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Journal

American Heart Journal, 104(1)

ISSN

0002-8703

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Publication Date

1982

DOI

10.1016/0002-8703(82)90636-6

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Left ventricular imaging with digital subtraction angiography using intravenous contrast injection and fluoroscopic exposure levels

First-pass left ventriculograms were obtained using digital subtraction angiography in 24 patients after intravenous injection of 30 to 40 ml of iodinated contrast material. An image processing computer was used to enhance the iodine signal in the image relative to the background soft tissue by digitizing each new frame of the fluoroscopic exposure and subtracting from it a stored "mask" image. Digital left ventriculograms were obtained in the 30-degree right anterior oblique (RAO) position using high fluoroscopic exposure levels [8 mA and 70 to 90 kVp] and compared to 30-degree RAO cineangiograms obtained at cardiac catheterization. Standard cineangiograms were performed in 33 patients at cardiac catheterization but six (18%) were excluded because of runs of ventricular tachycardia initiated by the standard intraventricular injection of 40 ml of contrast media. Digital subtraction angiography was attempted in the 33 patients and left ventriculograms of clinically useful quality were obtained in 30 (91%). There were close correlations between end-diastolic volumes ($r = 0.82$), end-systolic volumes ($r = 0.93$), and ejection fractions ($r = 0.96$). Multiple premature ventricular contractions occurred in a total of 10 of 33 (30%) patients during standard intraventricular cineangiography but did not occur in any patients during the intravenous first-pass technique. Wall motion abnormalities were visualized as well by digital angiography as by the standard method. Digital angiography appears to be an important new addition to diagnostic cardiology because it provides a less invasive outpatient method for obtaining contrast left ventriculograms which have much greater spatial resolution than radionuclide cineangiograms. (AM HEART J 104:20, 1982.)

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Digital subtraction angiography is a technique which utilizes a high-speed digital computer to enhance radiographic images.¹ This technology increases the visibility of iodinated contrast agents by the method of mask subtraction.^{2,3} The mask subtraction technique utilized for cardiac imaging involves generating a brief fluoroscopic image of a part of the body, converting the image into a matrix of digital numbers, and storing the resulting digital image (called a "mask") in the memory of a special image processing computer. After the initial image is stored, a continuous fluoroscopic exposure is obtained during injection of iodinated contrast material. Each frame of the fluoroscopic exposure is

digitized and the stored mask is subtracted from it in real time. The subtracted digital image is amplified and converted into an analog video image for storage on a video tape recorder or video disc.⁴ If no dye is injected between the time the mask is obtained and the second radiographic exposure is performed, and if the subject does not move, the result of the subtraction will be blank images. However, if iodinated contrast material is injected after the mask is obtained and during the fluoroscopic exposure, the iodine signal will be the only information left in the image after the subtraction of the mask. As a result, the iodine signal is more clearly visualized in the subtracted image. Because the iodine signal is amplified prior to storage, it is not degraded significantly by analog storage on a videotape recorder.⁵ The improved contrast resolution obtained with this computer enhancement of radiographic images permits vascular angiography to be performed with intravenous injections of 30 to 40 ml of iodinated contrast material.⁶ Several groups have reported the use of this technique in visualizing carotid, renal, or peripheral arteries.⁷⁻⁹

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Supported in part by a grant from the American Heart Association, California Affiliate.

Received for publication Feb. 16, 1982; accepted March 2, 1982.

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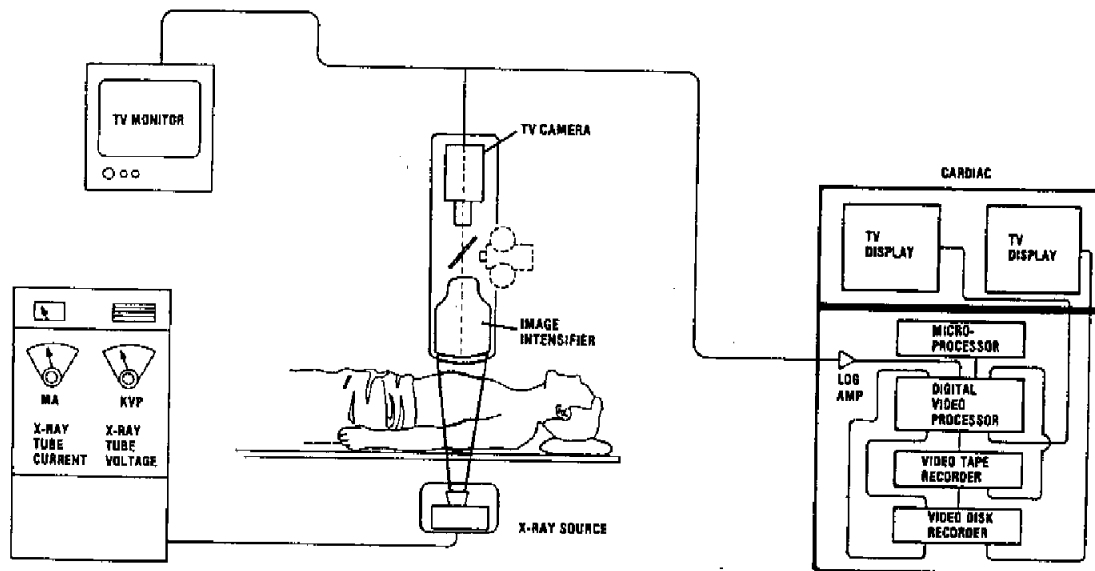


Fig. 1. System diagram. The *left side* of the diagram represents the components of a traditional angiographic room, including the x-ray control module, x-ray tube, and image intensifier. Cineangiograms can be recorded on film or the image can be processed through a television camera and displayed on a monitor. On the *right-hand side* is a schematic of the digital processing unit. The video signal from the television camera is amplified logarithmically and is then digitized by the video processor. Images can be recorded on video tape or video disc and fed back from these recorders into the video processor for preprocessing of the image after the studies are completed.

For cardiac imaging, the bony structures and soft tissues overlying the heart are subtracted from each radiographic frame. Therefore the iodinated contrast material can be more easily visualized as it passes through the heart. Because of the subtraction process and selective amplification of the dye signal, the cardiac chambers can be imaged adequately with a relatively small concentration of contrast material.¹⁰ In the present study we interfaced a portable digital angiography system to the video output of the image intensifier in our cardiac catheterization laboratory and used it to process ventriculographic images. The purpose of the study was to determine if first-pass ventricular angiograms of clinically adequate quality could be obtained utilizing high fluoroscopic x-ray exposure levels and peripheral intravenous injections of standard amounts of iodinated contrast material. In addition, left ventricular (LV) volumes calculated from these intravenous angiograms were compared to volumes calculated from standard cineangiograms to determine if digital angiography can be used to assess quantitatively LV size and function.

METHODS

Imaging system. The components of the imaging system used in our studies are shown in Fig. 1. The catheterization laboratory is equipped with a Siemens Cardioskop U-arm x-ray unit and a swivel table. The image obtained

on the image intensifier is visualized with a Plumbicon TV camera and transformed into a video signal. For the digital angiography studies, the video signal from the Plumbicon camera was connected to the input of the digital angiography system (Cardiac 1000, American Edwards Laboratory) where it was logarithmically amplified and then digitized by a digital video image processor into a $512 \times 512 \times 8$ bit deep pixel matrix at standard TV rates (30 frames/sec). Before any iodinated contrast material was injected, a $\frac{1}{2}$ second (16 frame) digital mask image of the heart and thorax was obtained and stored in the memory of the computer. Immediately after the mask was stored, iodinated contrast material was injected and each new frame of the video image was digitized and the stored mask was subtracted from it in real time. The subtracted digital image was amplified and reconverted from digital into analog format and stored on videotape (Sony Betamax model SL0323MD $\frac{1}{2}$ -inch recorder) or videodisc (Sony VM-1200 LV). The subtracted images were also displayed on the video screens in the catheterization laboratory during each study.

The digital angiography system used in the present study had several features that facilitated obtaining and analyzing the images. A computer-generated menu was available to specify the number of frames that would be digitized and averaged for the stored mask image. In the present study, 16 consecutive frames were averaged for the mask. Since motion can produce artifact in subtraction images, it is preferable to summate a large number of frames for the mask so that misregistration due to cardiac motion will be minimized. The memory depth of the

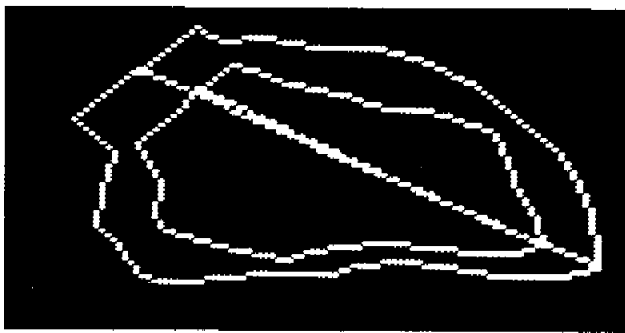


Fig. 2. Graphic video display of hand-traced boundaries of digital left ventriculograms. Traced boundaries both at end-diastole and end-systole are shown. The computer utilizes these traces for calculations of ventricular volumes using the area-length method.

computer was 12 bits per pixel and the images were digitized at eight bits per pixel, which left four bits for summation. These four bits were used to integrate the 16 frames of the mask, since the number of frames that can be summed is equal to 2 raised to the power of the number of bits available, i.e., $2^4 \text{ bits} = 16 \text{ frames}$. After the mask specifications had been entered, data acquisition and mask subtraction were completely automated. The digital angiography system displayed the subtracted image on the video screens in the catheterization laboratory during each study.

Another useful feature of the system was that the subtracted images stored on videotape could later be replayed through the digital angiography system and redigitized for postprocessing. Therefore the contrast and gray scale could be manipulated after the study had been performed to enhance visibility of the iodine-filled chambers. The digital angiography system also contained a graphical tracing system which allowed the boundaries of the ventricular chamber to be outlined at end-diastole and end-systole during postprocessing for computation of ventricular volumes (Fig. 2).

Angiographic studies. Patients undergoing left ventriculography during cardiac catheterization for clinically indicated reasons were asked to participate in this study. Informed consent was obtained from the patients who agreed to participate. Each patient received a 30-degree right anterior oblique (RAO) left ventriculogram during his routine cardiac catheterization. A dose of 42 ml of Renografin 76 was injected over 3 seconds by a Medrad Mark IV power injector into the LV via a No. 7 French Cordis pigtail catheter. Cineangiographic images were obtained with the kVp between 70 and 90 and the mA between 150 and 250. LV images were recorded on 35 mm cineangiographic film at 30 frames/sec for subsequent analysis. 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 and used to derive magnification factors. LV volumes at end-diastole and end-systole were calculated

by the Sandler-Dodge area-length formula, corrected for magnification with the grid using the method described by Kennedy et al.^{11, 12}

On the day following the cardiac catheterization, the patient was brought back to the cardiac catheterization laboratory. In all but one patient a percutaneous puncture of the right femoral vein was performed with the Seldinger technique.¹³ A No. 6 French USCI introducing catheter sheath was passed into the femoral vein and the patient was placed in the same position as in the previous day's LV study. The height and angulation of the x-ray tube and image intensifier also were identical to those used during the previous left ventriculographic study. The patient was asked to hold his/her breath and a mask image was collected just prior to the injection of contrast material. Thirty or 40 ml of Renografin 76 or Hypaque 75 was then rapidly hand injected through the No. 6 French introducer. The duration of contrast injection was less than 3 seconds. All digital angiography images in the present study were obtained at high fluoroscopic exposure levels of 8 mA, which is approximately twice the standard fluoroscopic tube current. The kVp ranged between 70 and 90 kVp, depending on the size of the patient. A 5 mm thick aluminum filter was used to eliminate low energy radiation which results in less patient exposure than in standard fluoroscopy. The maximum incident exposure rate on the image intensifier was 50 $\mu\text{R}/\text{frame}$. A fluoroscopic exposure of approximately 20 seconds was required to record the contrast material as it passed through the right heart chambers into the pulmonary circulation and then through the LV. The subtracted fluoroscopic video image of the first-pass intravenous angiogram was recorded on $\frac{1}{2}$ -inch videotape for subsequent analysis. After the study, an 8 × 8 cm grid was also fluoroscopically imaged, recorded on videotape, and used to correct for magnification.

LV volume analysis. The cardiac images recorded on video tape were reviewed and the heart beat in which the greatest concentration of dye was seen in the LV was chosen for analysis. Images from this cardiac cycle were then digitized by the digital angiography system so that the boundary of the LV could be traced directly on the video image. An end-diastolic frame was chosen by identifying the image with the largest iodine-filled area, and the end-systolic frame was identified as the image with the smallest contrast filled area. End-diastolic and end-systolic volumes were calculated by the computer using the area-length method. LV volumes were obtained from the cineangiograms by projecting the filmed image from a Vanguard projector onto a piece of paper, hand tracing the boundary, and then planimetrying the traced area with an x-y tracing tablet on the digital angiography computer. The single-plane area-length formula was used to calculate LV volumes. The end-diastolic (EDV) and end-systolic (ESV) volumes and ejection fraction (EF) obtained from the standard LV cineangiograms were compared to those obtained by digital intravenous angiography. Statistical analysis was performed by a least-squares linear regression analysis for two variables.

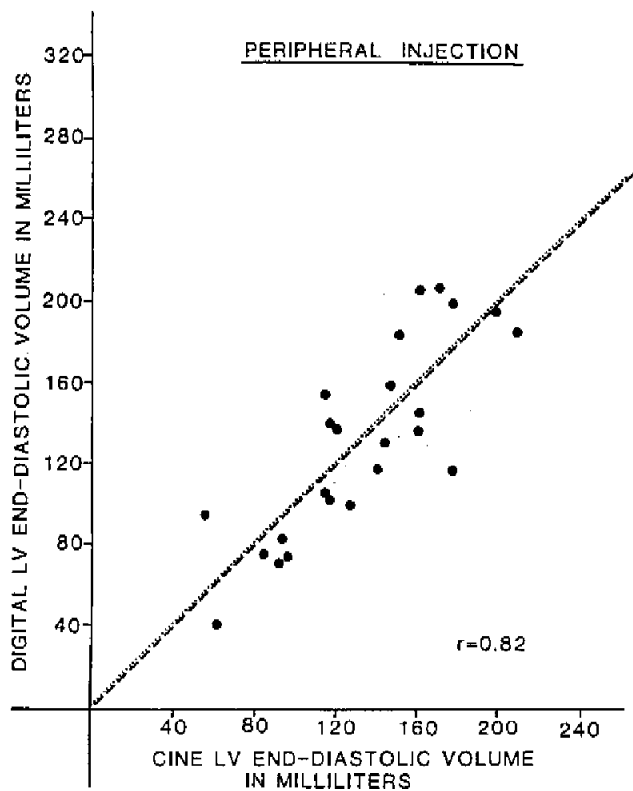


Fig. 3. Comparison of left ventricular (LV) end-diastolic volumes obtained by intravenous digital angiography (vertical axis) and intraventricular cineangiography (horizontal axis). The line of identity is shown as the heavy dashed line and the regression equation is represented by the dotted line.

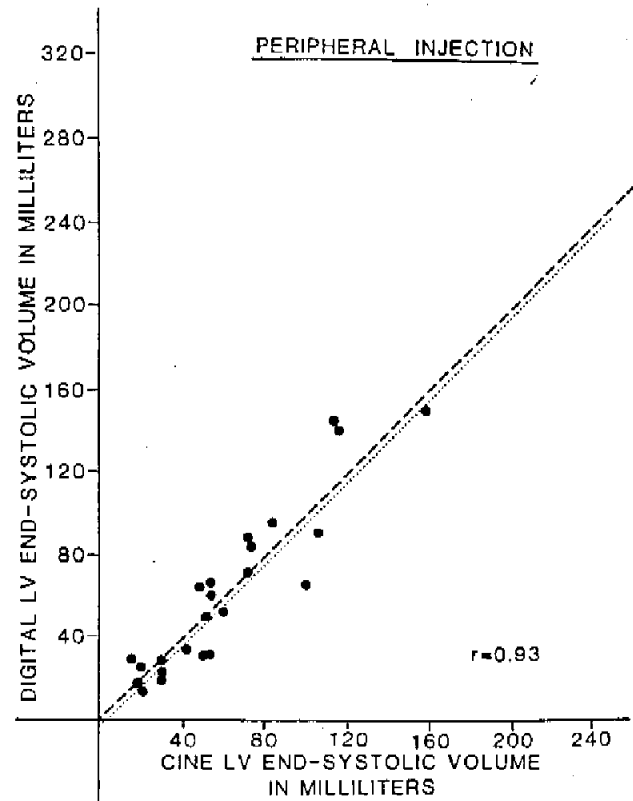


Fig. 4. Comparison of left ventricular (LV) end-systolic volumes obtained by intravenous digital angiography (vertical axis) and intraventricular cineangiography (horizontal axis). The line of identity is shown as the heavy dashed line and the regression equation is represented by the dotted line.

RESULTS

Study patient characteristics. Thirty-three consecutive patients who were undergoing left ventriculography for clinical reasons and who agreed to participate in the digital intravenous angiography protocol were studied. Multiple premature ventricular contractions (PVCs) occurred during the standard intraventricular cineangiograms in 10 of 33 (30%) patients. In six of these patients there was a continuous run of PVCs during the intraventricular injection of contrast such that the computation of ventricular volumes and EF was 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 PVC was chosen for analysis. PVCs did not occur during any of the 33 intravenous angiograms.

Because six patients were excluded due to ventricular tachycardia during the routine cineangiograms, a total of 27 patients were available for comparison. Right ventricular (RV) visualization was accomplished in 25 of these 27 patients following the

intravenous injection. LV boundary detection was readily appreciated in 19 (70%) patients during first-pass digital angiography. In eight studies, the mitral and aortic valve planes were indistinct or portions of the ventricular boundary were insufficiently visualized. These images were postprocessed with the digital angiography system to increase contrast in the images. This postprocessing permitted adequate visualization of the LV in five studies that initially were thought to be suboptimal. Thus diagnostically useful images which were sufficient to allow LV boundary tracing were obtained in 24 of 27 (89%) patients studied. These 24 patients comprised the study group. There were 15 men and 9 women in the study whose age averaged 55.7 years (range 38 to 77 years), and whose mean weight was 77.0 kg (range 44 to 120 kg). Nineteen of the individuals had coronary artery disease and five had chest pain with normal coronary arteries.

In three patients, diagnostically useful images were not obtained despite attempts at postprocessing. These unsuccessful tests were in three of the

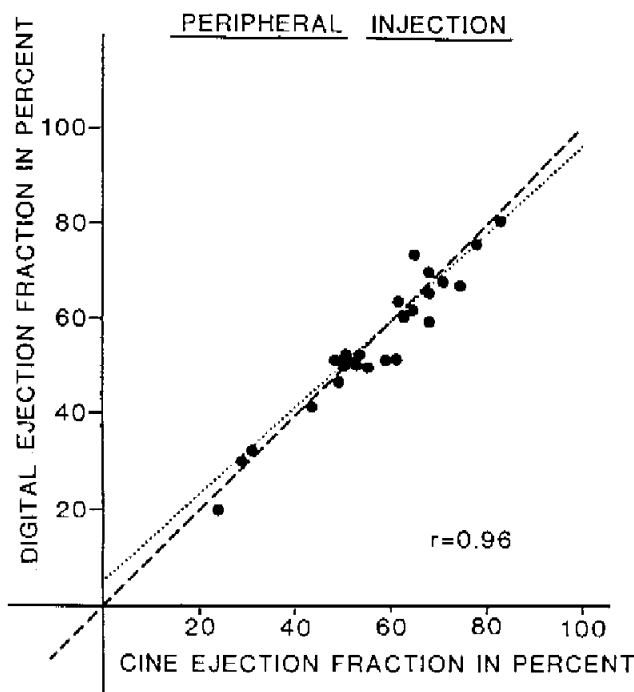


Fig. 5. Comparison of left ventricular (LV) ejection fraction obtained by intravenous digital angiography (*vertical axis*) and intraventricular cineangiography (*horizontal axis*). The line of identity is shown as the *heavy dashed line* and the regression equation is represented by the *dotted line*.

initial five patients studied. Of these, one patient did not receive an adequate bolus of contrast material during the injection and a second patient had the contrast material administered into the left basilic vein. In this second patient the venous flow was probably insufficient to maintain a reasonably compact bolus through the LV phase. The third patient had tricuspid regurgitation. Also, all three unsuccessful attempts occurred in patients with dilated ventricles and markedly reduced LV function (EFs of 24%, 22%, and 21%).

LV volume and ejection fraction results. Ventricular volumes were able to be calculated both from standard LV cineangiograms and from intravenous digital angiograms in 24 patients. The results are plotted in Figs. 3, 4, and 5. The EDVs calculated from the standard cineangiograms were related to volumes calculated from the digital angiograms by the equation: digital EDV = (0.99) (cine EDV) + 0.6 ml. These volumes were closely correlated with $r = 0.82$ (Fig. 3). ESV were closely correlated ($r = 0.93$) and related by the equation: digital ESV = (1.0) (cine ESV) - 1.7 ml (Fig. 4). EFs calculated from the two techniques also were closely correlated ($r = 0.96$) and related by the regression

equation: digital EF = (0.92) (cine EF) + 4.9% (Fig. 5).

LV wall motion abnormalities. Six of the 24 patients had significant wall motion abnormalities. Qualitative assessment of wall motion abnormalities revealed that hypokinesia or akinesia was appreciated equally well by digital angiography or standard cineangiography in five of the six patients. The other patient had an isolated LV apical aneurysm that was well visualized during the intravenous angiogram, but initially was not appreciated during direct intraventricular injection because of inadequate mixing of dye and incomplete filling of the LV apex. The intravenous injection permitted adequate mixing of contrast prior to ventricular filling (Fig. 6).

DISCUSSION

Our results indicate that first-pass RV and LV angiograms of acceptable quality for clinical use can be obtained with an intravenous hand injection of iodinated contrast material and high fluoroscopic x-ray exposure levels. The amount of contrast material injected into the vein was equal to or less than the amount usually injected directly into the LV during standard cineangiography. Despite the decreased blood concentration of dye obtained with intravenous injection of contrast material, the mask subtraction technique allowed the dye to be clearly visualized as it passed through the cardiac chambers and great arteries.

Benefits of digital angiography for assessing LV function. There are several benefits of this digital angiographic technique for assessing LV size and function. First, the intravenous injection did not induce any PVCs, whereas direct injection into the LV induced single or multiple PVCs in 10 of 33 (30%) patients studied. A second advantage of the technique is that it is less invasive because it only requires injection of dye into a peripheral vein, as compared to the need for an arterial puncture and catheter placement directly into the LV.¹⁴ This may be especially useful in those patients in whom it is difficult to enter the LV with a catheter, such as patients who have mechanical prosthetic valves in the aortic position. During the time period of the present study, we utilized digital intravenous angiography to obtain left ventriculograms in two such patients. Although a standard left ventriculogram could not be obtained in these patients, there was good correlation between the intravenous technique and a gated radionuclide cineangiogram. The less invasive aspects of the study also means that studies can be performed on an outpatient basis because

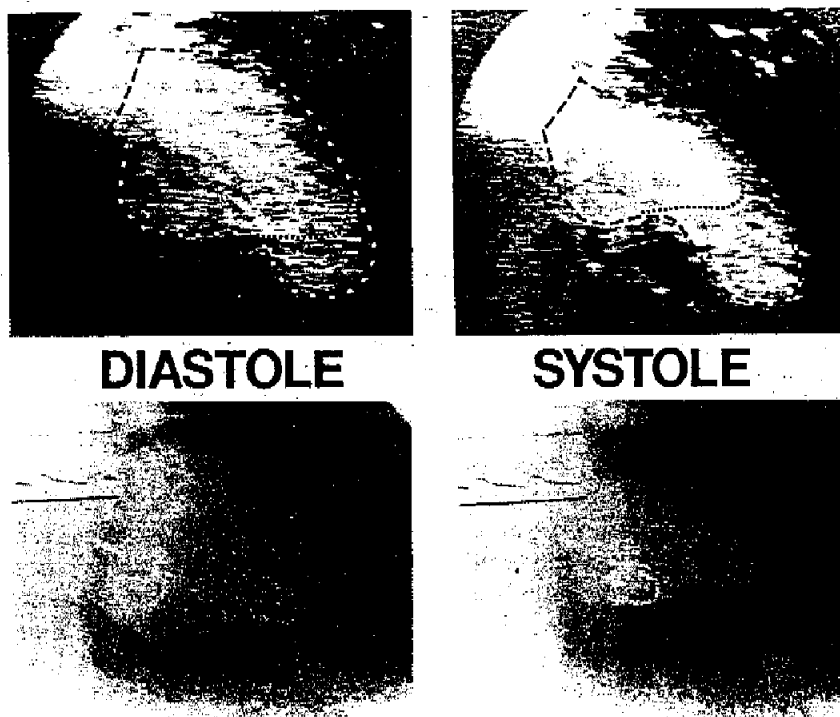


Fig. 6. Intravenous digital angiograms (upper panels) and intraventricular cineangiograms (lower panels) from the same patient. Both studies were performed with 40 ml of contrast material. The intravenous technique provided better mixing of contrast and allowed the apical aneurysm to be better visualized. The left ventricular boundaries that were appreciated on the standard intraventricular cineangiograms have been superimposed on the digital angiogram and outlined with the *small dots*, while the boundaries appreciated on the digital angiogram have been outlined by the *heavy dashed lines*.

patients may leave the hospital shortly after the procedure is performed.

A third advantage of the method is that the digital angiography system we used provided sufficient improvement in contrast resolution to allow satisfactory ventricular imaging with high fluoroscopic exposure levels. Because fluoroscopic levels can be used and the equipment is portable, intravenous angiograms can be obtained at the bedside. This feature should prove particularly useful for studying critically ill patients such as those patients hospitalized in a Coronary or Intensive Care Unit.

Another significant advantage of digital angiography is the ability to easily postprocess the video image and improve contrast visualization for boundary detection. Postprocessing images in this manner obviates some of the problems with traditional cine film developing, such as poor quality control, erratic film processing, and the necessity to choose between either high or low contrast film prior to the study. Potentially, digital angiography may be developed to the point where it could replace cine film entirely, thus making film processing obsolete and negating the increasing cost of silver based x-ray film.¹⁶

Because the contrast information is preserved by the technique, it is possible to display either high or low contrast images as desired during postprocessing. Wall motion abnormalities also were well visualized by the digital intravenous angiographic technique. Areas of hypokinesis or dyskinesis were appropriately identified by intravenous angiography in all patients who had these anomalous contraction patterns demonstrated by standard LV angiography.

Our approach to digital intravenous angiographic imaging differs significantly from other reported methods and from standard cineangiography, in that the x-ray energy levels to which the patient is exposed is considerably less with our technique. We utilized high fluoroscopic exposure levels of approximately 8 mA and 70 kVp whereas other laboratories have used cine mode exposure levels of 150 to 300 mA and 60 kVp.⁶ We chose to use fluoroscopic exposure levels because they provided satisfactory spatial and contrast resolution for visualization of LV contour. Since the LV silhouette encompasses a large portion of the image (i.e., a large number of pixels), we were able to obtain adequate ventricular contrast levels. The spatial resolution capacity of

our digital angiography system was 1 to 2 mm depending on the contrast levels and focal spot on the x-ray tube. The usual spatial resolution of radionuclide images is approximately 10 mm. Therefore with regard to spatial resolution, images obtained by digital angiography have 5 to 10 times greater spatial resolution than images obtained with nuclear angiography.

Difficulties of digital angiography. We encountered two main problems in obtaining high quality intravenous angiograms of the LV. If the patient breathed during the study, movement of the diaphragm and soft tissues created misregistration between the background soft tissue densities obtained in the mask and the soft tissue densities obtained in each fluoroscopic frame during passage of the iodinated contrast material. This misregistration resulted in inadequate cancelling of bone and soft tissue in the subtracted images and resulted in streaks and noise in the image. This problem was minimized by training the patient to take a deep breath and maintain the diaphragms at a stable position. By visualizing the patient's diaphragm on the subtracted video image during the study, the operator was able to instruct the patient about the depth of breathing and thereby help the patient keep his/her diaphragm motionless during the injection. This method minimized misregistration artifact.

The second major problem pertains to difficulty in obtaining an adequate concentration of contrast material in the LV. Patients who had a low cardiac output and markedly reduced LVEF had spreading of the dye bolus in the venous system. They also had greater dilution of the dye as it moved into the dilated LV. This problem is exemplified by the fact that good quality peripheral angiograms were obtained in all 20 patients with LVEFs above 45% compared to satisfactory studies in only four of seven patients with EFs less than 45%. Similarly, a patient who had tricuspid regurgitation had spreading of the bolus of contrast material which resulted in an inadequate concentration of dye in the LV. In addition, tricuspid regurgitation resulted in some contrast material remaining in the RV during the time that dye was appearing in the LV. Since the RV overlies the LV in the RAO position, it interferes with visualization of the LV, particularly along the medial and inferior boundary of the LV. Because of this problem, we now perform first-pass intravenous angiograms in the angulated 30-degree left anterior oblique position in patients who are suspected of having tricuspid regurgitation.

Difficulty in obtaining adequate visualization of

the LV during our initial studies caused us to inject the contrast agent into the femoral vein rather than into the basilic vein. We are currently reevaluating the option of arm injections as well as pulmonary artery injection. The arm injections are being performed with higher than fluoroscopic x-ray energy levels because more iodine signal information may be obtained at the higher radiation dose. We are also exploring higher x-ray exposure levels because they might enhance the image and still be well below the x-ray exposure used during cine mode angiography.

Conclusions. Angiographic imaging of the LV using intravenous injection and the mask subtraction technique is now feasible because of recent advances in high-speed computer technology. Digital angiography results in high resolution images of the LV and allows visualization of wall motion abnormalities and quantitation of ventricular volumes and EF. The digital angiography technique can be performed by hand injection of dye into a peripheral vein, thus obviating the problem of PVCs and the complications of arterial punctures and intraventricular catheterizations. The equipment is portable, operates at fluoroscopic exposure levels, and provides images that have much higher resolution than radionuclide images. For these reasons, digital intravenous angiography is an important diagnostic advance that should have multiple applications to clinical cardiology.

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Detection and assessment of severity of regional ischemic left ventricular dysfunction by digital fluoroscopy

Digital intravenous ventriculography (DIV) was used to detect and assess the severity of regional and global left ventricular (LV) function in the presence of graded levels of coronary stenosis. DIV was performed on six anesthetized dogs with a coronary blood flow probe and micrometer controlled occluder on the circumflex coronary artery (CXA) and pairs of sonic dimension crystals in the posteroinferior (ischemic area) and anterior (control area) walls of the LV in the control state, with subtotal occlusion of the CXA (STEN), and with CXA occlusion (OCL). Global analysis at each stage included area-length calculation of end-diastolic volume (EDV), end-systolic volume (ESV), and ejection fraction (EF). Regional analysis included calculation of area displaced by anterior wall (AA), and posteroinferior wall (IA), average amplitude of excursion of the anterior wall (AE), and posteroinferior wall (IE). STEN caused significant increase in AA ($14.4 \pm 2.2\%$) and decreases in EF ($-19.7 \pm 2.5\%$), IA ($-36.6 \pm 4.2\%$), and IE ($-30.8 \pm 5.3\%$) ($p < 0.05$). With OCL, there were significant increases in EDV ($78.7 \pm 7.6\%$), ESV ($225 \pm 20.6\%$), AA ($42.6 \pm 10.3\%$), and AE ($25.5 \pm 4.3\%$); with further fall in EF ($-42.4 \pm 2.1\%$), IA ($-94.3 \pm 6.6\%$), and IE ($-84.7 \pm 9.4\%$) ($p < 0.01$). Regional functional indices derived from DIV detected regional wall motion abnormalities, when these were shown to be present by sonocardiometer measurements of myocardial segment length and extent of shortening in the ischemic region of the LV. We conclude that DIV is a sensitive technique for the detection and assessment of severity of regional and global LV dysfunction in ischemic heart disease. (*AM HEART J* 104:27, 1982.)

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Supported by United States Public Health Service Career Development Award Grant No. 1K04HL2001 (Dr. Higgins) from the National Heart, Lung and Blood Institute.

Received for publication Feb. 26, 1982; accepted March 3, 1982.

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Contrast left ventriculography is generally considered the most precise technique for the evaluation of left ventricular (LV) anatomy and function. Left ventriculograms can be obtained without cardiac catheterization by digital processing of fluoroscopic images of the heart obtained after central intravenous injection of contrast media (digital intravenous