Correlation of 10-milliliter digital subtraction ventriculograms compared with standard cineangiograms

Left ventriculograms were obtained with the use of 10 ml of contrast media by passing fluoroscopic video images through a video image processor. The low concentration of dye in the left ventricle was enhanced by the technique of mask mode subtraction, and the images were postprocessed to increase visibility by manipulation of the gray scale and contrast levels. These digital subtraction angiograms were compared to standard cineangiograms by means of 40 ml of contrast media. Of 30 patients studied, six (20%) had runs of ventricular tachycardia during the cineangiogram and had to be excluded. In the remaining 24 patients, there was a good correlation between the two techniques for left ventricular end-diastolic volume ($r = 0.77$, end-systolic volume ($r = 0.95$), and ejection fraction ($r = 0.97$). Spatial resolution in the digital studies was adequate to appreciate wall motion abnormalities that were visualized on the cineangiograms. Left ventricular end-diastolic pressure (LVEDP) did not change after the 10 ml injection, but the mean LVEDP rose 6.0 mm Hg after the 40 ml cineangiograms ($p < 0.01$). Digital subtraction angiography can be used to obtain left ventriculograms with one-fourth the amount of contrast media and one-fourth the x-ray exposure compared to standard cineangiograms. This technology will permit multiple left ventriculograms to be obtained which, in turn, will allow intervention studies to be performed in the catheterization laboratory. (Am Heart J 105:946, 1983.)

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Digital subtraction angiography is a new method which employs high-speed computer technology to enhance angiographic images so that adequate visualization of vascular structures can be obtained with lower concentration of contrast media compared to standard angiography.[1] With this method, high-resolution angiograms of peripheral arterial systems have been obtained by means of intravenous injection of contrast material.[2-4] As a result, the technique is applicable as a screening method for patients with suspected carotid, aortic, femoral, or renal artery lesions.[5-7] Peripheral arteries usually do not move significantly during imaging and, consequently, motion artifact is minimal in the process of digital subtraction. Cardiac imaging is theoretically a more difficult area in which to apply digital subtraction techniques because of the rapid cardiac motion during each heart beat.[8] If adequate cardiac imaging with digital subtraction angiography could be obtained, it would likely find many clinical applications because digital left ventriculograms could be performed with less contrast material and less radiation exposure compared with standard cineangiograms.

Recently, we have been able to obtain good quality left ventriculograms with digital subtraction angiography by means of intravenous injection of 30 to 40 ml of iodinated contrast media.[9] In the present study, we evaluated the use of this technology as a method for obtaining left ventriculograms following intraventricular injection of lower amounts of contrast media. The purpose of this study was to assess whether digitally processed left ventriculograms could be obtained with 10 ml of contrast media injected directly into the left ventricle by means of

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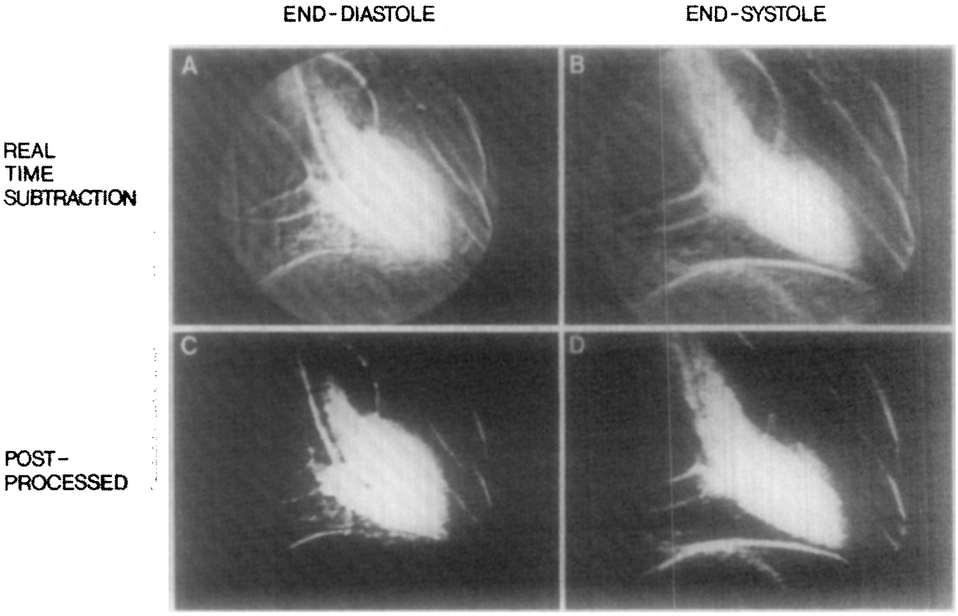

Fig. 1. End-diastolic and end-systolic images of the left ventricle obtained by injecting 10 ml of contrast material into the left ventricle and processing the video signal in real time by digital subtraction. *A*, End-diastolic and *B*, End-systolic image prior to postprocessing. *C* and *D*, The same images after contrast enhancement.

fluoroscopic x-ray exposure levels and whether quantitative analysis of these images would yield results comparable to those obtained from standard 40 ml cineangiograms.

METHODS

Digital angiography technique. Digital angiography was performed by means of the method of mask mode subtraction which involves the acquisition of an x-ray image of the chest, known as a "mask," prior to contrast injection.[10] This mask image was obtained by using an image-processing computer (Cardiac 1000, American Edwards Laboratories, Santa Ana, Calif.) to digitize the incoming video image into a $512 \times 512 \times 8$ bit image matrix at a rate of 30 frames/sec. Each frame of the digitized image was stored in a $512 \times 512 \times 12$ bit computer memory which allowed a 16-frame (½ second) fluoroscopic exposure to be summed and stored as the mask. The stored mask image, therefore, represented the soft tissues and bones of the thorax. After the mask was stored, the fluoroscopic exposure was continued and each new video frame was digitized and the stored mask was subtracted from it in real time. If perfect subtraction occurred, the resultant image would be blank because any soft tissue or bones would be subtracted from the image. Iodine contrast media was then injected during fluoroscopy and the results were recorded on video tape. This permitted adequate contrast of iodine compared to soft tissues despite even low concentrations of contrast material.

Our cardiac catheterization laboratory is equipped with a Siemens Cardioskop U-arm x-ray unit. The imaging chain consists of a cesium iodide 7-inch image intensifier and a plumbicon television camera with 525 horizontal scan lines. The video output of the television camera is connected to the input of the image-processing computer. The subtracted fluoroscopic images are displayed in real time on television monitors in the catheterization laboratory.

In this study, ventriculography was performed by means of a fluoroscopic exposure level of 8 mA and 70 to 90 kVp depending on the size of the subject. This was accomplished by modifying the equipment in our cardiac catheterization laboratory to provide up to 8 mA in the fluoroscopic mode. Eight mA is two to three times higher than standard fluoroscopic currents. Since 5 mm of aluminum filtration was added, the overall exposure rate was only 40% higher than conventional fluoroscopy. The video signals from the television camera were logarithmically amplified prior to computer digitization and processing. After processing, the images were reconverted to analog format for storage on videotape (Sony Betamax, Model SL0323MD, ½ inch recorder). Following completion of the study, the images could be redigitized by the computer for postprocessing. Among other advantages, postprocessing permitted manipulation of the contrast and gray scale levels through the computer to enhance visualization and boundary detection. In addition, the computer contained software programs to calculate left ventricular volume and ejection fraction. A more comprehensive description of our imaging system is described in a previous report.[9]

Clinical studies. Patients undergoing left ventriculography during cardiac catheterization for clinically indicated reasons were asked to participate in this study. Informed

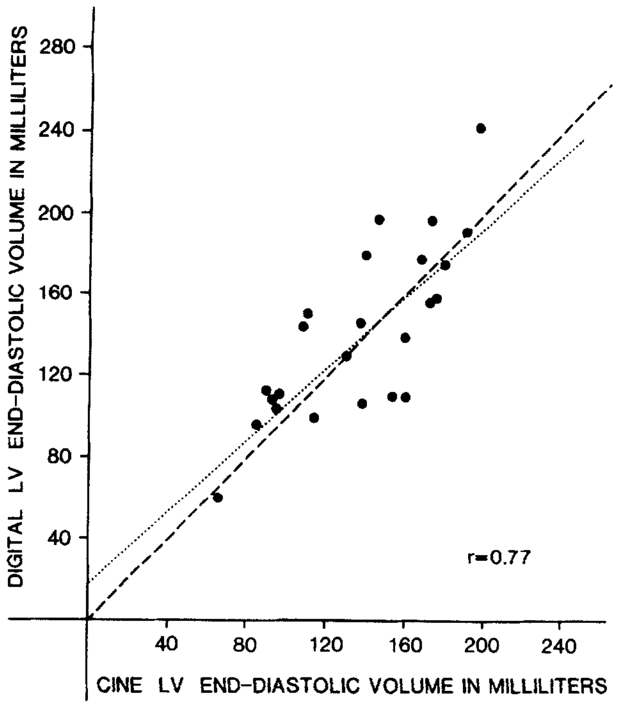

Fig. 2. Comparison of left ventricular end-diastolic volumes obtained with 10 ml digital subtraction angiography and 40 ml cineangiography. The line of identity is the heavy dashed line and the regression equation is represented by the dotted line.

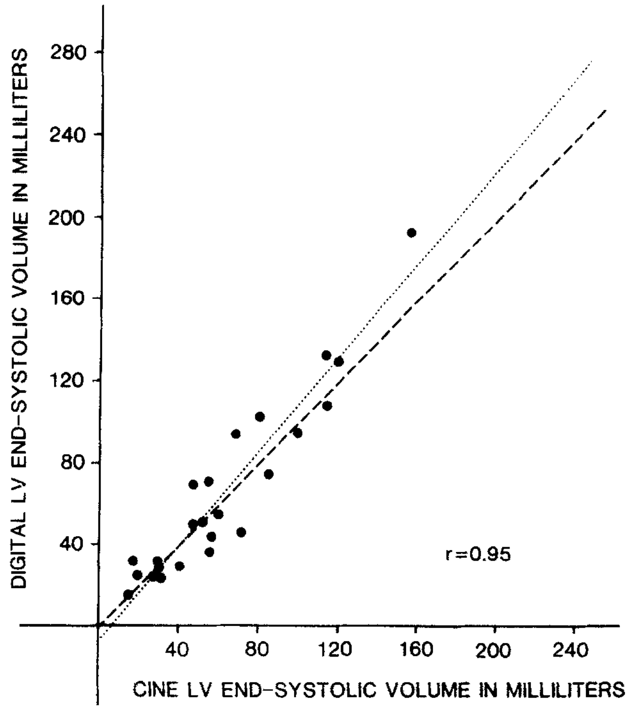

Fig. 3. Comparison of left ventricular end-systolic volumes obtained with 10 ml digital subtraction angiography and 40 ml cineangiography. The line of identity is the heavy dashed line and the regression equation is represented by the dotted line.

consent was obtained for each patient who agreed to participate. During our routine cardiac catheterization studies, coronary angiography was first completed. Then, a 7-French Cordis pigtail catheter was passed retrograde across the aortic valve into the left ventricle and the patient was positioned in the 30-degree right anterior oblique (RAO) position. Immediately prior to injection of dye, the patients were asked to hold their breath in order to prevent misregistration artifact from occurring during the study. A ½-second sequence of fluoroscopic mask images (16 frames) was digitized, summed, and stored in the computer memory. After the mask was obtained, the fluoroscopic exposure of the heart was continued and the computer was automatically switched to the subtracted mode as the contrast media was injected. During the present study, digital angiography was performed by injecting 10 ml of Hypaque-75 or Vascoray directly into the left ventricle at a rate of 5 ml/sec by means of a Medrad Mark IV power injector. While in the subtraction mode, the computer subtracted the mask from each new frame in real time at television rates of 30 frames/sec. The subtracted image was displayed on a monitor in the cardiac catheterization laboratory and was also recorded on videotape for later analysis.

Standard 35 mm cineangiography of the left ventricle was performed after the 10 ml injection was obtained. The patient remained in the same position and the height of the table and image intensifier were kept constant. Cineangiograms were obtained at the rate of 30 frames/sec with an exposure rate of 150 to 250 mA and 70 to 90 kVp. For the cineangiograms, 40 ml of Hypaque-75 was injected at a rate of 13 ml/sec over 3 seconds by a Medrad Mark IV power injector. After the study, an 8×8 cm grid was placed on the patient table at a height above the table corresponding to one half the distance of the patient's anterior-posterior thoracic dimension. A brief image of this grid was obtained on the 35 mm cine film as well as on the digital angiography video tape. This grid was used during subsequent analysis to correct for magnification factors. The left ventricular pressure was recorded through the 7-French pigtail fluid-filled catheter and a Statham P23ID transducer. The left ventricular end-diastolic pressure (LVEDP) was interpreted as the onset of the rapid upstroke of the left ventricular contraction pressure wave. Pressure measurements were recorded before and within 2 minutes after the 10 ml and the 40 ml injections of contrast media.

Analysis of angiograms. The 35 mm cineangiograms were reviewed on a Vanguard projector. End-diastolic and end-systolic frames were chosen, projected onto a piece of paper, and the boundary of the left ventricle was hand traced onto the paper. Left ventricular volumes at end diastole and end systole were calculated by the Sandler-Dodge single-plane area-length formula corrected for magnification with the grid technique of Sandler and Dodge[11] and Kennedy et al.[12]

The digital subtraction cardiac images recorded on video tape were reviewed and a 10-second segment of the video tape containing the ventriculogram was transferred onto a video disc (Sony VM-1200 LV). The cardiac images could then be analyzed during playback from the video disc in a frame-by-frame mode at variable speeds, and contrast and gray levels could be manipulated to enhance the visibility of the ventricular contour. End-diastolic and end-systolic images of the left ventricle were chosen and traced by hand onto a piece of acetate which had been placed over the video disc screen. As with the cineangiogram tracing technique, indistinct portions of the left ventricular boundary could be more clearly visualized by playing the image back and forth on the video monitor until the correct boundary was chosen. The hand-traced acetate outlines of the left ventricular boundaries were then planimetered on an x-y tracing tablet that is part of the digital angiography computer. The Sandler-Dodge single-plane area-length formula was also used to calculate left ventricular volumes for the digital angiograms.

The end-diastolic and end-systolic volumes and ejection fractions obtained from the standard left ventricular cineangiograms were compared to those obtained from the 10 ml digital subtraction angiograms. Statistical comparison of the measurements was performed by a least-squares linear regression for two variables.

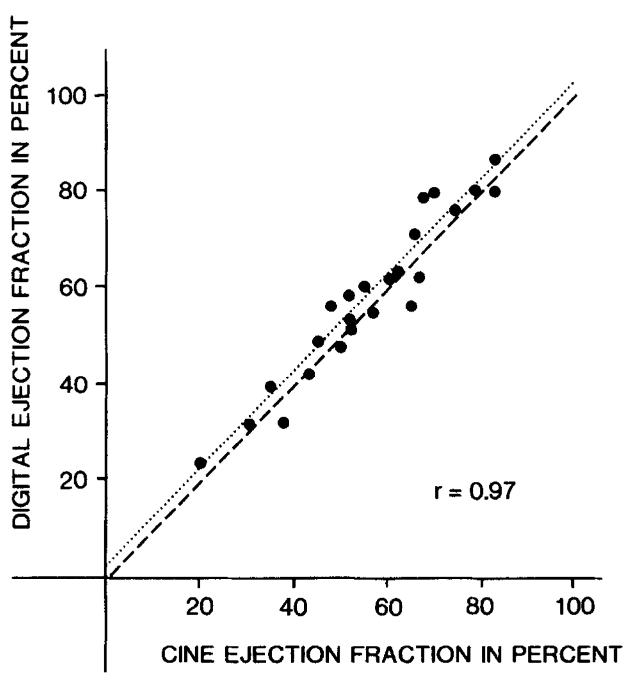

Fig. 4. Comparison of left ventricular ejection fraction obtained with 10 ml digital subtraction angiography and 40 ml cineangiography. The line of identity is the heavy dashed line and the regression equation is represented by the dotted line.

RESULTS

Study group. Thirty patients who were undergoing left ventriculography for clinical reasons and who agreed to participate in the digital angiography protocol were studied. Multiple premature ventricular contractions occurred during the standard 40 ml cineangiograms in 10 of 30 (33%) patients. In six (20%) of these patients, there was a continuous run of premature ventricular contractions during the intraventricular injection of contrast, such that the ventricular volumes and ejection fractions were not representative of the basal state. These six patients were excluded from the study. In the other four patients, the second sinus beat after a premature contraction was chosen for analysis.

Premature ventricular contractions occurred in 4 of the 30 (13%) patients during the 10 ml intraventricular injections used to obtain the digital subtraction angiograms. However, there were no continuous runs of premature ventricular contractions during the 10 ml injections and no patient had to be excluded because of premature contractions that occurred with the 10 ml injections. An example of a 10 ml intraventricular injection with and without computer enhancement is demonstrated in Fig. 1.

After the six patients who had runs of premature ventricular contractions were excluded, 24 patients were available for comparison of the standard 40 ml cineangiograms and the 10 ml digital subtraction angiograms. There were 15 men and 9 women whose ages averaged 53.3 years (range 36 to 77 years) and whose mean weight was 81.3 kg (range 45.5 to 120.5 kg). Thirteen patients had coronary artery disease and eight of these had a history of a myocardial infarction. There were two patients with idiopathic hypertrophic subaortic stenosis (IHSS), two patients with alcoholic cardiomyopathy, and two patients with rheumatic valvular disease. Five patients were catheterized for evaluation of chest pain but were found to have normal coronary arteries on selective coronary angiography.

Quantitative analysis. Comparisons between the 10 ml digital and the 40 ml cineventriculograms are depicted in Figs. 2, 3, and 4. The end-diastolic volumes calculated from the standard cineangiograms were related to end-diastolic volumes calculated from the digital angiograms by the equation: digital end-diastolic volume = ([0.88] [cine end-diastolic volume]) + 22.9 ml (Fig. 2). These volumes were correlated with $r = 0.77$, $p < 0.005$. End-systolic volumes were more closely correlated ($r = 0.95$, $p < 0.005$) and related by the equation: digital end-systolic volume = ([1.1] [cine end-systolic volume]) − 7.2 ml (Fig. 3). Ejection fractions calculated from the two techniques also were closely correlated ($r = 0.97$, $p < 0.005$) and related by the regression

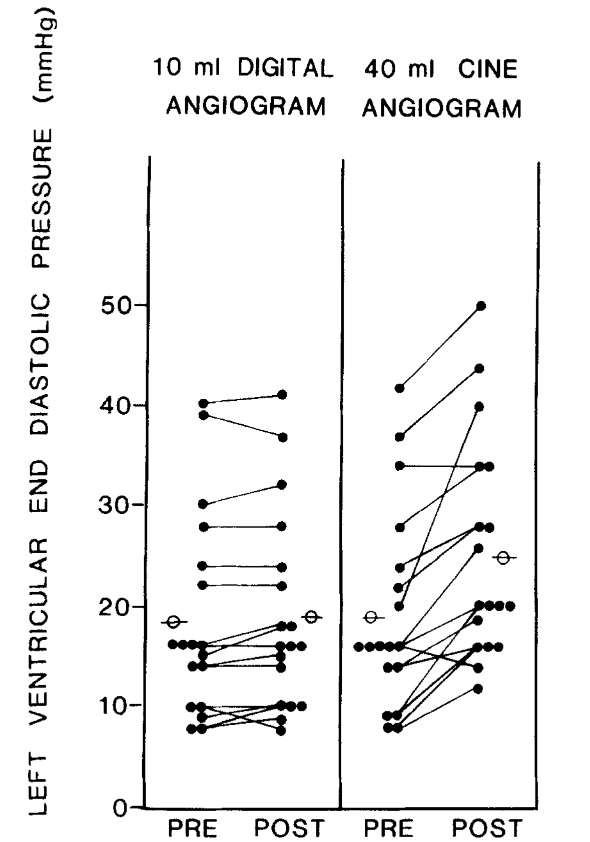

Fig. 5. The left ventricular end-diastolic pressure is demonstrated before and after the 10 ml intraventricular injection in the left-sided panel. The panel on the right side demonstrates the left ventricular end-diastolic pressure before and after the standard 40 ml cineangiogram injection.

equation: digital ejection fraction = ([1.0] [cine ejection fraction]) + 1.0% (Fig. 4).

Nine of the 24 patients had significant wall motion abnormalities. Four of these nine patients had diffuse hypokinesis of the left ventricle. One patient had a large anterior apical aneurysm and one patient had akinesis of the inferior wall with anterior hypokinesis. The remaining three patients had hypokinesis of the apical, inferior, or basal segment of the left ventricle. Qualitative assessment of wall motion abnormalities in the RAO view revealed that diffuse or localized hypokinesis or akinesis was appreciated equally well by the digital 10 ml angiograms or the standard cineangiograms in all nine patients.

Pressure measurements. Left ventricular pressure measurements were recorded before and after both the 10 ml and the 40 ml injection of contrast material in 18 of the 24 (75%) patients. The results of these observations are depicted in Fig. 5. The mean pressure was 18.4 ± 10.2 mm Hg at rest and did not change significantly after the 10 ml injection (18.9 ± 10.0 mm Hg). Prior to the 40 ml injection of contrast media, the mean LVEDP was 19.2 ± 10.4 mm Hg (no difference compared to initial baseline) and after the 40 ml injection the mean LVEDP increased an average of 6.0 mm Hg ($p < 0.01$).

DISCUSSION

Our results indicate that acceptable quality left ventriculograms can be obtained with direct injection of 10 ml of contrast media into the left ventricle when the image is processed by a digital subtraction angiography computer. This 10 ml injection represents one fourth the standard amount of contrast material usually utilized to obtain left ventriculograms. Despite the decreased blood concentration of contrast media, the mask subtraction process allowed the contrast media to be clearly visualized in the left ventricle.

Quantification of LV volumes. A quantitative analysis of left ventricular volume revealed a close correlation ($r = 0.95$) between the end-systolic volumes derived from the cineangiograms and the 10 ml digital angiograms. The ejection fractions calculated from the two techniques also correlated closely ($r = 0.97$). The end-diastolic volumes had a weaker correlation coefficient ($r = 0.77$). One possible explanation for this weaker correlation is that mixing of contrast media and blood is poorer with the 10 ml injection so that there is insufficient filling of the ventricle in end diastole. If this were true, one would predict that the 10 ml digital end-diastolic volume would be consistently lower than the calculated 40 ml cineangiogram volume. However, our data do not show this because measurements fall equally on both sides of the line of identity (Fig. 2). Another consideration is that the 40 ml injection over 3 seconds could add a significant volume to the left ventricular blood pool in some patients and produce an overestimation of basal ventricular volume. Again, our data do not demonstrate a consistent overestimation of volume by the 40 ml injections. Moreover, Sasayama et al.[13] from Kyoto University have presented data which suggest that a 40 ml injection over 3 seconds does not significantly alter the left ventricular volume. They reported their results with injecting 5 ml of contrast media into the left ventricle. They did not use real time subtraction but after the injection was made, the images were post processed by digital subtraction. In 16 patients, they obtained very close correlation between standard cineangiograms and 5 ml digital angiograms both for end-diastolic volumes ($r = 0.95$) and for end-systolic volumes ($r = 0.98$). In our experience with the use of real time subtraction, we could not consistently obtain adequate visualization of the left ventricle by means of 5 ml of contrast media and thus we chose an injection rate of 5 ml/sec for a total of 10 ml. One possible reason for the good experience of Sasayama et al.[13] with 5 ml injections is that they excluded patients with left ventricular volumes above 150 ml. We did not exclude patients on this basis. The largest ventricle in our series was 252 ml at end diastole.

Advantages of digital angiography. There are several benefits of the digital angiographic technique for assessing left ventricular size and function. First, because adequate left ventriculograms can be obtained with 10 ml of contrast material, the left ventricle can be visualized in multiple views during cardiac catheterization without increasing the total amount of contrast material compared to standard cineangiography. In addition, the fluoroscopic exposure levels we employed exposed the patient to less than one-fourth the amount of radiation compared to a standard cineangiogram. Thus, approximately four times the number of left ventriculograms can be obtained during routine cardiac catheterization without increasing the total amount of x-ray exposure to the patient compared with standard cineangiography.

A second important benefit of the technique is that the injection of 10 ml of contrast media has less hemodynamic effect than injection of 40 ml of contrast. This was demonstrated by the fact that left ventricular pressures did not rise significantly after the 10 ml injection but did increase a mean of 6.0 mm Hg ($p < 0.01$) following the 40 ml injection. These observations are similar to the data of Sasayama et al.[13] They found that the 5 ml injections did not elevate the left ventricular end-diastolic pressure whereas the standard 25 to 40 ml injection raised the pressure an average of 7 mm Hg (from 12 to 19 mm Hg) within 1 to 3 minutes after injection. This feature of digital subtraction angiography would be useful when intervention studies are performed to assess ventricular function in the cardiac catheterization laboratory. For example, atrial pacing studies or drug intervention studies are feasible and could be performed with less alteration of the baseline hemodynamics due to the injection of contrast material. For these reasons, digital subtraction angiography is particularly attractive as a method for performing cardiac catheterization in the pediatric age group or in adults with diminished renal clearance who have intolerance to high doses of contrast material.

Another important advantage of digital subtraction angiography is that it produced fewer premature ventricular contractions than the standard cineangiographic study. Twenty percent of patients who had standard cineangiograms developed runs of ventricular tachycardia during the injection. This resulted in an inadequate assessment of ventricular function in these patients because it made the analysis of ventricular volumes and ejection fraction impossible. In contrast, none of the 30 patients developed runs of ventricular tachycardia during the 10 ml digital angiograms. Therefore, it appears that digital ventriculograms performed with injection of 10 ml of iodinated contrast material will allow ventricular function to be assessed in a much higher percentage of patients during routine cardiac catheterization.

Conclusions. Our results demonstrate that left ventriculograms of adequate quality can be obtained with 10 ml of contrast material injected into the left ventricular cavity when the fluoroscopic image is processed through a computer. The visibility of the lower concentration of contrast media is enhanced by cancelling out background soft tissue and bones of the thorax via a process called mask mode subtraction. In addition, visualization of the iodine is improved by manipulating the contrast gain and gray levels of the digitized image. Digital subtraction left ventriculograms can be obtained with one-fourth the standard amount of contrast media and one-fourth the x-ray exposure to the patient compared to cineangiograms. There is much less interference in the assessment of ventricular function because premature ventricular contractions occur less commonly and left ventricular end-diastolic pressure is less affected compared to standard cineangiograms. These attributes permit the angiographer to use less contrast media which is particularly useful in patients who have a low tolerance for contrast media such as diabetic patients, patients with impaired renal function, or patients with pulmonary hypertension. Moreover, several digital left ventriculograms can be obtained to assess either left ventricular wall motion from multiple views or the left ventricular response to physiologic or pharmacologic interventions. For these reasons, digital subtraction angiography will have multiple applications in clinical cardiology.

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Pulmonary hypertension in isolated secundum atrial septal defect: High frequency in young patients

Out of 709 consecutive patients with isolated secundum atrial septal defect, the pulmonary artery systolic pressure was >50 mm Hg in 118 patients (17%). Pulmonary hypertension was present in 13% of patients under 10 years and in 14% aged 11 to 20 years. The Eisenmenger reaction was present in 9% of the 709 patients. The frequency of the Eisenmenger reaction was high in young patients and was not significantly different in patients in the first and second decades as compared to older patients. None of our patients with pulmonary hypertension resided at high altitude. The high frequency of pulmonary hypertension in our young patients cannot be satisfactorily explained. Autopsy studies suggest that in some, pulmonary hypertension is due to the persistence of the fetal pulmonary vascular pattern. (AM HEART J 105:952, 1983.)

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There are variations in the natural history of certain cardiac conditions which cannot be easily explained, and our observations show that unlike other reports, pulmonary hypertension is common in our young patients with isolated secundum atrial septal defect. Pulmonary hypertension (PH) as a result of pulmo-