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Measurement of Left Ventricular Ejection Fraction by Videodensitometric Analysis of Digital Subtraction Angiograms

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Left ventricular ejection fraction (LVEF) was calculated from 25 first-pass digital subtraction angiograms using a densitometric analysis. Digital subtraction angiograms are obtained in a computerized format; therefore, they can be readily analyzed with computer software to measure the density of the iodine signal within the image. The video signals from the image intensifier were logarithmically amplified so that there was a linear correlation between the video signal intensity and the depth of

the iodine contrast material represented by that video signal. LVEF was also calculated by the area-length method from the same digital subtraction angiograms. There was close correlation between these two techniques ($r = 0.94$, standard error of the estimate = 5.04%). The videodensitometric EF technique is simple to perform, it correlates well with the standard area-length method, and is not dependent on geometric assumptions of LV geometry. (Am J Cardiol 1983;52:871-875)

An angiogram of the left ventricle represents a 2-dimensional (2-D) projection image of a 3-dimensional object; therefore, mathematical assumptions are needed to derive a quantitative measurement of left ventricular (LV) volume and ejection fraction (EF).¹ Densitometry is an alternative approach to LV volume analysis. This method has been used primarily during radionuclide angiography by counting the density of photons emitted from the volume of technetium-labeled red blood cells within a region of interest drawn around the left ventricle.² Videodensitometry of radiographic images is a technique that may be able to combine the computational simplicity of radionuclide densitometry with the improved resolution capabilities of x-ray imaging devices. Videodensitometry involves analyzing a video (television) scan of a radiographic image and assigning a number to the various densities of soft tissue, bone or iodine at each point in the image.^{3,4}

Recent developments in computer technology have resulted in the ability to convert angiographic images directly into a digital format in real time by using the video signal obtained directly from the x-ray image intensifier.⁵ The computer format allows various methods for computer processing and enhancement of images such as digital subtraction angiography.^{6,7} In the present study, we obtained digital subtraction angio-

grams from 30 patients and analyzed them using a videodensitometric technique. The EF calculated by this videodensitometric method was then compared with the EF derived from standard area-length analysis of the same angiographic images.

Methods

Patients: Thirty patients who were undergoing cardiac catheterization for clinical indications agreed to participate in this study. Adequate first-pass digital angiograms were obtained in 25 of the 30 patients (83%). The average age of the 25 patients was 56 years (range 38 to 77) and the average weight was 74 kg (range 44 to 121). Fourteen were men and 11 women. Twenty patients had coronary artery disease and 5 had chest pain syndrome with normal coronary arteries.

Digital subtraction angiography: First-pass digital angiography was performed after completion of the standard cardiac catheterization. Digital angiograms were acquired with a Cardiac 1000 computer (American-Edwards) using the image processing method of mask mode subtraction.⁸⁻¹⁰ A complete description of our methods for obtaining digital subtraction angiograms has been reported.¹¹ Fluoroscopic images were digitized in real time at 30 frames/s into a $512 \times 512 \times 8$ bit deep matrix. An initial 0.5-second image (16 fluoroscopic frames) of the heart was stored in the computer memory as a mask. After the mask was obtained, iodinated contrast material was injected intravenously. In the present study, 30 ml of iodinated contrast material (Hypaque 75® or Vascoray®) was injected intravenously through a No. 6Fr introducing catheter sheath placed percutaneously into the right femoral vein. Mask mode subtraction was continued during a 15-second fluoroscopic exposure in order to observe the first pass of the contrast agent through both the right- and the left-heart phases. During this time the patients had to continue holding their breath.

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Studies were performed in a catheterization laboratory, which is equipped with a Siemens Cardioskop U-arm x-ray unit. The first-pass left ventriculograms were performed in a 30° right anterior oblique projection. Images were focused on a 7-inch cesium iodide image intensifier and the images were converted into a video signal by a Plumbicon television camera. For this study, the fluoroscopic exposure level was set at 8 mA and 70 to 90 kVp, depending on the size of the subject. The 8-mA setting is 2 to 3 times the tube current typically

used in fluoroscopy. The measured incident exposure rate on the image intensifier was 2 to 17 $\mu\text{R}/\text{frame}$, depending on the kilovolt peak and patient thickness. After mask mode subtraction processing, the images were reconverted to analog format for storage on videotape (Sony Betamax, Model SL0323MD, $\frac{1}{2}$ -inch recorder).

The video signal of the fluoroscopic image was logarithmically amplified before computer digitization because x-rays are attenuated in an exponential or logarithmic manner. By logarithmic amplification of the signal coming from the image intensifier, it is possible to reestablish in an accurate manner a linear proportionality between the amplitude of the video signal and tissue densities or the depth of iodine that the x-ray beam traversed¹² (Fig. 1). After logarithmic amplification, the video signal was digitized so that the amplitude of the signal in each picture element (pixel) of the image was converted into 1 of 256 numbers. Since this signal was logarithmically amplified before digitization, each pixel number represented the x-ray density of the structures within that pixel. By summing the amplitudes of the video signal in all pixels over the area of interest and properly correcting for x-ray densities due to non-iodine-containing structures, a density count could be generated that was proportional to the blood volume in which the iodine was mixed.

Videodensitometry technique: In the first 20 angiograms, studies were redigitized into a 126×126 matrix by an HP-85 computer and stored on a digital magnetic tape. Because of the limitations of storage and the time required for transfer, only every other frame of the videotape study was used. The digitized images were then transferred from the digital magnetic tape into a NOVA-3 computer (Data General). In the last 5 patients, a newer version of the digital postprocessing algorithms was written so that the original Cardiac 1000 computer could also analyze the images videodensitometrically without the necessity for transfer to digital magnetic tape. In these 5 studies, the full 512×512 image matrix was used and every frame was analyzed in real time.

Figure 2 demonstrates how the videodensitometric calculation was performed. An end-diastolic frame was chosen by the operator as the frame with the largest area of iodine in the left ventricle. A region of interest was outlined such that the border of the ventricle was included (approximately 1 cm beyond the visual border of the iodinated area). The aortic and mitral valve planes were used as the medial boundary (Fig. 2A). To subtract any noniodinated signals, the average x-ray density in a background area was also determined by first superimposing the diastolic region of interest outline on the end-systolic image of the left ventricle. Next, a second region of interest was drawn around the systolic boundary of the left ventricle with the aortic and mitral valve planes as the medial boundary. The area from which the background density was computed was chosen as the region between the end-diastolic and end-systolic regions of interest (Fig. 2B). An average background density was determined from the end-systolic frame by summing the x-ray densities from each pixel within the background area of interest and dividing by the number of pixels within the background area. This method of computing average background density was chosen because we believed that the area between the end-diastolic and end-systolic boundaries would correspond most closely to the densities due to x-ray attenuation by structures anterior or posterior to the LV chamber. In addition, some of the iodine passes through the coronary arteries into the LV myocardium during the passage of contrast medium through the heart. The density of this myocardial blush varies from beat to beat. Therefore, a new background density was calculated for each heartbeat.

FIGURE 1. Incident x-rays that penetrate an object such as a step wedge are absorbed or attenuated in an exponential fashion. The image intensifier (II) and television camera (TV) record the densities of the step wedge as an exponentially attenuated video signal. If this video signal is processed by a logarithmic amplifier (log amp), the exponential attenuation can be compensated for so that the contrast densities in the video signal output are linearly related to the depth of contrast material in the step wedge.

FIGURE 2. The technique for determining the area of interest for the background from a first-pass digital subtraction angiogram. **A**, the end-diastolic frame is outlined to include all of the iodine within the left ventricle and the boundaries of the aortic and mitral valve planes are used as the medial boundary. **B**, the end-systolic frame is then chosen and the area around the end-systolic border is outlined. The background region of interest is taken as the area between the end-diastolic and end-systolic regions of interest.

END-DIASTOLE

END-SYSTOLE

Each frame of the first-pass study was then analyzed by measuring the density of the video signal within the diastolic area of interest and generating a density versus time curve (Fig. 3). Maximal and minimal density values for each heartbeat were determined corresponding to end-diastole and end-systole. A density-time curve was also generated for the background area of interest so that beat-to-beat variations in the background could be counted. These density values were used to calculate an EF for each heartbeat using the formula:

$$EF = \frac{(ED - [Bkg \cdot ED \text{ area}]) - (ES - [Bkg \cdot ED \text{ area}])}{(ED - [Bkg \cdot ED \text{ area}])}$$

where ED = end-diastolic or maximal value; ES = end-systolic or minimal value from the density-time curve; Bkg = average value per pixel for the background region of interest; and ED area is the number of pixels in the end-diastolic region of interest. The total density values for the end-systolic or end-diastolic images were counted from the pixels within the original end-diastolic region of interest; therefore, the average background must be subtracted from the entire end-diastolic region (ED area). This formula is simplified to:

$$EF = \frac{ED - ES}{ED - (Bkg \cdot ED \text{ area})}$$

An EF was also calculated using the area-length method of Sandler and Dodge¹³ as modified by Kennedy et al.¹⁴ The image with the largest iodine-filled area was used as the end-diastolic frame and the image with the smallest iodine-filled area was used as the end-systolic frame. The boundary of the iodine-filled area was outlined by the operator using the mitral and aortic valve planes as the medial boundary. X-ray magnification factors were corrected by placing a centimeter-ruled grid on the x-ray table at one-half the patient's anterior-posterior thoracic dimension and filming the grid with the image intensifier and x-ray source at the same position at which the angiographic study was performed.

EF determined by the area-length method was compared with the EF calculated by videodensitometric analysis of the same images. A correlation coefficient was derived by a least-squares linear regression analysis.

Results

Adequate first-pass digital subtraction angiograms were obtained in 25 patients. Angiographic studies were

performed in 5 other patients but were inadequate to clearly delineate the LV boundary because of misregistration artifact or low concentration of contrast. These 5 patients were excluded from the study. The results of the calculated EF by the area-length and videodensitometric techniques are shown in Figure 4. The correlation coefficient between the 2 techniques was 0.94 and the calculated EF were related by the equation: Videodensitometric EF = (1.04 · area-length EF) - 2.95. The standard error of the estimate was 5.04.

Discussion

The area-length method has been the most widely used technique for calculating LV volumes and EF from

FIGURE 3. A density-time curve is generated by the computer after the first-pass left ventriculogram is replayed and superimposed on the end-diastolic and background regions of interest. The maxima and minima points for the curve are automatically determined by the computer and these densities are used to calculate ejection fraction as described in the text. The background density values during each end-systolic frame are used to derive the average background density for the determination of ejection fraction from each heart beat.

FIGURE 4. Correlation of ejection fraction determined by the area-length method compared with ejection fraction determined by videodensitometry. SEE = standard error of the estimate.

cineangiograms.¹⁵ In most cases it yields reliable results that correlate closely with measured volumes of heart casts. As a result, it has become the standard against which other methods are compared. However, all methods of measuring LV volume and EF are based on assumptions that, under certain circumstances, may not be accurate.¹⁶ For example, the area-length method assumes an ellipsoid geometric shape for the LV cavity. This may be a good approximation for normal ventricles. However, diseased hearts usually dilate and become more spherical.¹⁷ In addition, cineangiograms are 2-dimensional images that tend to obscure volume-occupying structures in the LV cavity, such as muscular trabeculations, papillary muscles and the mitral valve leaflets. Also, frequently the LV silhouette is significantly foreshortened (especially in the left anterior oblique projection), which causes inaccuracies in the dimensional measurements used in the equations for an elliptical volume.^{18,19}

Densitometry is an alternative method of calculating LVEF that does not depend on assumptions of ventricular geometry. This method has been used to calculate EF from radionuclide angiograms by measuring the density of photons from the labeled cardiac blood pool and assuming this density to be proportional to the volume of blood within the cardiac chamber of interest.²⁰⁻²³ Until now, densitometry could not be easily applied to iodine contrast angiograms because the images were recorded on standard cineangiographic film, which may display the iodine signal in the saturated portion of the film-exposure curve to increase visibility of the ventricular boundary. When the gray scale of a black and white radiograph is saturated to a maximal white level, the density information of the contrast signal is lost.

Digital subtraction angiography circumvents this problem by preserving numerical information about the x-ray density in various regions of the images while still allowing the black-white levels in the image to be adjusted during playback. In addition, the digital subtraction images can be used for videodensitometry because the electronic signal is logarithmically amplified before digitization.²⁴ This permits the video x-ray signal to be linearly proportional to the x-ray density of the material in the path traversed by the x-ray beam. A major advantage of using digital subtraction images for videodensitometry is that much of the background densities due to x-ray attenuation from overlying structures such as ribs, lung tissue and soft tissues are subtracted from the image during image acquisitions. The density value remaining in each pixel corresponds linearly to the depth of the iodine contrast material within the blood volume of the area of interest. By adding the iodine signal in all the pixels of the area of interest, such as the left ventricle, a number is derived that is proportional to the volume of blood in the ventricle. Although the concentration of iodine in the left ventricle must be known accurately to derive absolute ventricular volume, EF is a relative number, and therefore, it is only necessary to know the relative volume of the LV at end-diastole and end-systole to calculate EF.

However, the average background density over the region of interest must be known in order to calculate relative ventricular volume. The method used in this study to obtain the background density takes advantage of the good spatial resolution in digital angiograms and is different from the method usually used in calculating EF from radionuclide angiograms. In this method, the area between the boundaries of the LV silhouette at end-diastole and end-systole was used as the background area, the average density within this region was computed and this average value was taken as the background density. This background area was used because we believed it would most closely represent the noniodinated video signal from soft tissues and bones that lay anterior or posterior to the ventricular chamber. In the end-systolic image, this region also includes densities corresponding to the LV muscle. As contrast medium passes through the heart, some iodine will enter the coronary arteries and the average background density may increase because of iodine within the ventricular myocardium. The region of interest that we used to obtain the background takes into account this variability that results from myocardial perfusion during the first pass of iodine through the heart.

As with any method of calculating EF, there are several potential problems with videodensitometry. The major problem is that good-quality angiograms are essential for analysis. Several factors can produce poor-quality digital subtraction angiograms, including misregistration caused by patient motion between the time the initial mask is taken and subsequent fluoroscopic images are recorded and very low concentrations of iodine in the left ventricle, as may occur in patients who have a low cardiac output. Despite these potential dif-

difficulties, 25 of 30 patients (83%) had first-pass digital angiograms that were adequate for evaluation. Most of the angiograms in this study were performed with a prototype digital image processing computer. More recent experience with an improved version of the computer indicates that adequate first-pass angiograms can be obtained in >90% of our patients. In addition, the more recent software programs allow the videodensitometric analysis to be performed by the image processing computer as the videotape of the first-pass study is replayed in real time. This allows the computer to measure the density in each pixel of the 512 X 512 matrix at 30 frames/s and generate a density-time curve. The computer then automatically chooses the maximums and minimums from the curve, subtracts the background densities, and calculates an EF for each beat. This automation of the videodensitometry calculations significantly reduces the time required for measuring EF.

Another potential problem with the videodensitometric method relates to physical factors that could prevent x-ray attenuation by iodine from being linearly proportional to the depth of iodine contrast material traversed by the x-ray beam. These physical factors include beam hardening, beam scatter and veiling glare. Our initial studies of these factors indicate that they cause an underestimation of EF by, at most, 15%.²⁵ Another possible source of error in the videodensitometric technique is nonlinearities in the imaging chain. This problem should be less significant for large areas of interest over the image intensifier, as are used to calculate LVEF.

Counterbalancing these potential problems are several advantages of videodensitometric analysis of digital subtraction angiograms that make this method attractive for routine clinical use. First, digital subtraction angiography permits the computational and theoretical simplicity of radionuclide angiography to be used to measure EF from high-resolution iodine contrast angiograms. Second, the densitometric technique may prove more accurate than methods based on geometric assumptions, especially when the left ventricle is dilated or irregularly shaped. Another advantage of videodensitometry is that once the initial region of interest is outlined, several beats can be evaluated to yield a beat-to-beat measurement of EF that is useful during an irregular rhythm, such as atrial fibrillation or premature ventricular contractions. Finally, the videodensitometric method does not require the skill and experience that is necessary to accurately outline the LV silhouette when using the area-length method. In addition, the same densitometric analysis can be applied to the right or left anterior oblique projection without altering the formula, because no geometric assumptions are made.

Although further clinical experience is necessary, videodensitometric analysis of digital subtraction angiograms may find widespread clinical use because it combines the computational simplicity of radionuclide angiography with the high resolution of radiographic imaging.

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