes resulting from premature contraction, as determined by angiographic and epicardial marker methods, showed close agreement.

The data from the present study, derived from measurements of distances between epicardial markers, do not demonstrate a statistically significant change in left ventricular end-diastolic volume, end-systolic volume, stroke volume or ejection fraction during contrast medium injection and ventricular opacification. By the seventh postinjection beat, a decrease in ESV produces a statistically significant increase in SV and EF, but the changes are small in both (6.4 ml and 0.04 ml, respectively) and are probably of little clinical importance.

Qualitative animal data from cineradiographic observations of LV wall motion⁴⁵ or of metallic epicardial markers⁴⁶ have not demonstrated significant changes in LV dimensions during the period of contrast medium injection, although one study using ultrasonic measurements did demonstrate an increase in LV diameter.¹⁸ Quantitative volume estimates, using intramyocardial markers² or epicardial strain gauges,¹ have shown an immediate, transient increase in LV volume during the period of injection. The absence of this transient effect of injected volume in our patients may be partly explained by the fact that the volume of contrast material administered in this study, 0.37-0.78 ml/kg body weight (mean 0.67 ml/kg), was approximately two-thirds of the 1 ml/kg body weight generally employed in animal studies.

Similarly, the amount of contrast material per ml of EDV is different for animal and human studies. In two studies using dogs¹,¹⁴ mean body weight was 17 kg, mean LVEDV was 27 ml and the amount of contrast material was 1 ml/kg; thus, 0.63 ml of contrast material per ml of LVEDV was used, which was nearly twice that used in our
CONTRAST MEDIUM EFFECT ON LV VOLUMES/Vine et al.

Human study (0.36 ml/ml LVEDV).

Two previous studies in humans of ventricular volume change during contrast medium injection compared the EDV and SV of the first opacified beat with those of each of a series of subsequently opacified beats.5, 4 Hammermeister et al. found no significant volume change during the first three-to-five opacified cycles following contrast injection.4 Carleton found a significant increase in EDV by the third opacified beat.3 The results of the present study, the first study in humans to compare volumes of beats immediately preceding the onset of contrast injection with volumes during and after opacification, are consistent with the data reported by Hammermeister et al.4 and show no significant change in left ventricular volume during the period of contrast injection or ventricular opacification. In the present series, the angiographic beat chosen for clinical purposes to compute LV chamber volume varied between the second and sixth postinjection beat, and in no case differed significantly in volume from the control preinjection beat.

The present data differ from those reported by Carleton.5 Whether this difference is due partly to the fact that Carleton employed more rapid injection rates (30 ml/sec) than Hammermeister et al. (20 ml/sec) or the present study (25 ml/sec), or is due to the larger dose of contrast per ml of EDV (0.51 ml in Carleton’s study vs 0.36 in ours) is not known.

Considering the data of the present study, combined with those of Carleton5 and of Hammermeister et al.,4 there is agreement that no significant change in left ventricular volume occurs for at least the first two opacified cardiac cycles after contrast injection and that the ejection fraction remains unchanged throughout the period of injection and subsequent opacification. While Carleton’s data suggest that large injected volumes may produce significant changes in

![Figure 5](image1.png)

**Figure 5.** Mean change (± sd) from control beat 0 in EDV and ESV(A) and in SV and EF(B) for the 10 patients through postinjection beat 7. There is a statistically significant increase from control by beat 7 in both SV and EF.

![Figure 6](image2.png)

**Figure 6.** Volume curve derived from clip measurements in a patient who inadvertently performed a Valsalva maneuver, showing a progressive decrease in volumes.
end-systolic, end-diastolic and stroke volumes during the third-to-fifth opacified cycles (approximately the fourth-to-sixth postinjection beats), other studies of LV hemodynamics and contractility in man demonstrate no significant change during the period of opacification. In the present study, small changes of stroke volume and ejection fraction were observed by the seventh postinjection beat.

Data from five of the 15 subjects were omitted from analysis because of decreasing ventricular volumes consistent with a Valsalva effect. An example of this is shown in figure 6. That a partial Valsalva maneuver occurs frequently during angiography in patients specifically instructed to maintain inspiration without Valsalva was demonstrated by esophageal manometry and was recently reported. Although there has been considerable concern and effort to determine the effects of contrast material on ventricular volume and performance, it is likely that unrecognized or inadvertent Valsalva maneuvers have a more important effect on the results of clinical ventriculography as usually performed than do the effects of the contrast medium.

While the present study does not define the complex interplay of the acute changes in preload, afterload and contractility produced by the sudden injection of contrast material into the left ventricular cavity in man, it does quantitate the net effect of contrast injection on left ventricular volume, stroke volume and ejection fraction. We conclude that the injection of moderate amounts of contrast medium (0.6–0.8 ml/kg) at rates of 20–25 ml/sec does not cause significant changes in left ventricular volume or ejection fraction through the sixth postinjection beat.

Acknowledgment

The authors acknowledge the assistance of our surgical colleagues, Drs. D. H. Dillard, L. C. Winterscheid, E. A. Hessel II and Donald W. Miller, Jr., in placing the epicardial markers; the technical assistance of Ms. Carol Ross, Mr. Albert L. Keller and Mr. H. Tracy Dodge III; the editorial assistance of Ms. M. Alison Ross, and the secretarial assistance of Ms. M. Kay Johnson and Ms. Lucile Jones.

References

1. Sanmarco ME, Fronke K, Philips CM, Davila JC: Continuous measurement of left ventricular volume in the dog. II. Comparison of washout techniques with the external dimension method. Am J Cardiol 18: 584, 1966
11. Hallerman FJ, Rostall GC, Swan HJC: Comparison of left ventricular volumes by dye dilution and angiographic methods in the dog. Am J Physiol 204: 446, 1963
Immediate effect of contrast medium injection on left ventricular volumes and ejection fraction. A study using metallic epicardial markers.

D L Vine, T D Hegg, H T Dodge, D K Stewart and M Frimer

Circulation. 1977;56:379-384
doi: 10.1161/01.CIR.56.3.379

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1977 American Heart Association, Inc. All rights reserved.
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/56/3/379

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/