The Complementary Roles of M-mode Echocardiography and Scintigraphy in the Evaluation of Adults with Suspected Left-to-Right Shunts

Additional Observations on the Role of Two-dimensional Echocardiography

Elias H. Botvinick, M.D., and Nelson B. Schiller, M.D.

SUMMARY We sought to determine the relative clinical abilities and roles of echocardiography and scintigraphy in left-to-right shunt diagnosis. M-mode echocardiographic and scintigraphic studies were analyzed in 37 adults presenting diagnostic difficulties with suspected left-to-right shunts. The historic, physical, radiographic and electrocardiographic data were frequently ambiguous. An enlarged right ventricle on M-mode echocardiography was a sensitive (100%) but not specific (55%) indicator of atrial septal defect (ASD). M-mode lacked sensitivity for ventricular septal defect (VSD) and patent ductus arteriosus (PDA). In a few studies, two-dimensional echocardiography provided additional specific and clinically important anatomic information. Scintigraphic analysis demonstrated complete diagnostic accuracy and excellent localizing and quantitative abilities in all patients studied.

Because it is extremely sensitive to ASD, free of any exposure to radioactivity, entirely noninvasive and may be simply and visually analyzed, echocardiography is the study of choice in the preliminary evaluation of patients presenting diagnostic difficulty with suspected ASD. Scintigraphy is the study of choice in the preliminary evaluation of patients presenting diagnostic difficulty with suspected VSD and PDA and is the logical response to the finding of echocardiographic right ventricular enlargement when the diagnosis remains in doubt.

LEFT-TO-RIGHT SHUNTS in adults can generally be diagnosed from the history and physical exam, but diagnosis may be difficult.1 History, physical findings and radiographic and electrocardiographic examinations may often be suggestive but not diagnostic of such intracardiac shunting and may be especially ambiguous in the case of suspected atrial septal defect (ASD).2 The new, noninvasive cardiac diagnostic methods of echocardiography3 and scintigraphy4 provide the clinician with techniques that supply further objective evidence for or against this diagnosis. We sought to determine the place of these noninvasive tests in the evaluation of adults with possible intracardiac left-to-right shunts and to compare the relative clinical value of M-mode and two-dimensional (2D) echocardiography and scintigraphy.

Methods

We studied 37 adult patients who were clinically suspected of having an intracardiac left-to-right shunt. All patients presented some degree of diagnostic difficulty. In 30 patients, shunt diagnosis was suspected but was not secure after history, physical examination, chest x-ray and ECG. In the remaining seven patients, diagnosis was unclear and the possibility of shunt was suspected only after M-mode echocardiographic study. Each patient underwent M-mode echocardiography using one of several commercially available systems. When a Varian 2D phased-array sector scanner became available, the last 10 patients studied underwent 2D echocardiography in the standard parasternal, apical, subxiphoid and suprasternal views.5 Full assessment of echocardiographic studies was made, including measurement of wall chamber dimensions, wall motion and thickness. In all 2D studies, agitated saline was forcefully injected through a 22-gauge scalp vein needle into an upper extremity vein, the opacification of cardiac chambers was assessed and negative contrast effect6 was sought in an attempt to evaluate the presence, location and direction of shunting. Intracardiac left-to-right shunts were sought in each patient by evaluation of the first-pass radioangiogram performed in the anterior projection after the intravenous injection of 15-20 mCi of technetium-99m (Tc-99m) DTPA as a bolus.

All radionuclide injections were made through a small, 22-gauge scalp vein needle placed in an external
jugular vein in order to guarantee arrival of the radionuclide as a bolus in the central circulation. All images were performed on a Pho Gamma IV 37 phototube scintillation camera (Searle Corporation) using a high-energy, all-purpose, linear collimator at the 140-keV Tc-99m photopake using a 20% window. Sequential dynamic images of the central circulation, right lung and portions of the left lung field were obtained at half-second intervals for 1 minute using a PDP 1140 minicomputer (Digital Equipment Corporation).

Echocardiographic and scintigraphic studies were performed in all cases to resolve a diagnostic problem. Cardiac catheterization was also performed in 27 patients. Where noninvasive image evaluation supported the shunt diagnosis and clinical and quantitative assessment indicated a moderate-to-large shunt, catheterization was performed not to diagnose, but rather to seek associated lesions and accurate quantitation and localization of the shunt before surgical repair. Where no evidence of shunt was found, diagnostic catheterization was performed if otherwise clinically indicated. Patients with mild or no symptoms and small or absent shunts did not undergo catheterization.

Echocardiography and scintigraphy were performed within a 24-hour period, 1 day to 18 weeks before invasive study. Independent observers who had no knowledge of other findings evaluated the respective studies for the presence of intracardiac left-to-right shunt according to established objective criteria.

No M-mode echocardiographic sign was of itself considered diagnostic of left-to-right shunt. However, the echocardiogram was considered suggestive of left-to-right intracardiac shunt if it revealed evidence of right ventricular volume overload with right ventricular dilatation and a right ventricular end-diastolic dimension ≥ 25 mm in the minor axis in the supine position, with or without paradoxical septal motion. The size, anatomic integrity and orientation of all chambers and valves were also evaluated. A significant ASD would be expected to produce echocardiographic evidence of right-sided volume overload with right ventricular dilatation and possibly paradoxical septal motion. A small-to-moderate ventricular septal defect (VSD) may demonstrate no abnormality or only moderate left ventricular dilatation, with obvious dilatation only in the setting of large, advanced shunts. A patent ductus arteriosus (PDA) may also present no echocardiographic abnormality or may present with mild left atrial and left ventricular dilatation. A negative contrast effect demonstrated on 2D echocardiography indicated a left-to-right shunt at the level of visualization. The echocardiographic appearance of bubbles in a left-sided chamber after an i.v. injection of agitated saline indicated an element of right-to-left shunting proximal to or at the level of the chamber of appearance, consistent with the diagnosis of associated left-to-right shunt at this same level.

The scintigraphic diagnosis of intracardiac left-to-right shunt was suspected with the finding of incomplete or absent pulmonary clearance of the radionuclide in serial frames of the flow study and by the inability to identify a clear scintigraphic levophase. The diagnosis of an intracardiac left-to-right shunt was confirmed scintigraphically by computer analysis of the first-pass time vs radioactivity curve over a right pulmonary region of interest. Early tracer recirculation was documented and pulmonic-to-systemic flow (Qp/Qs) ratio was calculated using the gamma variate method for quantitative analysis of the pulmonary first-pass curve as generally performed.

Time vs radioactivity curves were similarly analyzed over other designated regions of the central circulation in order to localize the site of left-to-right shunt. The presence of a shoulder on the downslope of such curves provided evidence of early recirculation and was diagnostic of a left-to-right shunt at or proximal to the region of analysis. Evidence of such recirculation in the right atrial region served as an indicator of shunting at or proximal to the atrial level. In adults this would be most likely related to an ASD. A normal right atrial curve with evidence of recirculation in the right ventricular region would indicate shunting at the ventricular level, most likely related to a VSD. Evidence of recirculation only in the pulmonary curve would indicate a left-to-right shunt distal to the ventricles, most likely related to a PDA. Such regional scintigraphic shunt analysis was performed in 14 patients where such localization was requested for clinical reasons. A time vs radioactivity curve generated from the superior vena cava region of interest allowed assessment of the quality of the bolus injection in each case. An artifact in this bolus curve could give false-positive results.

Results

Among the 37 patients suspected of having a left-to-right intracardiac shunt, 26 patients had suspected ASD, eight had suspected VSD and three had suspected PDA. In those believed to have ASD, the historical, physical and basic laboratory evidence for shunt diagnosis was varied and nonspecific. While their history, presenting complaint, and basic laboratory data varied, all patients with suspected VSD or PDA presented with strongly suggestive auscultatory findings. Electrocardiographic patterns in each diagnostic subgroup were extremely heterogeneous.

Similarly, the chest x-ray was often ambiguous. The spectrum of radiographic presentation was broad and demonstrated the difficulty in relying on this single clinical measurement for objective evidence of left-to-right shunting.

Twenty patients among the 26 with suspected ASD underwent cardiac catheterization. Each of these 20 catheterized patients had echocardiographic evidence suggestive of left-to-right shunt. Shunt and ASD were confirmed in only 15 patients, including all seven patients initially suspected of having ASD on M-mode study. Scintigrams were abnormal and revealed shunts
in all 15 patients with proved ASD (fig. 1). Catheterization revealed no evidence of shunts in five other patients suspected of having ASD (fig. 2). Six other patients with clinical findings suggestive of ASD had negative scintigraphic and echocardiographic studies. Only two of these underwent catheterization when there was no evidence of shunt. Later in this study, 10 patients were evaluated by 2D echocardiography. An ASD was suspected and a consistent abnormal M-mode study was seen in nine of these patients. Each of these nine patients had evidence of right ventricular volume overload, two with a prominent pulmonary artery, two with anatomic evidence of a primum ASD (fig. 3), one with a visible secundum
defect, and one with Ebstein’s anomaly (fig. 4). Saline contrast study revealed evidence of right-to-left shunt in four of these 10 patients and failed to identify a right-to-left shunt in three patients with proved ASD. One contrast study in a patient with proved ASD demonstrated a negative contrast effect (fig. 3C). Saline contrast studies were negative in two other patients, one with Ebstein’s anomaly and one with a PDA.

Six of the eight patients clinically suspected of having a VSD showed scintigraphic evidence of such a shunt although they had a normal echocardiogram. Four of these patients were not further evaluated because they had few symptoms, and the noninvasive evaluation indicated a relatively small shunt, confirmed by the quantitative scintigraphic evaluation. Two patients had VSD confirmed at catheterization. Each of three patients with clinically suspected PDA had catheterization confirmation of this diagnosis and scintigraphic evidence of left-to-right shunt. The echocardiographic examination was normal in each of these patients. A 2D echocardiogram performed in one patient with PDA was entirely normal.

Figure 5 shows the results of echocardiographic, scintigraphic and invasive evaluation in all 37 patients who had suspected intracardiac left-to-right shunt, according to the nature of the suspected abnormality. Twenty patients presented with a clinical diagnosis of left-to-right shunt in the presence of echocardiographic signs of right ventricular volume overload. Only 15 of these had such a shunt, in each case an ASD. M-mode echocardiography was a sensitive (100%) but nonspecific (55%) indicator of ASD. Twenty-four patients had scintigraphic evidence of left-to-right shunt. Catheterization performed in 20 patients was confirmatory. Only 15 of these 24 patients (62%) also had an abnormal echocardiogram. Among 14 patients with clinically suspected left-to-right shunts and negative echocardiograms, nine with VSD or PDA showed catheterization and/or scintigraphic documentation of shunt. Among five patients presenting with an abnormal echocardiogram without scintigraphic or catheterization evidence of left-to-right shunt, three had pulmonary hypertension, two primary in origin and the other related to severe pulmonary disease, one patient had mitral valve disease and another had Ebstein’s anomaly.

The shunt was correctly localized in 12 of 14 patients with scintigraphic evidence of shunt. Among these 14, eight had ASD, four had VSD and two had PDA (fig. 6). In two patients with a diagnosis of VSD in whom scintigraphic shunt localization was attempted, there was no evidence of an interventricular communication but good right ventricular clearance in the presence of pulmonary recirculation. This flow pattern is more typical of PDA and may have been related to shunt streaming directly across a high VSD and through the right ventricular outflow tract to the pulmonary artery without significant right ventricular mixing.

Scintigraphic shunt quantification and the Qp/Qs ratio correlated well with catheterization findings ($r = 0.87$). The mean difference in Qp/Qs calculated by scintigraphy and catheterization was 0.3. There was no consistent evidence of left-sided chamber enlargement or hypertrophy in any clinical subgroup.
Discussion

While the history and physical examination may be extremely suggestive of an intracardiac left-to-right shunt in adults, the diagnosis may be difficult. To determine the value of echocardiography and scintigraphy in cases where the history and physical examination are nondiagnostic for left-to-right shunt, patients were evaluated who demonstrated symptoms, signs and basic laboratory data that were nonspecific for this diagnosis. The chest x-ray and ECG lacked sensitivity and specificity and often presented ambiguous and nondiagnostic findings, at least in part because of the selected population of diagnostically difficult cases.

Echocardiography was abnormal in all patients with ASD, consistent with previous reports. Echocardiography lacked specificity despite its high sensitivity. False-positive echocardiograms occurred in five of 20 (25%) patients in this series with ASD suspected before catheterization. The echocardiogram also lacked sensitivity for shunt diagnosis in adults with conditions such as VSD or PDA. Although Qp/Qs ratios in these patients were lower than in those with ASD, several of the former had moderate shunts. The diagnostic capabilities of M-mode and often of 2D echocardiography in the setting of left-to-right shunt depend on the indirect assessment of the pathophysiologic effects of shunting, as seen by evidence of chamber enlargement and other...
indications of right-sided volume overload. Conditions such as pulmonary hypertension, associated tricuspid regurgitation or Ebstein's anomaly can present M-mode echocardiographic pictures similar to those for ASD.\(^9\) In one patient (fig. 4), the clinical impression of ASD was so strong that electrocardiographic and M-mode echocardiographic findings suggesting Ebstein's anomaly were overlooked. Although our echocardiographic criteria for left-to-right shunting were fulfilled, a critical analysis of this study showing a large right ventricle, a large tricuspid diastolic excursion with decreased tricuspid diastolic slope and the intermittent appearance of delayed tricuspid closure would certainly have suggested the true diagnosis. However, the actual tricuspid closure point was difficult to establish and varied from place to place, likely a function of leaflet redundancy. Many of the other findings in the M-mode study were consistent with a large left-to-right shunt through an ASD. This M-mode echocardiogram was reviewed and interpreted differently after performance of a negative scintigram, and the subsequent performance of a diagnostic two-dimensional echocardiogram. Although this single study may have been differently interpreted by others, it was included here among that group with M-mode echocardiographic studies falsely positive for left-to-right shunt. This study provides an example of the ambiguities and difficulties inherent in the method, even in experienced hands. Although echocardiographic misdiagnosis in this single case may in part be an error of interpretation rather than a true lack of echocardiographic specificity, the case demonstrates another aspect of the vulnerability of the method compared with scintigraphy. However, in this case and in three others with visualized atrial shunts, two-dimensional echocardiogram provided a definitive anatomic diagnosis. With large VSD or PDA, left-sided volume overload with left-sided chamber enlargement and possibly hypertrophy might be expected.\(^10\) This was not seen in any of our patients and would likely be present only in the setting of extremely large or far-advanced shunting that was not present in these adult patients. In this study, the absence of echocardiographic evidence of left ventricular or right ventricular enlargement was consistent with a small-to-moderate VSD.

While M-mode echocardiography lacked diagnostic accuracy and provided no sound basis for shunt localization, 2D echocardiography has a firmer anatomic basis and could often accurately delineate the anatomy with localization of the site of atrial defect (fig. 3) or other pertinent pathology (fig. 4).\(^11\) As generally noted,\(^5,6\) subtle evidence of echo dropout in the mid-atrial septum was an unreliable indicator of ASD on 2D echocardiography. However, a prominent absence of septal echoes, especially in the lower region of the septum, proved to be a specific 2D echocardiographic marker for ASD of the primum variety.\(^5\) Two-dimensional echocardiography often lacked specificity with the finding of simple right-sided chamber enlargement. However, 2D saline contrast studies supported ASD diagnosis in several cases. Our findings support those of two recent studies\(^12,13\) that suggest improved diagnostic accuracy for left-to-right shunt diagnosis from right-sided echocardiographic contrast studies. M-mode and most 2D echocardiographic findings here identified as consistent with left-to-right shunt diagnosis are often not specific for that condition. Except possibly for a negative contrast effect on 2D study, there are no echocardiographic signs of left-to-right shunt, but only signs of right ventricular volume overload, right ventricular dilation or other anatomic or physiologic evidence that is frequently related to the presence of such a shunt. Nonetheless, these findings are consistent with the shunt diagnosis and can be important in establishing the diagnosis and directing the course of further diagnostic or therapeutic steps. While scintigraphy provides more specific evidence of left-to-right shunt, it is nonetheless appropriate to compare these techniques with the less specific findings of echocardiography, because both methods frequently aid the diagnosis of the difficult case with suspected shunt. Although only 10 patients in this study underwent 2D echocardiography, the observations made are valid and serve as the basis for future clinical evaluation of the method.

Scintigraphy appeared both sensitive to and specific for shunt diagnosis. Scintigraphic computer analysis could frequently localize the site of intracardiac shunt.\(^14,15\) In this study the scintigraphic diagnosis of intracardiac left-to-right shunts was again found sensitive to a level of 1.2:1 Qp/Qs ratio.\(^14\) Scintigraphic shunt quantitation correlated extremely well with catheterization values despite the frequent temporal separation of these studies. Shunt localization using analysis of time vs radioactivity curves over selected regions of interest is best performed in a left anterior oblique projection where ventricular cavities are separated.\(^14,15\) However, we were quite successful in localizing the site of shunt using the anterior projection alone. The anterior projection is most useful for visualizing large regions of the lung fields, which can be analyzed for diagnostic time vs radioactivity data without danger of sampling such data over the central circulation.

Scintigraphic diagnosis of left-to-right shunt agreed with catheterization in all 27 cases studied. Scintigraphic accuracy was likely one significant reason why 10 patients did not undergo catheterization evaluation. Further reliance on such noninvasive data in ambiguous clinical cases will probably lead to having fewer patients undergo diagnostic catheterization for suspected left-to-right shunt. Since scintigraphy and catheterization agreed so completely in patients evaluated by both measurements, the diagnostic sensitivity and specificity of echocardiographic study was judged on the basis of a combined scintigraphic-catheterization standard. A significant bias was introduced into this study because we dealt only with adult patients.

VSD and PDA generally were related to small-to-moderate Qp/Qs ratios. Chamber dimensions obtained by both M-mode and 2D echocardiography
Figure 4. False-positive echocardiogram. (A) M-mode echocardiogram in a patient believed to have an atrial septal defect (ASD). There was echocardiographic evidence of right ventricular dilatation (upper panel) with an opening tricuspid valve (TV) excursion (arrow points, lower panel), significantly greater than that of the mitral valve and a somewhat slowed diastolic TV closure rate. The apparent delay in TV closure seen here was minor and only present in some projections. Catheterization performed to document the ASD was negative, and subsequent scintigraphic study again showed no evidence of left-to-right shunt (B). Review of the history, physical and laboratory data, only then suggested the possibility of Ebstein's anomaly of the TV, which could cause the entire spectrum of findings in the absence of a shunt. Two-dimensional echocardiography documented the malposition of the tricuspid leaflet (C, black arrows) and the hemodynamic abnormality of Ebstein's anomaly was confirmed at a second catheterization study. RVW = right ventricular wall; RVC = right ventricular cavity; IVS = interventricular septum; LVC = left ventricular cavity; RAC = right atrial cavity; SVC = superior vena cava; RV = right ventricle; RA = right atrium; LV = left ventricle; LA = left atrium; mitral valve.
were normal, and echocardiography was of limited value for identifying such patients. While generally reliable in this group, in our population, physical signs were not classic, provided no diagnostic assurance and finally proved inaccurate for VSD diagnosis. However, in larger VSD or PDA, left ventricular or left atrial enlargement could supply useful indirect echocardiographic information regarding the size of the shunt. Patients with VSD and PDA present obvious differences clinically, anatomically and echocardiographically from ASD. However, these conditions are not always obvious, also require diagnostic assessment and can benefit from noninvasive evaluation. Since patients with suspected VSD or PDA, as well as those with suspected ASD are often sent for echocardiographic assessment, we evaluated difficult clinical cases in each of these diagnostic categories. In our patients, the echocardiogram was obviously of less value among patients with suspected VSD or PDA than among those with suspected ASD.

Scintigraphic technique is important. A bolus injection of the radionuclide is critical to the successful analysis of the study. We and others have found that as many as one-third of injections made via the basilic vein fail to arrive in the central circulation as a bolus. Injections made into a hand or wrist vein will likely have a higher failure rate. For this reason we use the external jugular vein for all studies and evaluate the bolus on our computer display (fig. 1). This site is generally easily accessible, may be less painful, promotes hemostasis, achieves a successful bolus injection and is surprisingly acceptable to the patient. A good bolus injection is mandatory because a poor injection could produce false-positive scintigrams. This injection need not be made directly into the central circulation. The scintigraphic method does not then require long lines and catheterization techniques, but merely an i.v. injection of the imaging agent, so it may be categorized, as may contrast echocardiography, as noninvasive.

The patients we studied consisted of a group suspected from physical findings and laboratory tests of having a left-to-right shunt. In no case was the diagnosis secure before noninvasive imaging was conducted. This patient population may have brought some bias to our study, reducing the apparent diagnostic accuracy and increasing the apparent ambiguity of the physical examination, chest x-ray and ECG. In cases in which the diagnosis is obvious from all measurements, the physical examination and basic laboratory studies may be sufficient to make the diagnosis. This was not a consecutive series. Occasional patients with clinically obvious shunts were evaluated and catheterized without full noninvasive imaging analysis. However, the patients do represent the majority of adults with suspected left-to-right shunts evaluated at our center during the investigation. They demonstrate the frequent ambiguity of
physical findings and basic laboratory assessment even in the hands of trained internists and cardiologists who evaluated these patients. The results of the study, then, support the value of noninvasive imaging evaluation for shunt diagnosis, especially in the patient presenting with some diagnostic difficulty. Of course, the quantitative value of scintigraphy may be of clinical use in all patients with left-to-right shunts.

It is certainly true that many patients with left-to-right shunts can be diagnosed with great security after historical, physical, radiographic and electrocardiographic assessment. However, often these basic data present some degree of diagnostic ambiguity that should be clarified, if possible, by further noninvasive assessment before considering invasive study. On the basis of the evidence presented here, we have formulated a rational, integrated, noninvasive approach to the diagnosis of left-to-right shunt in cases presenting diagnostic problems after historical, physical and basic laboratory evaluation. This approach uses echocardiography and scintigraphy in a complimentary fashion. Although scintigraphy was more accurate than echocardiography for left-to-right shunt diagnosis, the study requires radiation exposure, the placement of an i.v. needle, and computer analysis. Echocardiography requires none of these procedures and is extremely sensitive for ASD diagnosis; M-mode echocardiography is a simple, useful tool for shunt screening in patients with suspected ASD and is the noninvasive study of choice in the preliminary evaluation of patients presenting diagnostic difficulties with suspected ASD. Patients symptomatic with suspected ASD and negative M-mode echocardiograms probably do not have an ASD and need not be further evaluated for shunt in most cases. A normal echocardiogram is to be expected in the presence of a suspected left-to-right shunt due to a small-to-moderate VSD or PDA, so scintigraphy is the study of choice in the preliminary evaluation of patients presenting diagnostic difficulties with suspected VSD or PDA. Of course, complete clinical reliance should never be placed on a single test. Cases of ASD associated with negative echocardiographic studies may rarely occur, probably related to a small pulmonary flow.

Two-dimensional and contrast echocardiography appear to add specificity to shunt diagnosis and have value for localizing shunts. From this preliminary evidence, 2D echocardiography seems to add to our knowledge of the congenital anatomy but will probably not upset the synergistic relationship of echocardiographic and scintigraphic methods. Although the 2D technique appears promising, its value for shunt diagnosis and for further screening of suspected ASD and other lesions should be studied in a larger patient series.

The scintigraphic method demonstrated complete accuracy for left-to-right shunt diagnosis in the adult population studied here. Scintigraphy also localized and quantitated these shunts noninvasively. However, it involves a finite exposure to radioactivity and a somewhat complex method that may not be clinically available, so it should be used selectively in patients presenting diagnostic difficulty with suspected ASD.
and suggestive echocardiogram or in difficult cases with suspected shunts in the presence of VSD or PDA. Since none of these noninvasive methods reliably measure pulmonary vascular resistance, we cannot advocate dispensing with hemodynamic catheterization evaluation preoperatively in patients with larger shunts. However, catheterization studies may be avoided in many patients with noninvasive findings of small or absent left-to-right shunt.

References
The complementary roles of M-mode echocardiography and scintigraphy in the evaluation of adults with suspected left-to-right shunts. Additional observations on the role of two-dimensional echocardiography.

E H Botvinick and N B Schiller