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Intravenous Digital Subtraction Angiography in the Assessment of Patients With Left to Right Shunts Before and After Surgical Correction

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Pre- and postoperative structural changes and pulmonary to systemic flow (QP/QS) ratios were assessed using digital angiography in 34 patients documented to have a left to right shunt at cardiac catheterization. There were 16 men and 18 women whose ages ranged from 4 months to 60 years. The radiographic single mask mode was used for all digital subtraction angiographic studies with a typical radiographic sequence being 80 to 100 kV, 5 to 10 mA/frame at six frames/s for 15 seconds. Renografin-76 was used as a bolus injection at 0.5 to 1.0 ml/kg via an arm vein in most patients. The level of the left to right shunt and any associated anomalies were noted and compared with results from cardiac catheterization. Digital subtraction angiographic flow curves were generated from the pulmonary arteries, and QP/QS ratios were calculated pre- and postoperatively using the gamma variate fit method and compared with the QP/QS ratio from first pass radionuclide studies.

A strong correlation between preoperative digital subtraction angiographically derived QP/QS ratio and radionuclide-derived QP/QS ratio was found, with an r value equal to 0.89, $p < 0.0001$. Postoperatively, all patients had a QP/QS ratio less than 1.2:1.0 for both digital subtraction angiography and radionuclide studies. The level of left to right shunt was accurately assessed in all patients, and its absence observed postoperatively. Associated anomalies, such as a persistent left superior vena cava, coarctation of the aorta and partial anomalous venous return, were identified in all cases.

Intravenous digital subtraction angiography provides accurate quantitative and anatomic data in patients with a left to right shunt, is potentially an important outpatient method to assess adequate surgical correction and may suffice preoperatively to proceed to cardiac surgery without preoperative cardiac catheterization.

Quantification of left to right shunts using technetium-99m first pass studies has become a useful adjunct in the assessment of patients with a left to right shunt, both before and after surgical correction (1–3). Delineation, however, of the level of the shunt and definition of associated anatomic abnormalities has been very difficult using these methods because of their inherent poor spatial resolution. With the development of digital subtraction angiography, the subtraction of unnecessary background information provides an enhanced spatial resolution allowing identification of structures with low concentrations of intravenously injected iodine. At the same time, the ability to postprocess images and extract numbers from the images theoretically allows not only a structural analysis, but also a quantitative analysis of the cardiovascular system. Our system can readily discern a 1 ml vessel with 1% contrast medium. The resolution visualized by the television system is 2.3 line pair/ml in the 6 inch (15.24 cm) mode.

Considering the superior spatial resolution of digital subtraction angiography, it was the aim of this study to use digital subtraction angiography in patients with a left to right shunt before and after surgical correction to assess the presence and level of left to right shunting and any associated structural abnormalities and determine whether digitally generated flow curves reflect the presence and degree of shunting and its absence postoperatively. The results from the digital subtraction angiographic studies were compared with the data generated from technetium-99m first pass radionuclide studies and conventional cardiac catheterization.

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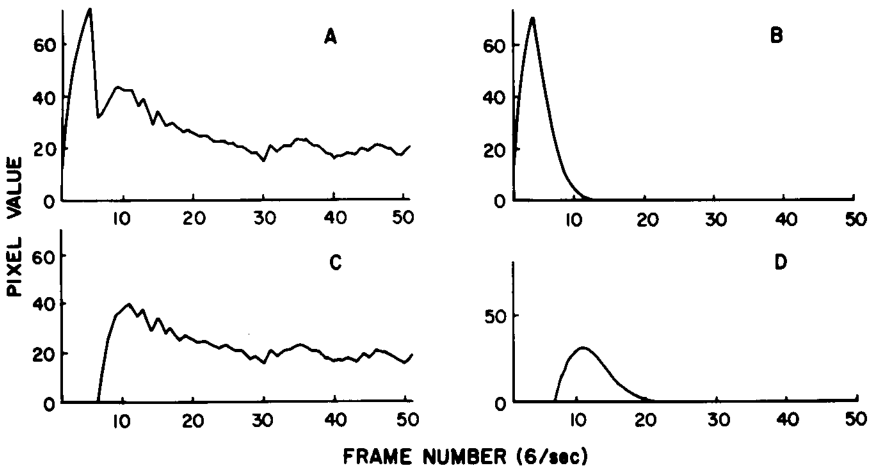


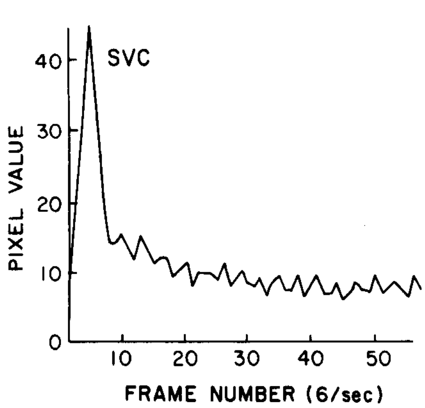
Figure 1. **A,** A typical left to right shunt curve generated over the pulmonary artery in a patient with an atrial septal defect. **B,** The result of a gamma variate fit to the primary curve. The area under this curve is proportional to the pulmonary flow (QP). This is then subtracted from the curve in **A** and a new curve generated in **C,** representing both systemic and shunt recirculation. This curve is fit to a gamma variate and a new curve generated in **D.** The area in **B** minus the area in **D** is proportional to the systemic flow (QS). Hence, B/(B − D) is proportional to the QP/QS ratio.

Methods

Study patients. The group studied comprised 34 consecutive patients documented to have a left to right shunt at cardiac catheterization. The defects studied were atrial septal defect in 20, ventricular septal defect in 9 and atrioventricular canal in 1. Associated anomalies present were partial anomalous pulmonary venous return in two patients, and total anomalous pulmonary venous return, coarctation of the aorta and a left superior vena cava draining into the coronary sinus, each in one patient. Sixteen of the patients were male and 18 female, with a mean age of 24.5 years (range 4 months to 60 years). Four of the patients were younger than 1 year of age and three patients were between 1 and 5 years of age. Ten of these patients (seven with an atrial septal defect and three with a ventricular septal defect) who proceeded to surgical correction also had postoperative digital subtraction angiography and radionuclide studies.

Equipment and imaging techniques. All digital subtraction angiographic studies were performed using a commercially available unit (DR960 DSA unit, Technicare Corporation) described previously (4). The radiographic single mask mode was used; typical radiographic sequences being 80 to 100 kV, 5 to 10 mA per frame (2 to 10 ms at 1,000 mA) with six frames/s for 15 seconds. The best mask available was then used for immediate postprocessing to provide optimal images for each study. The image matrix size used for all studies was 256 × 256 × 8 bits. Images were stored on a digital disk for immediate viewing and reprocessing, and on a digital tape for permanent storage.

Figure 2. A typical pixel value-time curve over the superior vena cava (SVC) showing a sharp rapid input bolus.



All measurements of radiation dose were obtained at a tabletop level underneath the attenuator (patient) so that all readings were recorded as entrance doses to the patient. The radiation exposure on a 12 second digital subtraction angiographic unfiltered study was 1,650 milliroentgens (mr) and with a 12 second filter study was 1,300 mr. This compares with a 12 second cine run at 60 frames/s (single plane) of 2,720 mr and a 12 second cine run at 30 frames/s (single plane) at 1,907 mr.

Ninety-five percent of the patients had a 17 to 20 gauge catheter (Intracath) introduced into an arm vein and 5% into the external jugular vein or superior vena cava. Most patients did not require medication before the study, but to avoid artifacts due to motion, the younger patients were sedated with meperidine, promethazine and chlorpromazine orally. Renografin-76 was used as a bolus injection at 0.5 to 1 ml/kg with a single dose ranging from 10 to 30 ml. A dextrose flush of 10 to 20 ml was used with each injection to ensure a rapid bolus. Two to four injections were administered to obtain standard cardiac views.

Assessment of left to right shunts. In the same manner as standard contrast angiography, a visual assessment was made to ascertain the presence of left to right shunting by following the sequence of clearance of contrast medium from the right-sided chambers into the right atrium, right ventricle or pulmonary artery. At the same time, chamber size and contractility and the presence of any associated anomalies were noted. An assessment of the absence of

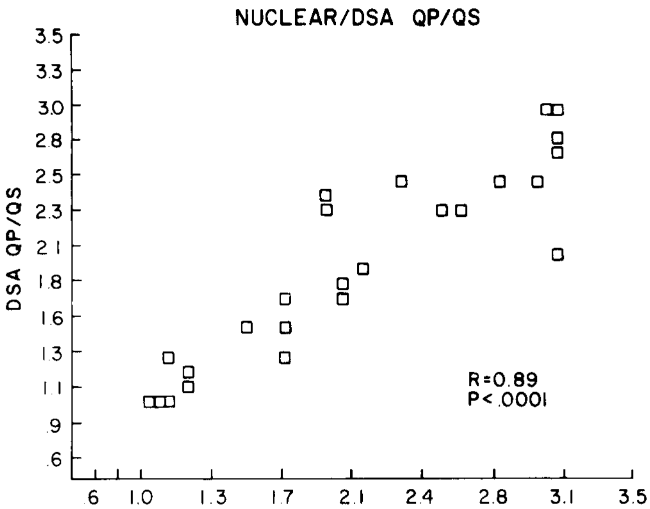


Figure 3. Correlation between radionuclide first pass-generated QP/QS ratio and digital subtraction angiographically (DSA) generated QP/QS ratio.

abnormal left to right recirculation and anatomic correction of preoperative anomalies was made postoperatively.

Left to right shunts were quantified by two observers blinded to the patients' history, by calculating the pulmonary to systemic flow (QP/QS) ratio from densitometric flow curves generated over the pulmonary artery. The pulmonary artery was chosen as the region to generate flow curves because more adequate mixing of contrast medium would be achieved. The optimal view of the pulmonary artery was chosen so that there were no overlapping cardiac structures in the field of interest. Furthermore, generating curves over the atria or in the ventricles was subject to wide variation, depending on the size of the region of interest and the portion of the chamber chosen. Changes in pixel value were plotted against time from regions over the main pulmonary artery. The region of interest chosen used only portions of the main pulmonary artery that were not overlapped by other cardiac structures. The pixel values generated in this region of interest represent the degree of attenuation of transmitted X-rays and were presumed to correlate with the amount of iodine in the region and, hence, flow. Correction for background was performed by generating a region of interest over a noninvolved area and subtracting this from the pixels within the region of interest. Corrections for scatter and veiling glare were not made during this study.

A typical pulmonary flow curve generated in the manner just described in a patient with an atrial septal defect is seen in Figure 1. From this curve, a pulmonary to systemic flow ratio was calculated by the method established by Askenazi et al. (2). From the primary curve, a gamma variate fit was applied (Fig. 1A). The derived curve (Fig. 1B) is then subtracted from the original curve and a new curve generated, representing both systemic and shunt recirculation (Fig. 1C). The new curve is fit to a gamma variate and a new curve is generated (Fig. 1). The area under the first curve (Fig. 1B) is proportional to the pulmonary blood flow (QP) and the area under the second curve (Fig. 1D) is proportional to the shunted flow. The difference between these two areas is then proportional to the systemic flow (QS). The ratio QP/QS is then derived from these calculations. To exclude the possibility of a fragmented or prolonged bolus, the adequacy of the injection of contrast medium was assessed by generating regions of interest over the superior vena cava. An example of an adequate bolus is seen in Figure 2.

Radionuclide technique. Technetium-99m radionuclide first pass studies were performed on all patients, both pre- and postoperatively. Pulmonary to systemic flow ratios were calculated by analyzing the lung dilution curves in a similar manner to that described for the digital subtraction angiographically generated curves. The details of the method used in our department have been reported previously (4). The results of the QP/QS ratio generated from digital subtraction

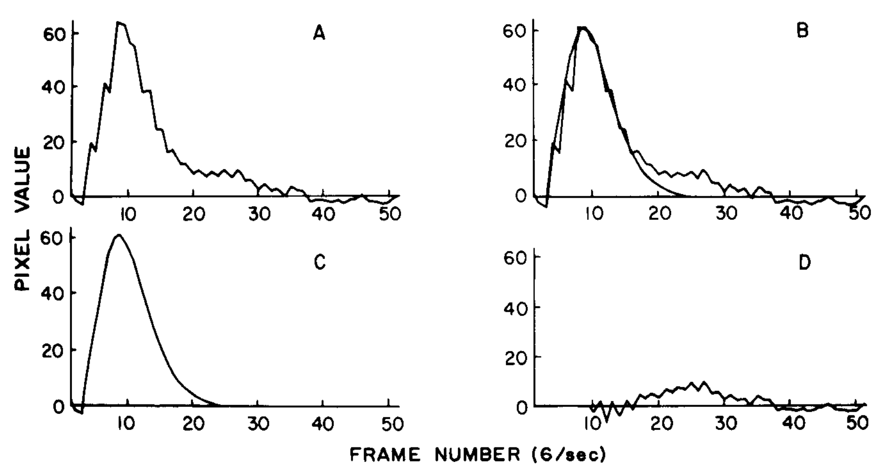


Figure 4. The pulmonary artery curve in the patient shown in Figure 1 after surgical repair of the atrial septal defect. Note that the area in **D,** representing shunted plus systemic recirculation, is trivial. The QP/QS ratio was calculated as 1.1:1.

angiography and radionuclide studies were then correlated using the Pearson product/moment correlation. The level of the left to right shunting and the presence of any associated anomalies were then correlated with the findings from cardiac catheterization.

Results

Calculation of QP/QS ratio. Five patients from the radionuclide studies and four from the digital subtraction angiographic studies were excluded from calculations of QP/QS ratio (although included in the structural analysis) because of a fragmented and very prolonged bolus as judged by the input curves generated over the superior vena cava. The four patients with an unsatisfactory study ranged in age from 26 to 55 years. Three of the patients had an atrial septal defect and one had a ventricular septal defect with pulmonary hypertension and a right to left shunt.

In 25 patients in whom successful studies were performed, a significant correlation was found when comparing radionuclide with digital subtraction angiographic QP/QS ratio, correlation coefficient (r) = 0.89, probability (p) < 0.0001 (Fig. 3). In all 10 patients studied postoperatively, the QP/QS ratio calculated was less than 1.2:1.0 for both radionuclide and digital subtraction angiographic studies (Fig. 4).

Structural analysis. Visual inspection of early recirculation of contrast medium accurately localized the level of shunting in all but three patients (Fig. 5A and B, 6A, B and C). These three patients (two with ventricular septal defects, one with patent ductus arteriosus) had a small shunt with a QP/QS ratio calculated from both radionuclide and digital subtraction angiographic studies to be less than 1.2:1.0. Postoperatively, in all 10 patients studied, the absence of recirculation of contrast medium was noted, having been significantly abnormal preoperatively. At cardiac catheterization, two patients had partial anomalous pulmonary venous return, one patient had total anomalous pulmonary venous return, one had coarctation of the aorta and one had a left-sided superior vena cava draining into the coronary sinus. All these associated anomalies were identified preoperatively by digital subtraction angiography, except in one patient with partial anomalous pulmonary venous return (Fig. 7A and B, 8 and 9). Postoperatively, their surgical correction was clearly delineated by digital subtraction angiography.

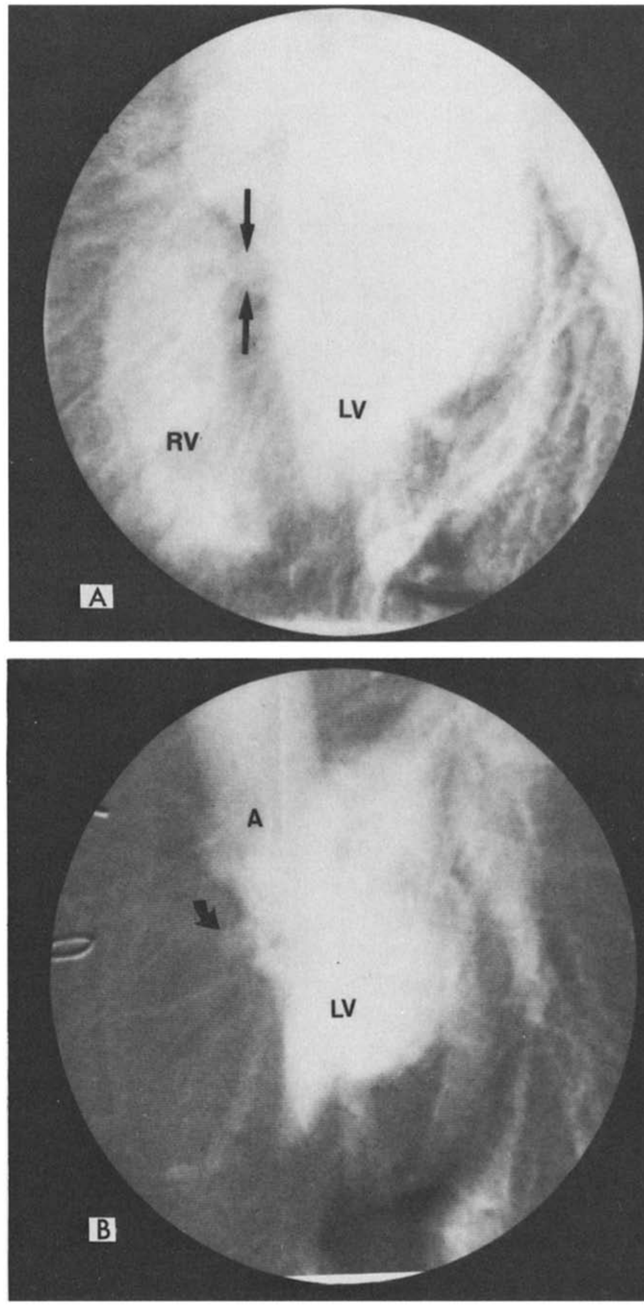
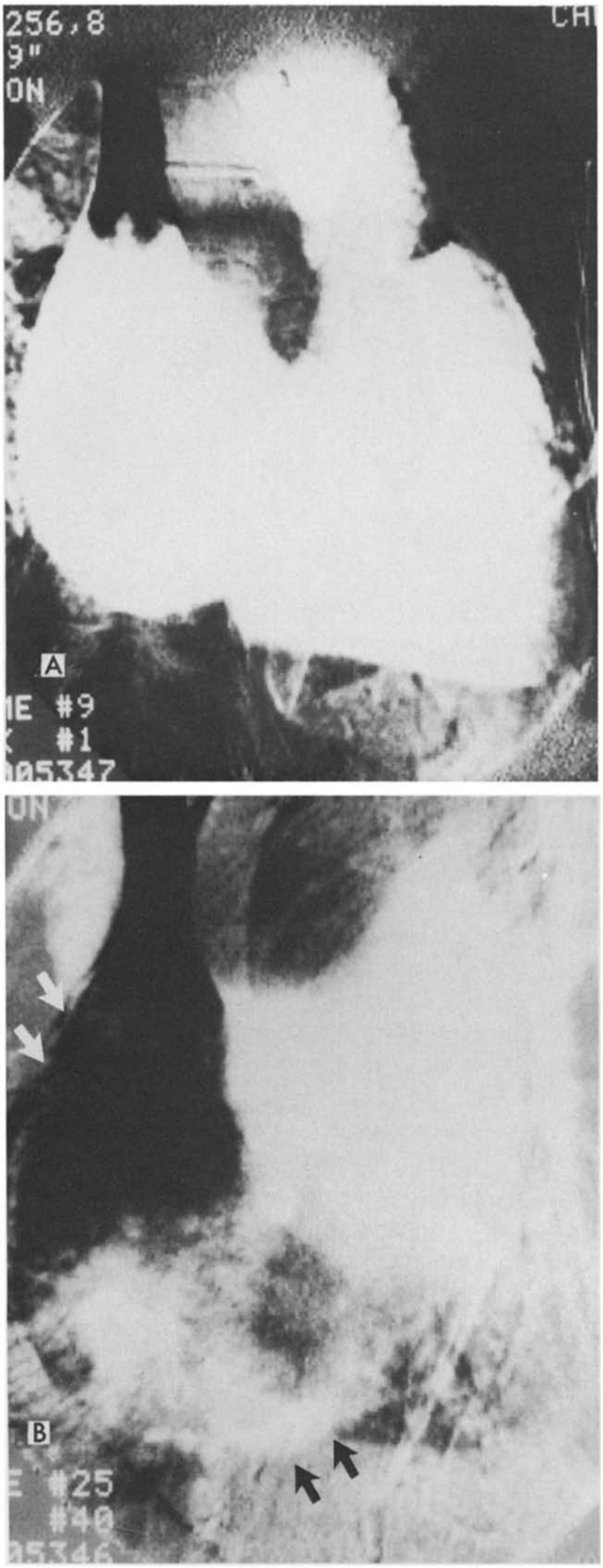


Figure 5. Ventricular septal defect. **A,** Digital subtraction angiogram, left anterior oblique view, craniocaudal angulation. **Black arrows** point to a small, high-lying membraneous ventricular septal defect. **B,** Postoperative film. **Small black arrow** points to a small ventricular septal aneurysm in the region of the previously described high-lying ventricular septal defect. A = ascending aorta; LV = left ventricle; RV = right ventricle.

Discussion

Comparison of digital subtraction angiography with the radionuclide method. Although radionuclide first pass assessment of the magnitude of left to right shunting was found a practical role in the management of patients with a left to right shunt, it is limited because it does not provide concomitant accurate structural information in these patients. In early experience described in this study, we found that use of curves similar to radionuclide curves generated digitally from the pulmonary artery permitted accurate quantification of the degree of left to right shunting in a manner



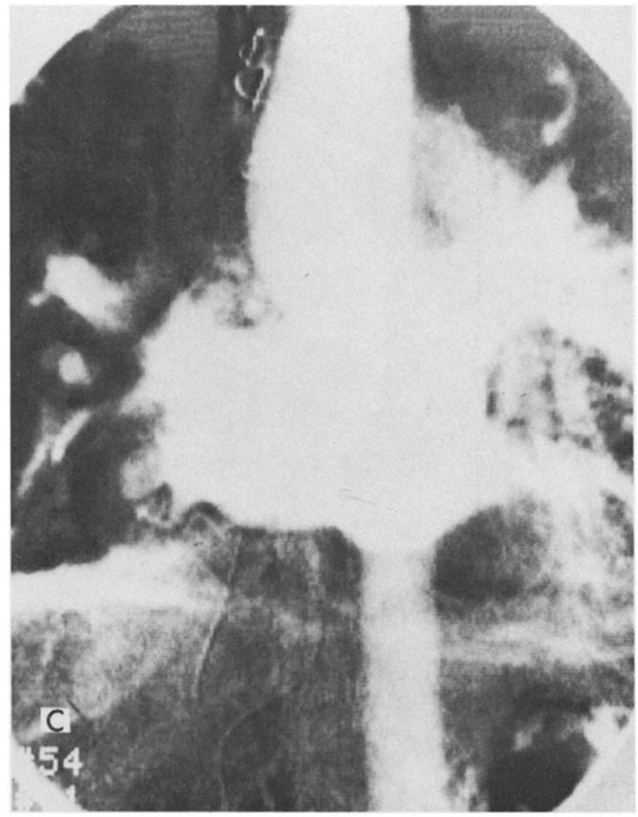


Figure 6. Digital subtraction angiogram in a 66 year old patient with an atrial septal defect. **A,** Anteroposterior projection demonstrating a dilated right atrium, right ventricle, right ventricular outflow tract and proximal pulmonary artery. **B,** Levophase demonstrating a large left to right shunt from the left atrium to the right atrium. White dye can be seen **(arrows)** in the previously subtracted black region of the right atrium **(white arrows). C,** Postoperative film. Levophase demonstrating normal pulmonary venous return into the left atrium with an intact atrial septum after patch closure of the atrial defect.

similar to that of the radionuclide studies. Although our method was not fully automated, the correlation between the digital subtraction angiographically-generated QP/QS ratio and the radionuclide QP/QS ratio was highly significant, both being similar methods of curve analysis. There has been much discussion as to the accuracy of digital numbers generated from a digital subtraction angiographic fluoroscopic unit in reflecting physiologic events (5,6). The effect of veiling glare and scatter clearly may play a role in reducing the accuracy of digital numbers in reflecting the amount of iodine and, hence, blood flow in a region of interest. Although correction for these factors has been suggested recently (6), we did not apply this at the time the patients were studied. However, in contrast to situations comparing curves from different areas of the image (as in attempts to assess myocardial perfusion [7] where the effect of scatter and veiling glare are different for each part of the image), in our case the error should be relatively constant because the changes in density were assessed over a fixed area of interest, the pulmonary artery. Furthermore, absolute values for flow were not sought, but simply the ratios of areas under the pulmonary artery curve.

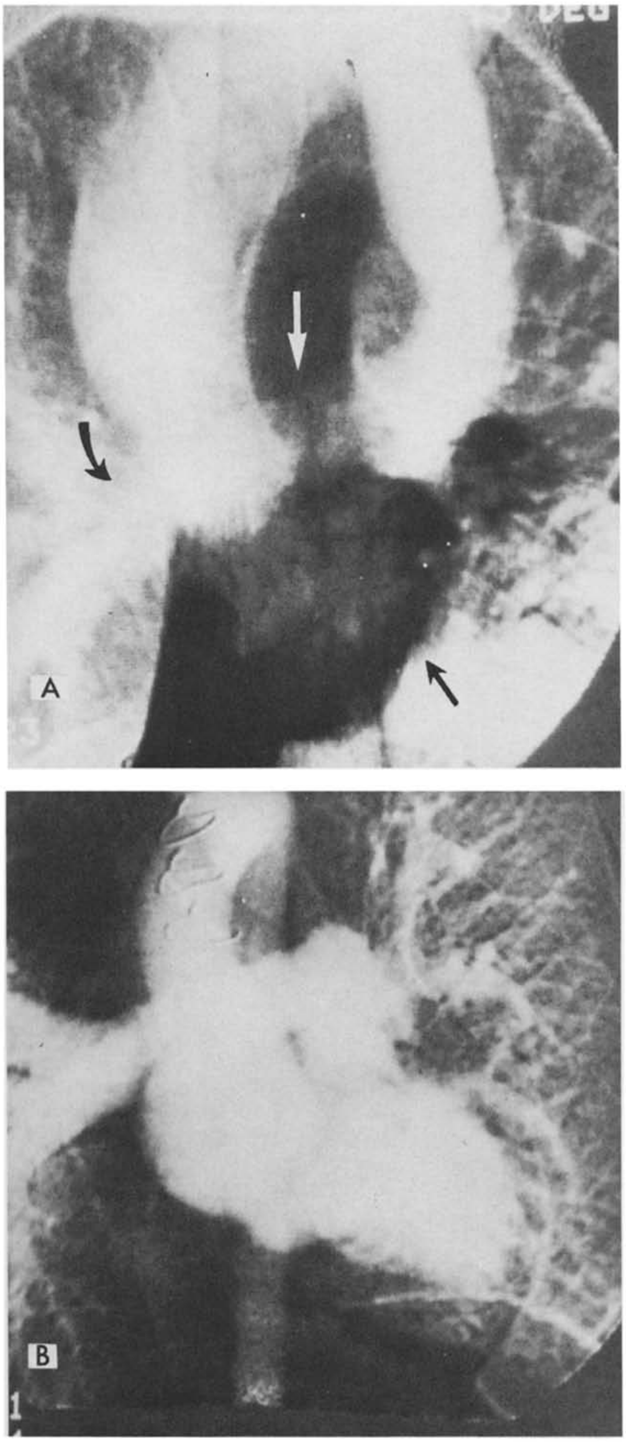


Figure 7. Digital subtraction angiogram in a 17 year old patient with total anomalous pulmonary venous return above the diaphragm. **A,** Anteroposterior projection. The **straight black arrow** points to the subtracted left atrium. The **curved black arrow** points to a confluence of right pulmonary veins draining into an abnormal horizontal vein **(white arrow)**, which is clearly not related to the left atrium. The anomalous vertical vein draining to the dilated superior vena cava is also well visualized. **B,** Postoperative film after correction of the total anomalous venous return with now normal appearing pulmonary venous drainage to the left atrium. The previously noted vertical vein has thrombosed.

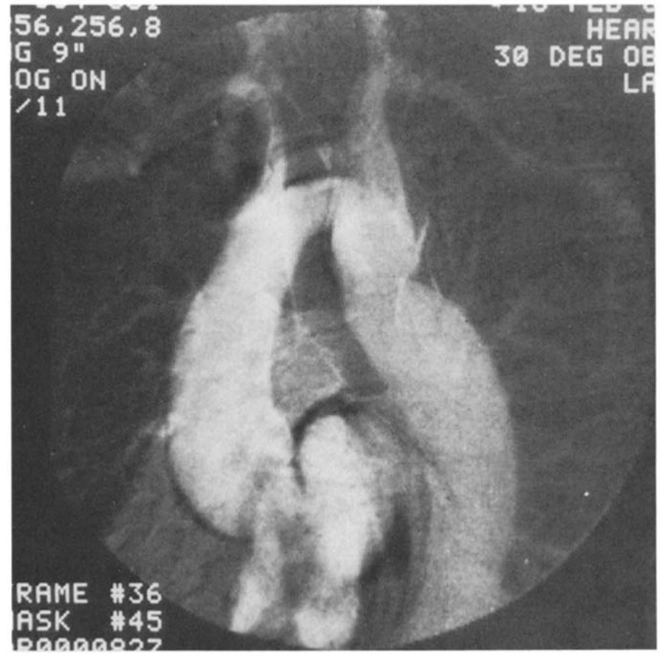


Figure 8. Intravenous digital subtraction angiogram demonstrating coarctation of the aorta in its usual position, just distal to the left subclavian artery. There is some post-stenotic dilation of the upper descending aorta.

Regardless of these theoretical considerations, the curves generated over the pulmonary artery in our patients had configurations typical of a left to right shunt curve (Fig. 10A and B); the correlation between the QP/QS ratio calculated in this manner and that from the radionuclide studies was significant, and the dramatic return of the curves to the expected normal pattern after the surgical correction strongly suggested that the curves reflected the recirculation of flow in our patients.

Accuracy and advantages of digital subtraction angiography. Because of its inherent superior spatial resolution, digital subtraction angiography also provides accurate information about the level of left to right shunting and the presence of any associated anomalies, and provides an opportunity to assess chamber size and contractility. Visual inspection of the sequence of appearance and reappearance of contrast medium in our patients accurately assessed the level of left to right shunting in all but three of our patients and its absence in all patients postoperatively. The majority of our patients studied had a large left to right shunt, often requiring surgical correction. In the cases of very small shunts, the ability of digital subtraction angiography to detect the left to right shunting by either visual inspection or the pulmonary artery-generated curves is probably not very sensitive, as evidenced by three of our cases where a small left to right shunt was missed.

With respect to ventricular septal defects, digital sub-

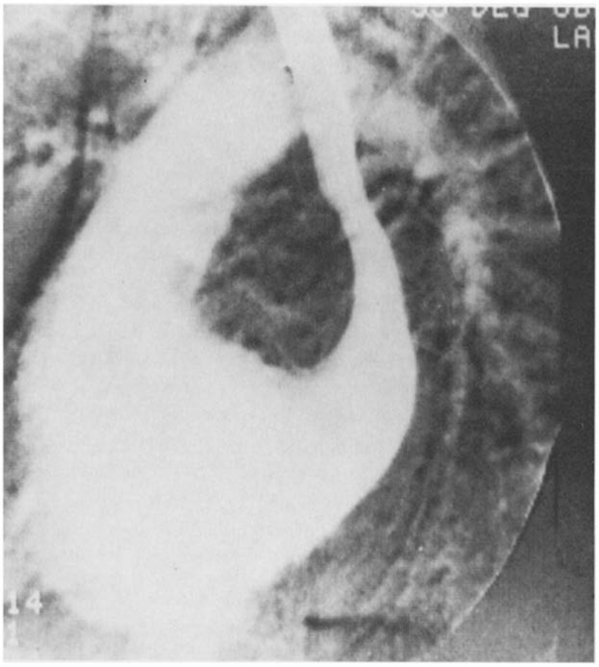


Figure 9. Intravenous digital subtraction angiogram with an injection into the left antecubital vein demonstrating a persistent left superior vena cava draining to a dilated coronary sinus.

traction angiography allows one to distinguish a muscular from a membranous defect, but only further experience can determine if this can be done in every patient. However, the method may not provide sufficient detail to separate a subpulmonary from a membranous defect.

Perhaps the most important advantage that digital subtraction angiography can provide in this group of patients is the ability to delineate structural abnormalities with a spatial resolution that is similar to that obtained from standard cardiac catheterization. The associated anomalies observed in our patients by digital subtraction angiographic studies were identical to those found at cardiac catheterization, excluding one instance of partial anomalous pulmonary venous return seen at cardiac catheterization, which was not obvious with digital subtraction angiography. In fact, this patient was one of the early patients studied when our experience in the application of digital subtraction angiography in congenital heart disease was limited. Furthermore, digital subtraction angiography provided an ideal relatively noninvasive outpatient method to assess the adequacy of surgical correction of not only the defect involved in each patient, but also the associated anomalies.

Although left and right ventricular function was not analyzed systematically in our patients, the ability of digital subtraction angiography to generate images of the right and left ventricle with a spatial resolution similar to that of conventional angiography provides an ideal opportunity to study their function both before and after surgical correction. The accuracy of digital subtraction angiography to assess ventricular function has already been established by others (8,9). The equipment used for our studies could not generate high frame rates necessary for accurate assessment of ventricular function, and gating was not available to us at that stage.

Conclusion. Digital subtraction angiography is a new, safe, relatively noninvasive method involving only peripheral injections of contrast medium. It is ideally suited to the outpatient setting and provides important quantitative and anatomic data in patients with a left to right shunt. At the same time, it is a potentially important outpatient method to assess the adequacy of surgical correction and follow up

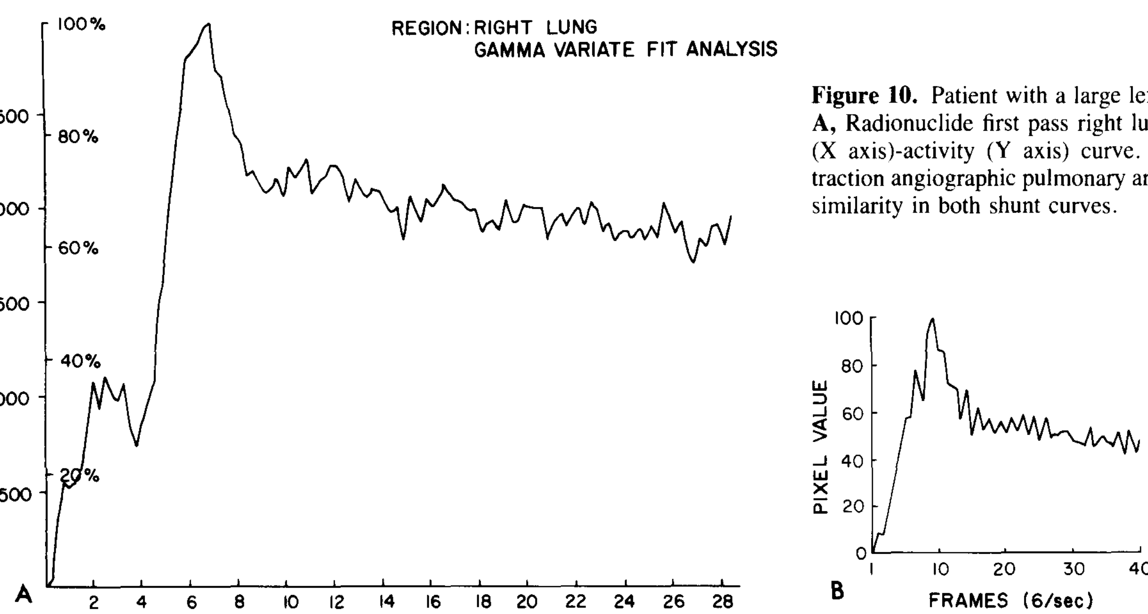


Figure 10. Patient with a large left to right shunt. **A,** Radionuclide first pass right lung dilution time (X axis)-activity (Y axis) curve. **B,** Digital subtraction angiographic pulmonary artery curve. Note similarity in both shunt curves.

patients after repair of a defect producing left to right shunting. Furthermore, in select patients, a combination of clinical, structural and functional information gained from digital subtraction angiography may suffice to proceed to cardiac surgery without cardiac catheterization.

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References

1. Hurwitz RA, Treves S, Keane JF, Girod DA, Caldwell RL. Current value of radionuclide angiocardiography for shunt quantification and management in patients with secundum atrial septal defect. Am Heart J 1982;103:421-5.
2. Askenazi JS, Ahnberg DS, Korngold E, Lafarge CG, Maltz DL, Treves S. Quantitative radionuclide angiocardiography: detection and quantitation of left-to-right shunts. Am J Cardiol 1976;37:382-7.
3. Houser TS, MacIntyre WJ, Cook SA, et al. Recirculation subtraction for analysis of left-to-right cardiac shunts—concise communication. J Nucl Med 1981;22:1033-8.
4. MacIntyre WJ, Pavlicek W, Gallagher JH, Meaney TF, Buonocore E, Weinstein MA. Imaging capability of an experimental digital subtraction angiography unit. Radiology 1981;139:307-13.
5. Shore CG, Ergon DL, Van Lysel MS, et al. Quantitation techniques in digital subtraction video angiography. In: Proceedings of the Society of Photo-optical Instrumentation Engineers, April 20-22, 1980. Washington, DC: Society of Photo-optical Instrumentation Engineers, 1981;314:121-9.
6. Shore CG, Chamberlain C, Bassano DA, Randall PA. Effects of radiation scatter and veiling glare on image quality in digital radiography using image intensified fluoroscopy. In: Proceedings of Radiological Society of North America, November 28-December 3, 1982. Chicago: Radiological Society of North America, 1982:160.
7. Tobis J, Nalcioglu O, Boone J, Roeck WW, Henry WL. Video densitometric assessment of myocardial perfusion using digital subtraction angiography (abstr). Circulation 1982;66(suppl II):II-230.
8. Tobis J, Nalcioglu O, Johnston WD, et al. Left ventricular imaging with digital subtraction angiography using intravenous contrast injection and fluoroscopic exposure levels. Am Heart J 1982;104:20-35.
9. Goldberg HL, Borer JS, Moses JW, Fisher J, Cohen B, Skelly NT. Digital subtraction intravenous left ventricular angiography: comparison with conventional intraventricular angiography. J Am Coll Cardiol 1983;1:858-62.