METHODS

Digital Subtraction Intravenous Left Ventricular Angiography: Comparison With Conventional Intraventricular Angiography

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Standard contrast left ventriculography with catheter placement into the left ventricle entails risks and inconvenience. Computer-based digital subtraction techniques now permit high contrast left ventriculography after intravenous administration of contrast medium. To compare the accuracy of intravenous digital subtraction left ventriculography with film-based, standard contrast ventriculography, we assessed left ventricular function by both methods in 32 patients (8 with valvular disease, 22 with coronary disease and 2 with atypical pain). Studies in 31 of 32 patients were considered. Left ventricular ejection fraction by standard contrast ventriculography ranged from 24 to 88%. Digital subtraction angiography was performed with bolus injection of radiopaque contrast material (30 cc at 20 cc/s) into the inferior vena cava. The two methods correlated closely in end-diastolic volume (correlation coefficient [r] = 0.96, probability [p] < 0.001), end-systolic volume (r = 0.97, p < 0.001) and ejection fraction (r = 0.98, p < 0.001). Segmental function was assessed visually; precise agreement existed between the two techniques in 123 (79%) of the 155 segments (p < 0.001). It is concluded that intravenous digital angiography provides left ventricular images of sufficiently good quality to allow accurate quantitative assessment of global left ventricular function and volumes as well as determination of regional function.

Angiographically determined size and systolic function are primary determinants of the results of both medical and surgical therapy in patients with ischemic (1), valvular (2) and cardiomyopathic (3) heart disease. Several imaging techniques are available for evaluation of left ventricular performance. Because of its intrinsically high spatial resolution and its capacity to permit visualization of all borders of the ventricle, X-ray transmission ventriculography during injection of radiopaque contrast medium directly into the left ventricular chamber is considered the standard method for such assessment. However, this technique necessitates left heart catheterization with its attendant risks and inconvenience for the patient and is often associated with catheter-induced ventricular ectopic rhythm, precluding optimal assessment of left ventricular function (4).

To avoid the difficulties associated with left heart catheterization, computer enhancement techniques, based on digitization of the photon density of the fluoroscopic image obtained during contrast injection (5–8), have been employed to provide high resolution images from the levophase of the cardiac angiogram obtained after intravenous bolus injection of contrast medium. Recently, this technology has been applied to a portable device that potentially allows high quality "digital subtraction angiograms" to be rapidly and easily obtained for clinical evaluation. We have employed this equipment to determine the extent to which intravenous digital subtraction left ventriculography can provide information previously available only with intraventricular contrast administration and film-based images.

Methods

Study patients. Thirty-two adult patients (≥ 37 years of age, 26 men and 6 women) underwent both standard left ventriculography and digital intravenous angiography as part of our routine cardiac catheterization procedure for evaluation of right and left ventricular function. No patient characteristics were employed for selection of patients for study with the exception that patients with an unstable clinical course, preexisting renal dysfunction or diabetes mellitus were excluded. All patients who underwent both standard and digital angiography between November 1981 and March 1982 were included in this study. Twenty-two patients had

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coronary artery disease, eight patients had valvular heart disease and two had chest pain with normal coronary arteries. Cardiac catheterization was performed at least 8 hours after the last food intake with the patient under sodium pentobarbital sedation (100 mg intramuscularly) with local lidocaine anesthesia. No nitrate vasodilators were administered within 4 hours of catheterization and no other vasoactive agents were administered for at least 12 hours before catheterization. No vasoactive drugs were given during angiography or between the two angiograms. Twelve patients underwent digital angiography before standard angiography; 20 patients underwent the standard procedure first. Temporal separation of the two angiograms ranged from 5 to 55 minutes (average, 16).

Standard ventriculography. Standard left ventricular cineangiography was performed in the right anterior oblique position with catheter entry into the femoral artery using the percutaneous Seldinger technique, with either a Judkins pigtail or Schoonmaker catheter. Between 30 and 35 cc of diatrizoate meglumine and diatrizoate sodium (Renografin 76) were injected at 6 to 12 cc/s, according to our standard clinical diagnostic protocol. All angiograms were recorded at 60 frames/s on 35 mm Kodak CFS film using a General Electric Fluorocon 300 system. Films were processed using a Jamieson 54 processor.

Digital subtraction left ventriculography. Ventriculograms were obtained in the right anterior oblique position after insertion of either a Berman angiographic, Gensini or Judkins pigtail catheter into the inferior vena cava by way of the femoral vein. Injection of 30 cc of Renografin 76 mixed with 15 cc of sterile saline flush solution was performed at a rate of 20 cc/s. Because saline solution and Renografin (the latter being the more dense of the two substances) are immiscible, when the mixture is injected in the usual manner with the injector syringe nozzle pointed downward, the contrast agent arrives in the vein first. Fluoroscopic energies were 4 to 8 mA, at 75 kVP.

To minimize diaphragmatic movement and obscuration of the heart by the diaphragm, patients were instructed to inspire fully just before injection of the contrast agent. When possible, patients were asked to maintain full inspiration until completion of the levophase (approximately 15 seconds). If patients were unable to comply with this request, expiration was allowed after right ventricular opacification and a second maximal inhalation was undertaken with the onset of left ventricular opacification. Data were collected in the microprocessor of an American Edwards Laboratory CarDIAC 1000 digital angiographic device. A block diagram of the equipment, as it interfaces with the fluoroscope, is shown in Figure 1.

To obtain a digital subtraction angiogram, the area of interest is imaged with fluoroscopy, forming a picture on the image intensifier. This picture is converted to an analog electrical signal by a television camera. The analog output from the television camera is presented to the CarDIAC 1000 microprocessor and the picture is converted to a digital format that can be processed by computer. This is accomplished by dividing the image into a 512 by 512 "pixel" (picture element) matrix. The brightness of each pixel is quantified; the quantity thus determined is proportional to the number of photons incident on the image intensifier. The brightness, or photon density, at each pixel is recorded and stored digitally in the microprocessor memory. This analog to digital (A to D) conversion is performed at a rate of 30 frames/s. An initial set of 16 frames is averaged, stored in memory and used to define the "background" radiation transmitted through the patient before contrast injection. The background image is termed a "mask." Fluoroscopy is repeated after contrast administration, resulting images are digitized as before and the mask is subtracted from the new image on a pixel by pixel basis. This technique results in subtraction or marked attenuation of all stationary structures in the chest and the relative enhancement of the image of the contrast medium within the field of view. The processed digital image is then converted back to an analog signal (D to A) for viewing on a standard television monitor.

Measurements. Left ventriculograms obtained by both techniques were assessed in an identical manner. A representative ventricular cycle was identified. End-diastolic and end-systolic silhouettes of the left ventricle were outlined on transparent plastic. With reference to the silhouette of a standard calibration grid, left ventricular end-diastolic and left ventricular end-systolic volumes were computed according to the Sandler-Dodge formula (9). Ejection fraction (EF) was calculated from the volumes (EF = [end-diastolic volume − end-systolic volume]/end-diastolic volume). Ventricular volume analysis was performed in a blinded fashion. Each ventriculogram was assessed by one of four investigators who are routinely involved in volume analysis in our laboratory.

Left ventricular segmental function was semiquantified on a 4-point scale (normal = 1, hypokinetic = 2, akinetic = 3 and dyskinetic = 4). The left ventricle was subdivided into 5 segments (anterobasal, anterolateral, apical, inferolateral and inferobasal),

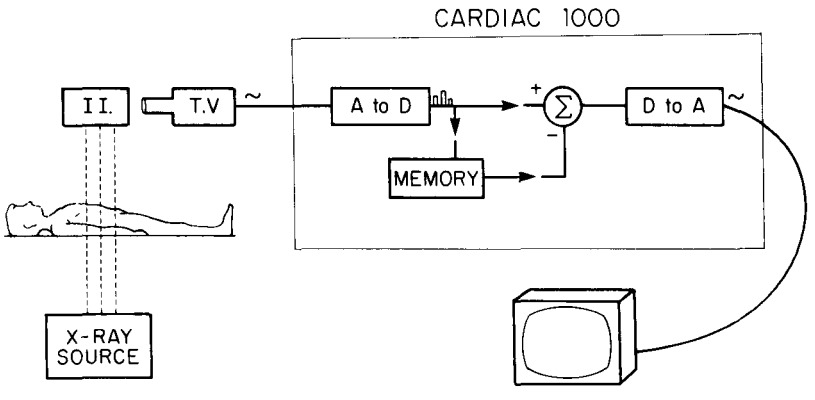


Figure 1. Schematic diagram depicting the functional components of the digital subtraction device (CarDIAC 1000) and its relation to the fluoroscopic imaging chain. See text for explanation. ~ = an analog signal; ⊓⊓ = a digital signal. A to D = analog to digital converter, D to A = digital to analog converter, I.I = image intensifier, Σ = microprocessor that "subtracts" the "mask," stored in memory, from the incoming signal.

and each segment was individually scored by one of three investigators.

To minimize interobserver bias, each investigator analyzed both the conventional and the digital subtraction angiogram on any single patient; the angiograms, however, were presented as part of a multipatient series so that the appropriate pairing of digital and conventional results was never identified to the investigator. To minimize memory bias, several days elapsed between interpretation of the two angiograms of a single patient.

Analysis of data. A least squares correlation was used to compare volumes and ejection fractions obtained by both techniques. The standard error of the estimate was determined for each correlation. Chi-square analysis was used to compare the frequency of agreement and disagreement in segmental wall motion between the two methods.

Results

Images of diagnostic quality were obtained in 31 of our 32 patients, the exception involving a patient who experienced a paroxysm of coughing during the administration of contrast medium. Among the 31 patients with evaluated studies, left ventricular ejection fraction determined by conventional contrast angiography ranged widely, from 24 to 88%. Left ventricular end-diastolic volume ranged from 84 to 322 cc^3 and left ventricular end-systolic volume from 18 to 132 cc^3, again from conventional contrast studies.

Left ventricular volumes and global ejection fraction (Fig. 2 to 4). Analysis of left ventricular end-diastolic volume by both techniques showed a close correlation (correlation coefficient [r] = 0.96, standard error of the estimate [SEE] = 17.3, probability [p] < 0.001, Fig. 2). The maximal difference between the two techniques was 36 cc, with a maximal percent difference (absolute difference/conventional angiographic volume) of 25%. In addition, there was a close correlation between left ventricular end-systolic volumes by both techniques (r = 0.97, SEE = 9.8, p < 0.001, Fig. 3). The maximal absolute difference between techniques was 21 cc and the maximal percent difference was 30%. As would be expected from the close correlation in volumes between the two techniques, there was an excellent correlation between ejection fractions (r = 0.98, SEE = 2.9, p < 0.001, Fig. 4). The maximal difference in ejection fraction was 6% and the maximal percent difference (absolute difference in ejection fraction/ejection fraction by conventional angiography) was 21%.

Segmental function. Of the 155 segments analyzed by conventional angiography, 87 segments were considered normal, 48 hypokinetic, 16 akinetic and 4 dyskinetic. There was absolute concordance in interpretation between the two methods in 123 (79%) of segments (p < 0.001 versus chance)

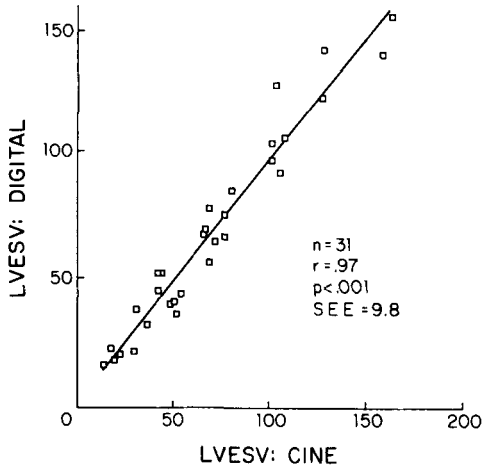


Figure 3. Left ventricular end-systolic volume (LVESV) as determined by both conventional intraventricular cineangiography (CINE) and digital intravenous angiography.

Figure 2. Left ventricular end-diastolic volume (LVEDV) as determined by both conventional intraventricular cineangiography (CINE) and digital intravenous angiography. n = number of studies, p = probability; r = correlation coefficient; SEE = standard error of the estimate.

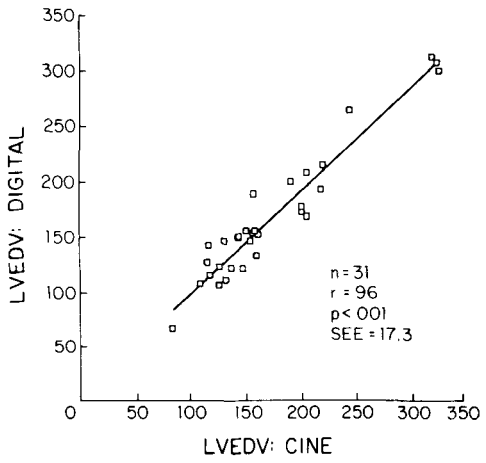
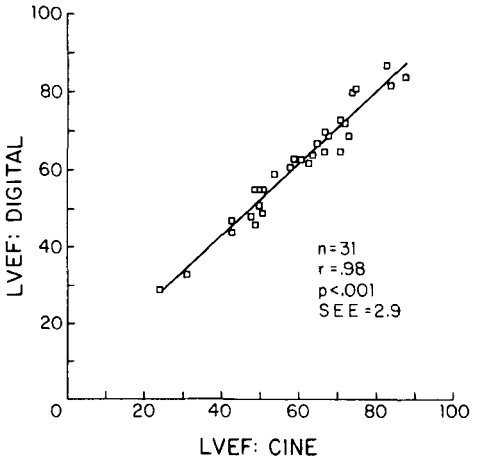


Figure 4. Left ventricular ejection fraction (LVEF) as determined by both the conventional and digital intravenous techniques.



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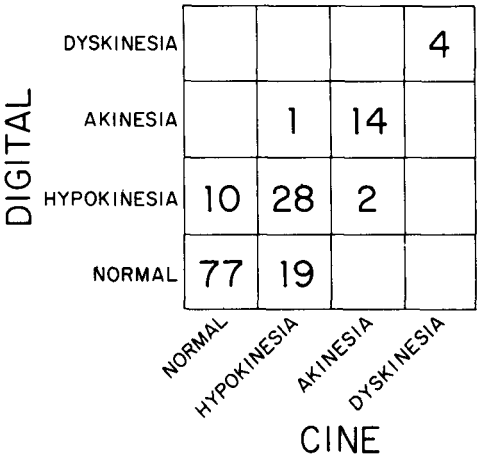


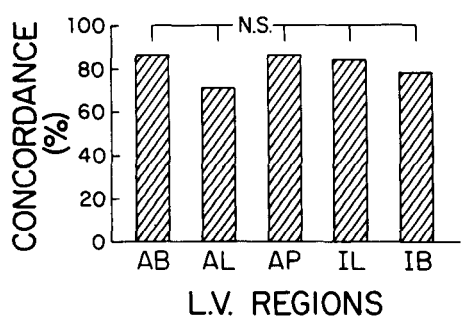
Figure 5. Concordance of left ventricular segmental function as determined by digital intravenous and conventional (CINE) angiography. Precise agreement was seen in 79% of segments.

(Fig. 5). Concordance between techniques was independent of the segment analyzed (Fig. 6).

Discussion

Comparison with previous studies. Our data indicate that left ventricular angiograms obtained during the levophase of an intravenous injection of contrast medium and displayed with the aid of the digital subtraction technique provide volumetric and global and regional functional information comparable with that obtained from conventional intraventricular contrast cineangiography. Our work confirms and extends the preliminary report of Kronenberg et al. (7), who reported similar excellent correlations in 5 patients; of Vas et al. (6), who reported comparative studies in 4 patients and of Tobis et al. (8), who reported on a series of 24 patients. However, Vas et al. also reported a systematic underestimate of left ventricular volume computed from the digital intravenous angiograms. We did not find such a discrepancy, nor can we explain this observation.

Figure 6. Concordance of segmental function, as determined for each of five left ventricular (L.V.) regions. The frequency of precise agreement between the two techniques was independent of the segment analyzed. AB = anterobasal; AL = anterolateral; AP = apical; IB = inferobasal; IL = inferolateral; N.S. = not significant.



Unlike Vas et al. (7), Tobis et al. (8) reported excellent correlations between conventional and intravenous digital techniques for end-systolic volume and ejection fraction. However, the correlation coefficient for end-diastolic volume observed by Tobis et al. was 0.82, somewhat lower than in our study. One possible explanation for the difference in results is that in our study both ventriculograms were performed during a single catheterization, whereas Tobis et al. performed the studies on two consecutive days, permitting the interposition of multiple physiologic alterations including changes in intravascular volume owing to the effects of contrast medium during the initial day of study. Tobis et al. were unable to obtain adequate images in 3 of their 27 patients, all of whom had a low ejection fraction ($\leq$ 27%) and, presumably, a relatively large central blood volume. We encountered no such difficulties in our initial studies, perhaps because we administered the contrast bolus directly into the inferior vena cava and employed a rapid, 1.5 second injection to maintain a tight bolus, while Tobis et al. injected into the femoral vein over a 3 second period. Although the correlation between conventional and intravenous digital approaches was excellent in our study, some individual patients manifested relatively large differences in volumes (up to 36 cc, or 25%) as determined by the two techniques; differences in ejection fraction were relatively smaller (maximal 6%).

Methodologic considerations. One possible source of systematic disagreement between conventional ventriculography and intravenous ventriculography is the different manner in which contrast medium is introduced into the left ventricle. It is unlikely that this technical difference accounts for the variation in our results, however, because in experimental animals, Norris et al. (10) have shown that although both techniques have significant effects on ventricular volume and function, such effects become evident subsequent to the point of maximal ventricular opacification. Similarly, in a study comparing the effects of standard and low contrast load left ventricular angiography, Sasayama et al. (11) showed that the hemodynamic effects of the former technique are not evident until after several cardiac cycles, during which time most information would be obtained. Moreover, variations in results of the magnitude noted in our study are within the range reported by Chaitman et al. (12) for interobserver variability in analysis of a single cineangiogram. Thus, although it is possible that differences in results are attributable to imprecision or systematic errors inherent in the intravenous digital subtraction technique, such inaccuracies are probably of sufficiently small magnitude so as to be lost in the "noise" introduced by interobserver and intraobserver variability.

Assessment of regional left ventricular function. Previous reports have not commented in detail on the accuracy of intravenous digital angiography in detecting abnormalities of regional left ventricular function. Our data

indicate that regional function assessment using the intravenous digital approach compares favorably with that using conventional intraventricular administration and analog information collection. Thus, results of analysis of digital ventriculograms agreed precisely with conventional angiography in 79% of the segments studied; the two techniques never differed by more than one grade. In 29 of the 32 segments over which disagreement existed, the segment in quesion was read as normal by one method and hypokinetic by the other. This degree of discordance in assessment of regional wall motion is comparable with that described by Chaitman et al. (12), when two observers subjectively analyzed the same series of ventriculograms; however, Chaitman et al. did not describe the amount of *intraobserver* variance in subjectively analyzed ventriculograms, the variable most appropriate with regard to our data.

Limitations of the method. Although results obtained in this study indicate clinical utility of the intravenous digital subtraction method, certain limitations and difficulties in acquisition and analysis are inherent in the technique. First, visual assessment of an intravenous, levophase left ventriculogram provides no information regarding mitral regurgitation, though application of digital computer-based methods now employed in radionuclide cineangiography theoretically could mitigate this difficulty (13). Moreover, though we obtained excellent quality angiograms in those patients in our series whose ejection fraction was depressed, very low forward cardiac output or tricuspid regurgitation, or both, could result in fragmentation of the contrast bolus, with resulting poor opacification of the left ventricle during the levophase presumably accounting for the difficulties in three studies encountered by Tobis et al. noted previously. In addition, the background correction requires precise pixel by pixel subtraction of the "mask" from the angiogram; therefore, movement of either the chest or the diaphragm can result in misregistration of pixels, with distortion or obscuration of the ventricular image.

Conclusion. Our studies indicate the feasibility and accuracy of intravenous contrast, computer-based digital subtraction angiography in comparison with conventional intraventricular contrast angiography requiring left heart catheterization. The ease of application of this new technique, which clearly is readily amenable to outpatient use, provides a convenient, high spatial resolution alternative to other ventricular imaging methods.

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