INTRAVENOUS LEFT VENTRICULOGRAPHY UTILIZING DIGITAL
SUBTRACTION TECHNIQUE

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To detect the left ventricular boundary in the intravenous ventriculography, we used a subtraction technique for background suppression. Images containing contrast medium and reference mask images were transferred to a computer through a flying spot scanner and stored on the digital disc. Stored reference mask images were subtracted from the digitized contrast images. The resulting images were then electronically enhanced to extract the left ventricular (LV) image. The LV boundary was delineated with an algorithm we have developed and the volume of the LV cavity was calculated automatically. The validity of this method was compared with data obtained from conventional left ventriculogram (LVG). In 11 patients, values for end-diastolic volume (EDV), end-systolic volume (ESV) and ejection fraction (EF) calculated from the intravenous LVG were correlated closely with those from the conventional LVG (128 ± 38 (SD) vs 133 ± 39 ml, r = 0.95; 50 ± 28 vs 53 ± 30 ml, r = 0.98; 63 ± 10 vs 62 ± 12%, r = 0.96, respectively).

Nine patients with valvular regurgitation were followed up serially after valve replacement. EDV index fell significantly after corrective surgery (145 ± 50 to 81 ± 33 ml/m², p < 0.02), whereas, EF was affected variably depending upon the preoperative state (58 ± 13 to 61 ± 11%, not significant).

Thus, this method is less invasive than conventional LVG and has successfully allowed for sequential determination of ventricular function on an out-patient basis.

CINEVENTRICULOGRAPHY is the most accurate and reliable method for an assessment of left ventricular (LV) contractile function. However, since performance of conventional cineventriculography requires hospitalization of patients and left heart catheterization technique is invasive in nature, the application of this method is limited. Accordingly in the present study, the cineventriculography was performed by less invasive intravenous injection of contrast material. Because the low contrast image limited boundary detection of the ventricle, we used a digital subtraction method to eliminate the background structures and enhance the diluted contrast medium by common minicomputers. We then processed the digitized images utilizing the algorithm we have developed for subsequent dimensional analysis. The validity of this method will be discussed in comparison with the

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Fig.1. End-diastolic (I-a) and end-systolic (I-b) images.
A: Reference mask image for the subtraction obtained after disappearance of dye. Each digitized image consists of 128 x 128 pixels with gray levels of 256 values.
B: Original digitized image of the left ventricle obtained in the 30 degree right anterior oblique projection with intravenous injection of 40 ml of contrast medium.
C: The result after subtraction with electronic enhancement.
D: Automatic-traced boundary of left ventricle.
TABLE 1 LEFT VENTRICULAR VOLUMES DERIVED BY INTRAVENOUS AND CONVENTIONAL ANGIOGRAPHY

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Diagnosis</th>
<th>Intravenous LVG</th>
<th>Conventional LVG</th>
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<tr>
<td></td>
<td></td>
<td>EDV</td>
<td>ESV</td>
</tr>
<tr>
<td>1</td>
<td>N</td>
<td>110</td>
<td>29</td>
</tr>
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<td>2</td>
<td>N</td>
<td>113</td>
<td>42</td>
</tr>
<tr>
<td>3</td>
<td>VHD</td>
<td>86</td>
<td>34</td>
</tr>
<tr>
<td>4</td>
<td>VHD</td>
<td>134</td>
<td>38</td>
</tr>
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<td>VHD</td>
<td>133</td>
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</tr>
<tr>
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<td>127</td>
</tr>
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<td>IHD</td>
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<tr>
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</tr>
<tr>
<td>9</td>
<td>IHD</td>
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<td>71</td>
</tr>
<tr>
<td>10</td>
<td>IHD</td>
<td>131</td>
<td>37</td>
</tr>
<tr>
<td>11</td>
<td>IHD</td>
<td>100</td>
<td>48</td>
</tr>
</tbody>
</table>

Mean: EDV = left ventricular end-diastolic volume (ml); ESV = left ventricular end-systolic volume (ml); EF = left ventricular ejection fraction (%); HR = heart rate (beats/minute); N = normal; VHD = valvular heart disease; IHD = ischemic heart disease; SD = standard deviation.

METHOD

Materials

Studies were performed in 15 patients undergoing diagnostic catheterization. Four subjects were considered normal by standard hemodynamic measurements and coronary arteriography, five had valvular heart disease and the remaining six patients had coronary artery disease.

Routine left heart catheterization, the selective left ventriculography (LVG) and coronary arteriography were performed either percutaneously through a femoral artery or via a right brachial arteriomy. LVG was performed in 30 degree right anterior oblique projection by injecting 30–40 ml of contrast medium (80% Angioconray), using a Phillips 9 inch image intensification system, films being exposed at a rate of 60 frames/sec with an Ari 35 mm cine camera.

Intravenous Angiographic Procedure

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A 16 radiopaque teflon catheter (Angiocath, The Deseret Company, Utah) was inserted into an antecubital vein and connected to a power injector (Angiomat 3000). Thirty ml of a 5% glucose solution was layered over 40 ml of contrast medium in the injector reservoir and injected at a rate of 12 ml/sec; this provided a means of propelling the bolus of contrast medium through the venous system. Following injection, the levophase ventriculograms were obtained with respiration held about ten to 15 seconds without Valsalva maneuver. The reference mask images were then obtained at the last part of the exposure with complete disappearance of dye from the ventricle. All these angiograms were obtained in exactly the same manner as in the conventional LVG. Intravenous LVG was performed following conventional LVG at least thirty minutes interval in 6 cases, and in remaining 5 cases, performed on a subsequent day within one week after conventional LVG, because the total dose of contrast medium was limited. Digital subtraction was not available in 4 patients because of occurrence of transient atrial fibrillation during angiography in one and malregistration due to movement of thorax during the exposure in other patients. Thus, data
Fig. 2. Comparison of ventricular volumes calculated from intravenous and selective left ventriculography (LVG). EDV = end-diastolic volume; ESV = end-systolic volume

Fig. 3. Comparison of ejection fractions (EF) from intravenous and conventional LVG.

were summarized in 11 patients.

Analysis of Data

In processing the intravenous ventriculograms, both images containing radiopaque material and reference mask images were transferred to a computer through a flying spot scanner and stored on a magnetic disc. As the reference for the registration, an external lead marker fixed on the image intensifier was employed (Fig. 1). Each digitized image consisted of 128 by 128 pixels with gray levels of 256 values (8 bits). The processing was performed using a Hewlett Packard 2108A (24KW) and 2100A (32KW) computers. The reference mask image was subtracted from the digitized ventricular image and electronically enhanced to produce the final images. The reference mask image was formed by summing all frames throughout one cardiac cycle. Conventional ventriculograms were directly processed to delineate the ventricular boundary without the subtraction technique.

The algorithm of boundary tracing we used has been described previously1–3 The LV volumes (Vo) were calculated by a modification of Kennedy’s formula5; Vo = 0.687 × C^3 × A^2 / L + 1.9 ml, where A is the area of the ventricle calculated from the number of pixels surrounded by the LV boundary; L is the longest measured length between the midpoint of aortic valve and the apex; C is the linear correction factor for the magnification of a unit of length (one pixel), which was derived from the comparison with the known area of the filmed 1 cm^2-grid placed parallel to tube where the heart was assumed to be one-half the anterior-posterior thoracic dimension.

Postoperative Study

We used intravenous LVG for postoperative assessment of LV function in patients who had regurgitant valvular disease. The nine patients have been followed for two to 38 months after valve replacement (15.4 ± 15.0 months). Four were pure aortic regurgitation, two were pure mitral regurgitation and the remaining three were combined valvular disease. Preoperative evaluation...
<table>
<thead>
<tr>
<th>Case No.</th>
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<td></td>
<td></td>
<td></td>
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<td>NYHA class</td>
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<tr>
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<td>40</td>
<td>M</td>
<td>AR</td>
<td>6</td>
<td>II</td>
</tr>
<tr>
<td>2</td>
<td>49</td>
<td>M</td>
<td>AR</td>
<td>4</td>
<td>II</td>
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<tr>
<td>3</td>
<td>35</td>
<td>M</td>
<td>AR</td>
<td>4</td>
<td>III</td>
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<tr>
<td>4</td>
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<td>M</td>
<td>AR</td>
<td>3</td>
<td>III</td>
</tr>
<tr>
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<td>AR + MR</td>
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<td>III</td>
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<tr>
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<td>AR + MR</td>
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<td>± SD</td>
<td>9</td>
<td></td>
<td></td>
<td>1.3</td>
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</table>

Abbreviations: cath-op = catheterization to operation (months); NYHA class = New York Heart Association functional classification; EDVI = end-diastolic volume index (ml/m^3); ESVI = end-systolic volume index (ml/m^3); EF = ejection fraction (%); HR = heart rate (beats/min); op-cath = operation to catheterization (months); M = male; F = female; AR = aortic regurgitation; MR = mitral regurgitation; AS = aortic stenosis; m = mean; SD = standard deviation; P = probability (values compared with those of preoperation); NS = not significant.
tion with right and left catheterization and angiography was performed using standard methods. All patients had significant valve regurgitation confirmed angiographically. Preoperative and postoperative symptoms were graded according to New York Heart Association (NYHA) functional classification. Prosthetic valve function was satisfactory in the nine restudied patients. All values were expressed as mean ± standard deviation. Regression lines were analyzed with a least squares method. Differences between volumetric and functional variables were evaluated by student t-test.

RESULTS

I. Comparison of Intravenous LVG with Conventional LVG

The complete results for comparison of volume data obtained by the two methods are given in Table I and Fig. 2. The end-diastolic volumes (EDVs) calculated from intravenous LVG ranges from 86 ml to 207 ml with mean value of 128 ± 38 ml which were not significantly different from those values obtained from the conventional LVG (ranging from 77 ml to 204 ml with average of 133 ± 39 ml). End-systolic volumes (ESVs) and ejection fractions (EFs) calculated from intravenous LVG and conventional LVG did not differ significantly (50 ± 28 vs 53 ± 30 ml and 63 ± 10 vs 62 ± 12%, respectively). Regression analysis of EDV, ESV and EF calculated from intravenous LVG and those from conventional LVG is given in Fig. 2 and Fig. 3. The coefficient of correlation is remarkably high, with small standard errors of the estimate.

II. Comparison of Pre- and Postoperative Data in Patients with Valvular Heart Disease

Results of valve replacement are presented in Table II and Fig. 4.

Preoperative data: EDV index of 9 patients were 145 ± 50 ml/m² and 66 ± 35 ml/m², respectively. EF was 58 ± 13% (range 43 to 80%).

Postoperative data: As a result of valve replacement, all patients who had been in NYHA class III and IV preoperatively were in class I after the surgery. There was significant decrease in EDV index (from 145 ± 50 to 81 ± 33 ml/m², p < 0.002) and ESV index (from 66 ± 35 to 35 ± 26 ml/m², p < 0.02). However, changes in EF were variable.

DISCUSSION

Intravenous angiography was first attempted in the 1930s, when Robb and Steinberg reported the intravenous injection of iodinated contrast medium for visualization of the cardiovascular system. However, opacification of the left ventricle was invariably poor with potential errors for dimensional analysis largely due to dilution of dye and superposition by the background or other cardiovascular structures containing dye. In order to improve the inherent limitations and disadvantages of levocardiogram, we employed the computer technology of subtraction after logarithmic conversion of the background and contrast images. The extracted LV images have sufficient contrast to allow subsequent automatic boundary detection of the left ventricle, as previously described. In a previous study, we performed LVG using extremely small doses of contrast medium with successful contrast enhancement of the image by the same subtraction method. Hemodynamic rearrangement was greatly minimized by the small doses. In the present intravenous LVG study, however, considerably larger amounts of contrast material are needed to obtain reliable LV opacification and pharmacological effects are inevitable.

Ferlinz et al. described considerable discrepancy between LV dimensions determined by the selective ventriculograms and those by levophase ventriculograms and they exaggerated significant underestimation of ejection characteristics by the latter because of inferior cine resolution with a right side injection. However, in the present study which used digital subtraction, no significant differences were observed in the dimensional and functional values obtained by selective and levophase ventriculograms, and these results were similar to those from Vas et al. In five cases, intravenous LVG was performed on separated days. In one patient (case 7), EDV and ESV obtained from intravenous LVG were substantially smaller than those obtained from conventional LVG. This patient developed angina and reversible asynergy with increased chamber volume and reduced EF during selective LVG.

The differences of the measured volumes in the two LVGs have been regarded largely as the result of poor cine resolution of levophase injection and the presence of irrelevant background structure. The digital subtraction technique we employed successfully eliminated nonspecific
Digital Subtraction Technique for Intravenous Ventriculography

image details and permitted extraction of the ventricular silhouette. Chaitman et al. showed that subjective estimation of ventricular volume, EF and wall motion had a significant error rate and that reproducibility and accuracy required objective analysis. In this regard, the on-line method for edge tracing and algorithm for subsequent ventricular volume calculation will reduce this potential source of human error.

Ideally, digital processing of fluoroscopic images are to be performed directly and the stored mask should be subtracted from these images in real time. This technique has been applied clinically for visualization of vascular lesions. This method usually provides formation of fifteen images per second by subtracting a mask from the sum of four fields. This sampling rate has been regarded as sufficient for volumetric determination of the left ventricular EF. However, dynamic analysis of rapid wall motion during systole is still limited by this rate. With more recent equipment, time interval difference (TID) mode is generally used with a recording rate of 25 to 50 images per second. Several investigators attempted to record the fluoroscopic images on videotape and later post-process them at rate of 30 frames per second. Though the noise introduced by the latter method is much greater than in real time processing, it does not interfere with assessment of wall motion of the left ventricle. We also obtained intravenous ventriculograms by a 35 mm cinefilm and processed it in the same manner by film subtraction. Our method has advantage of enabling conversion of X-ray information into subtracted digital images with the use of conventional cineangiographic equipment and common minicomputers. Digitized images stored in the computer are automatically processed along the algorithm we have developed for edge tracing, volume measurement or segmental wall motion analysis.

In the subtraction procedures for previous selective ventriculography obtained by minimal doses of contrast medium, the mask images were related to the corresponding cardiac phase using electrocardiographic gating. However, this gated subtraction was relatively difficult in intravenous angiography because of periodic temporal variation of reference images in several cardiac cycles during the passage of contrast material from a peripheral vein to the left ventricle. Respiratory movement of thorax and diaphragm is one of the major sources of registration artifacts which obscure the signals associated with dye flow, then we exclude three patients because of malregistration due to movement of thorax by cough or difficulty of holding respiration. To improve these malregistrations, mask images are shifted correspondingly to ventricular images, then we will be able to get proper subtraction images. TID mode, on the other hand, was relatively insensitive to both patient motion and respiration, but in this method, the electronic enhancement is greater than in temporal subtraction and the inferior wall of the left ventricle is sometimes obscured by the diaphragm. Brennecke et al. noted significant variation of pixel brightness due to overlap of the diaphragm shadow on the cardiac silhouette. They succeeded in suppressing the large nonspecific signals by respiration-gated subtraction. In order to extract the cardiac structures independent of respiratory artifacts, we determined the mask by an integration of several images taken immediately after the passage of contrast material from the left ventricle and while the patient was holding breath continuously. An integrated mask is preferred over one of shorter duration because it reduces overall noise of the subtracted images. This procedure also allowed not only adequate cancelling of background in the subtracted images but also minimized alteration of physiological pump function of the ventricle induced by the Valsalva maneuver.

Digital intravenous angiography is particularly advantageous for assessment of LV dimension and function, since it is less invasive than selective angiography which requires heart catheterization; it thus greatly reduces the risk attendant upon the conventional method. Moreover, intravenous angiography has been shown to be better tolerated by high risk patients, including even a blue baby who was successfully identified as having cyanotic congenital heart disease with this method following injection of 3 ml of dye. Premature ventricular contractions frequently associated with selective LVG are completely eliminated by this method. Injection of dye has been done safely without derangement of blood pressure. But the injection technique will be not optimal, because of the risk of contrast medium extravasation at the injection site. To eliminate this problem, it will be necessary to use a long catheter percutaneously advanced into the superior or inferior vena cava.

As part of the present study, a postoperative follow-up study was conducted on an outpatient
basis. The spatial resolution of the subtracted images was far superior to the resolution obtained by other noninvasive methods and, despite relatively enlarged chamber, the delineation of morphologic change was accurate and informative. In nine patients with LV volume overload, both EDV and ESV decreased postoperatively, but EF was affected variably depending upon the preoperative state. In seven patients, EF had been reduced preoperatively but returned to normal level postoperatively. In the remaining two patients (case 3, 9), EF failed to be improved, this might have been due to irreversible myocardial damage caused by the mechanical overloading.

Thus, intravenous angiography provided the measurement of cardiac dimension and function on an outpatient basis less invasively than the conventional method, and enabled determination of LV volume serially over a period of time. Other investigators have reported that X-ray energy level could be reduced in digital intravenous angiography to the extent that it can be obtained at the bedside. Thus, this method will be an important diagnostic tool and open a new field of cardiac radiology.

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