Selection for Surgery of Patients with Ventricular Septal Defect and Pulmonary Hypertension

By James W. Dushane, M.D., and John W. Kirklin, M.D.

Estimation of pulmonary blood flow relative to systemic blood flow is a critical point in selecting patients with ventricular septal defect and severe pulmonary hypertension for operation. A detailed medical history, physical examination, thoracic roentgenograms, careful interpretation of electrocardiograms, cardiac catheterization, and biopsy of the lung provide approaches to the problem. In borderline cases, decision still may be extremely difficult. The authors usually favor operation, however, with recognition that this decision may be in error. Obviously proper evaluation for operation cannot assure uniformly good results. Method of conduct of operation, perfusion, and post-operative care determine the results.

Considerable difference of opinion apparently exists concerning the important matter of selecting for operation patients who have intracardiac or extracardiac shunts and pulmonary hypertension. These differences are prominent with regard to patients with ventricular septal defect and severe pulmonary hypertension. Lillehei,1, 2 for example, has expressed the view that it is desirable to operate on nearly all patients with ventricular septal defect and pulmonary hypertension, and has implied that no patient within this group should be considered inoperable. This is in contrast to our own experience. It seemed warranted, as an introduction to a subsequent paper3 on open-heart surgery, to present the methods that we have employed for evaluation of patients with ventricular septal defect.

Basic Premises

In patients with forms of congenital heart disease allowing shunting between the systemic and pulmonary circulations, severe pulmonary hypertension may exist in the presence of relatively normal pulmonary vascular resistance because of a pulmonary blood flow that is abnormally high in relation to the systemic blood flow. Or, pulmonary hypertension may exist in the presence of a normal or reduced pulmonary blood flow because of excessively high pulmonary vascular resistance. Variations between these two extremes occur.

It is presumed that any immediate reduction in pulmonary artery pressure after closure of a patent ductus arteriosus, atrial septal defect, or ventricular septal defect occurs as a result of reduction in pulmonary blood flow produced by the repair and possibly also as a result of reduction in pulmonary venous pressure. In some patients a reduction in pulmonary vascular resistance appears to occur in the weeks and months after operation and to contribute still further to a reduction in pulmonary artery pressure. It is believed that only when operation results in a reduction of pulmonary blood flow or pulmonary venous pressure is there an opportunity for such a later reduction in pulmonary vascular resistance.

In patients with ventricular septal defect, a reduction in pulmonary blood flow after operation can result only if pulmonary flow was greater than systemic flow prior to repair, that is, in patients in whom the shunt was predominantly left to right. If a shunt across a ventricular septal defect were bidirectional and truly equal in the two directions, repair of the defect should not result in change in pulmonary blood flow relative to systemic blood flow. On the basis of the available evidence, it is believed that under such circumstances neither an immediate nor a late reduction in pulmonary artery pressure would...
result. Although further elevation of pulmonary vascular resistance might be prevented by operation, improvement of the general status of the patient is not certain. For example, his ability to increase systemic blood flow during exercise, albeit by an increased right-to-left shunt while the defect is open, may be abolished or reduced by repair.

When pulmonary blood flow is less than systemic blood flow, the shunt being predominantly right to left, ablation of the shunt will result, not in a reduction of pulmonary flow relative to systemic flow, but in an increase. Since the greatly elevated pulmonary vascular resistance does not fall under these circumstances, pulmonary artery pressure must rise after repair unless total cardiac output falls. Either result is probably detrimental to the patient, and operation should be avoided. When the shunt is bidirectional and of equal magnitude in the two directions, surgical intervention is believed to be of questionable value, since reduction in pulmonary artery pressure cannot be expected to occur.

When pulmonary blood flow is greater than systemic blood flow in the presence of severe pulmonary artery hypertension, pulmonary artery pressure will be lowered by operation and the patient will be improved or returned to normal health. Operation is, in this situation, clearly indicated.

Emphasis on levels of pulmonary artery pressure in management of patients with ventricular septal defect can be misleading. To quote the extremes, it has been the experience at the Mayo Clinic that patients who have ventricular septal defect with essentially equal aortic and pulmonary artery pressure can be cured by operation at a low risk if pulmonary blood flow is large in relation to systemic blood flow. Equal aortic and pulmonary artery pressures also may occur in patients at present considered inoperable, that is, not amenable to improvement by operation, if pulmonary blood flow is small with a predominantly right-to-left shunt. The first group is characterized by pulmonary vascular resistance less than systemic vascular resistance, the latter by pulmonary vascular resistance greater than systemic resistance.

Methods of Estimating Pulmonary Blood Flow in Patients with Ventricular Septal Defect and Pulmonary Hypertension

It is our belief that the estimation of pulmonary blood flow relative to systemic blood flow with its implications as to pulmonary and systemic resistances becomes a critical point in the selection for operation of patients with ventricular septal defect and severe pulmonary hypertension. This problem can be approached from several aspects.

History

A detailed medical history may provide important leads concerning pulmonary blood flow. In patients with ventricular septal defect, a history of persistent cyanosis usually is obtained when systemic arterial oxygen saturation is 85 per cent or less. Cyanosis that exists when the patient is at rest is highly suggestive of a predominantly right-to-left shunt and, thus, of inoperability. Patients without a history of cyanosis usually have predominantly left-to-right shunts, although some have bidirectional shunts that are predominantly right to left but of a magnitude insufficient to produce cyanosis.

A history of repeated respiratory symptoms, often frankly associated with cardiac failure, is strongly suggestive of a continuing, large left-to-right shunt in patients with ventricular septal defect and pulmonary hypertension. At operation, such patients usually have high left atrial pressure that is restored promptly to normal by closure of the defect. High left atrial pressure and a history of continuing respiratory distress are not found in patients with ventricular septal defect and pulmonary hypertension whose shunts have become predominantly right to left. Patients with a history of pulmonary congestion and growth failure in early life, who later become asymptomatic and healthy in appearance, often exhibit this misleading apparent improvement because of marked increase in pulmonary vascular resistance and consequent reduction of the left-to-right shunt.
VENTRICULAR SEPTAL DEFECT

Roentgenogram of thorax of a 6-year-old patient with ventricular septal defect and severe pulmonary hypertension. Note that the lung fields are hyperemic and that there is general cardiac enlargement. Preoperative cardiac catheterization showed femoral artery pressure of 122/67 and pulmonary artery pressure of 109/74. A large left-to-right shunt was demonstrated. The ventricular septal defect was repaired. Fifteen months later, cardiac catheterization showed pulmonary artery pressure of 33/14 and no intracardiac shunt.

Physical Examination

Certain features of the physical examination may give additional clues regarding intracardiac hemodynamics. A small, frail-appearing child with ventricular septal defect and pulmonary hypertension is likely to have a large pulmonary blood flow and to be greatly benefited by operation. Patients with ventricular septal defect and pulmonary hypertension whose hearts are overactive and exhibit a systolic thrill and a long, loud systolic murmur usually have a large pulmonary blood flow. Such patients often have an inflow diastolic murmur at the apex.

When physical examination reveals the heart to be quiet, without a thrill, and with only a short, soft precordial systolic murmur, the pulmonary flow is usually not large although further study may reveal it to be slightly or even moderately in excess of systemic blood flow.

Roentgenogram of Thorax

Assessment of cardiac size and contour and of pulmonary vascular shadows by means of roentgenograms of the thorax may provide valuable information concerning pulmonary blood flow and relative size of shunts. In patients with ventricular septal defect and pul-

Figure 1
Roentgenogram of thorax of an 11-year-old patient with ventricular septal defect and severe pulmonary hypertension. Note that the lung fields still give evidence of being hyperemic but not so strikingly as in the case shown in figure 1. Catheterization elsewhere had disclosed pulmonary artery pressure of 96/65 while brachial artery pressure was 85/55. A left-to-right shunt of only moderate degree was demonstrated and there was considerable elevation of pulmonary resistance to 5290 dynes, sec. cm. At the time of operation, before repair, pressure in the right ventricle was 115/6 and that in the left ventricle 113/9; immediately after repair, right ventricular pressure was 62/6 and left ventricular pressure 87/8. In spite of equalization of pressures in the 2 ventricles, this patient was clearly operable because of evidence of increased pulmonary blood flow. The patient has done well.
monary hypertension having a large pulmonary blood flow, the left ventricle is enlarged and the right ventricle is dilated as well as hypertrophied (figs. 1 and 2). In patients having bidirectional shunts of approximately equal magnitude in the two directions, the left ventricle is not significantly enlarged and the right ventricle is not enlarged or dilated although its wall is considerably hypertrophied (fig. 3). The posteroanterior roentgenogram of the thorax under these latter circumstances fails to reveal significant ventricular enlargement in contrast to the enlargement usually noted in patients with high pulmonary flow.

Enlarged pulmonary artery shadows that extend well out into the lung fields are evidence of large pulmonary blood flow. In a patient with ventricular septal defect and pulmonary hypertension, a roentgenogram that gives evidence in the lung fields of large pulmonary flow and evidence for enlargement of the ventricles would indicate that the shunt in the patient in question is predominantly left to right and that operation is indicated.

Lack of evidence of hyperemia of the lungs and a cardiac silhouette that is not enlarged, save for the pulmonary silhouette, do not give clear evidence against the presence of a left-to-right shunt but do alert one to the possibility that pulmonary blood flow may not be large relative to systemic blood flow (fig. 4).

**Electrocardiogram**

Careful interpretation of the electrocardiogram can prove to be of considerable help in assessing the hemodynamic situation in patients with ventricular septal defect with pulmonary hypertension. Correlation of the electrocardiogram with preoperative physiologic studies and with the measured changes occurring in pulmonary artery and systemic pressures after surgical closure of the defect in a large number of children has been of considerable value in establishing and validating criteria for right and left ventricular hypertrophy or overloading.

Pulmonary hypertension resulting from any cause, whether mainly from increased pulmonary blood flow, increased pulmonary vascular resistance, or elevated pulmonary venous pressure, is reflected electrocardiographically by evidence of right ventricular hypertrophy of the systolic overloading type alone or in combination with diastolic overloading patterns. Thus, evidence of right ventricular hypertrophy is noted in virtually all cases of ventricular septal defect with severe pulmonary hypertension and is not helpful in determining whether or not the patient has increased pulmonary blood flow.

Figure 3

*Roentgenogram of the thorax of a 10-year-old patient with ventricular septal defect and severe pulmonary hypertension. The roentgenogram does not give clear evidence of hyperemia of the lungs or of enlargement of the right and left ventricles. Preoperative cardiac catheterization disclosed pulmonary artery pressure of 100/67 and femoral artery pressure of 95/63; however, since pulmonary blood flow was calculated to be 6.3 liters per minute and systemic flow 4.4 liters per minute, operation was advised. Immediately after repair of the ventricular septal defect, pressure in the left ventricle was 108/5 and that in the right ventricle 76/3. The child was in satisfactory condition on dismissal from the hospital.*
Ventricular Septal Defect

Roentgenogram of thorax of a 4-year-old patient with ventricular septal defect and severe pulmonary hypertension. Note the absence of hyperemia in the lung fields and normal-sized cardiac silhouette. Cardiac catheterization showed pulmonary artery pressure of 96/68 and femoral artery pressure of 96/55. The shunt across the ventricular septal defect was purely right to left and pulmonary flow was less than systemic flow. Operation was considered inadvisable.

The most important electrocardiographic contribution to the proper assessment of pulmonary blood flow in patients with ventricular septal defect and pulmonary hypertension is the information afforded concerning the left ventricle. If a dominant left-to-right shunt exists, left ventricular work is increased, but if the shunts are balanced or predominantly right to left, the left ventricle has only its normal work load. Thus, the status of the left ventricle is most important and can usually be correctly evaluated by proper interpretation of the electrocardiogram. Evidence of left ventricular increased work is detected in several ways. Leads representing left ventricular potential may have deep Q waves (more than 3.5 mm.) ; tall R waves (more than 25 mm.) ; tall, peaked T waves; prolonged intrinsicoid deflection times, or any combination of these features (fig. 5 a and b). Usually the left preordial leads (V5 or V6) best show these characteristics, although sometimes the leads

Figure 4

Electrocardiogram of a 3-year-old child. Deep Q (11 mm.) and tall R (54 mm.) waves in lead V6 constitute evidence for increased left ventricular work. A large left-to-right shunt was present and systolic pressures were 55 mm. of mercury in the pulmonary artery and 90 mm. in the femoral artery before operation with a change to 30 mm. and 110 mm., respectively, after repair of the defect.

Figure 5a

Electrocardiogram of an 8-year-old child. Tall, peaked T waves in lead V6 indicate left ventricular overloading (note the small q and normal R waves). Cardiac catheterization studies indicated a left-to-right shunt of 55 per cent and the pressure in the pulmonary artery was identical with that in the aorta before operation. After repair, pulmonary artery pressure was normal.
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1. Figure 6

The electrocardiogram of a 2-year-old child. Deep Q and T waves in leads II, III, and aV<sub>R</sub> indicate left ventricular overloading in this patient. Often the left ventricular potential is better represented in young children by these "vertical" leads than by the left precordial leads. A left-to-right shunt of 50% was demonstrated by cardiac catheterization studies, and equal pressures in the pulmonary artery and aorta were detected. After operation, the pulmonary artery systolic pressure was 50 mm, while that in the aorta was 115 mm, of mercury.

representing vertical ventricular vectors (leads II, III, and aV<sub>R</sub>) reflect the left ventricle more accurately in infants and young children (fig. 6). A small r and deep S wave in right precordial leads (V<sub>1</sub> and V<sub>3R</sub>) indicate left ventricular overwork in infants and young children. Vectorial analysis of the QRS complexes of the electrocardiogram has been of considerable aid in detecting increased left ventricular work in infants and in young children less than 3 years of age. The characteristic features of these vectors are a counterclockwise QRS loop in the frontal plane with a mean QRS axis ranging from +60 to -60 degrees, normal findings in a few older children and many adolescents but usually indicative of left ventricular overloading in infants (fig. 7).

Electrocardiographic evidence of left ventricular overwork, in the absence of mitral insufficiency or aortic stenosis or insufficiency, indicates a left-to-right shunt in patients with ventricular septal defect regardless of the level of pulmonary hypertension and the degree of right ventricular hypertrophy reflected by the electrocardiogram. In some patients with nearly balanced but dominant left-to-right shunts, the electrocardiographic features of left ventricular overloading may be minimal or undetectable and thereby inconclusive, but these constitute a small percentage of cases.

**Cardiac Catheterization**

The most direct way of gathering data concerning pulmonary and systemic blood flow in patients with ventricular septal defect and pulmonary hypertension is by cardiac catheterization. Use of the Fick principle and of techniques employing indicator-dilution curves has resulted in data of unquestioned value in patients who can be studied without heavy sedation or anesthesia. Depression of ventilation and systemic hypotension as well as possible transient changes in pulmonary vascular resistance, which sometimes occur with heavy sedation or anesthesia, may, on occasion, render difficult the interpretation of data concerning shunts in infants and small children. Catheterization performed in children without sedation or anesthesia may result in an unsteady physiologic state and may invalidate the formulas used to calculate pulmonary and systemic blood flows. Because of the reliability of the clinical criteria of increased pulmonary blood flow, it is not necessary to catheterize all patients with ventricular septal defect and pulmonary hypertension prior to operation. When these clinical criteria suggest that pulmonary blood flow is increased little, if any, but do not clearly indicate a reduced pulmonary blood flow, then, on clinical grounds alone, one cannot decide concerning operability. A mild to moderate increase in pulmonary blood flow may exist without being reflected in the findings at physical examination, in the thoracic roentgenogram, or in the electrocardiogram, although the instances are uncommon. Such patients should be studied by cardiac catheterization, particularly if it
VENTRICULAR SEPTAL DEFECT

can be done without sedation or anesthesia, in order to collect further data on pulmonary and systemic blood flow.

Biopsy of Lungs

It has been demonstrated that patients with ventricular septal defect and pulmonary hypertension have changes in the small blood vessels of the lungs. These changes vary in type and degree and can be correlated with the ratio between calculated pulmonary resistance and systemic resistance. Likewise, they can be correlated roughly with the immediate change in pulmonary artery pressure that occurs with repair of the defect, although there is considerable overlap except at the extremes.

Information could be gained concerning pulmonary resistance and thus concerning pulmonary blood flow in patients with ventricular septal defect by histologic study of the pulmonary vasculature, although it might not be definitive in the individual case. Also, the reliability of other criteria of operability has rendered the need for such study unnecessary. A further reason for not resorting to biopsy of the lungs in borderline cases is the difficulty in making generalizations concerning the pulmonary vasculature from study of a small specimen from the lung.

Comment

A basic concept of operability in patients with ventricular septal defect and pulmonary hypertension has been presented. It is based not only on experience with operation in cases of ventricular septal defect but also on experience with operation in patients with pulmonary hypertension associated with patent ductus arteriosus, atrial septal defect, and other intracardiac defects. This concept would become invalid should some pharmacologic method become available for favorably affecting over a long period the severely elevated pulmonary resistance in patients who are considered at present to be inoperable.

Although the concept is clear, in occasional patients with severe pulmonary hypertension and ventricular septal defect it is difficult, in practice, to be certain of the relative magnitudes of pulmonary and systemic blood flow. In borderline cases, decision may be extremely difficult in spite of the utilization of all techniques for assessing operability, including complete cardiac catheterization. In such borderline cases, we usually decide in favor of operation, with recognition of the possibility that this decision may be in error.

An obvious final fact is that proper evaluation for operation in cases of ventricular septal defect and pulmonary hypertension cannot assure uniformly good results. The method of conduct of the operation, the perfusion, and the postoperative care determine the results.

Commentario in Interlingua

Es presentate un criterio fundamental del operabilitate de patientes con defecto ventriculo-septal e hypertension pulmonar. Illo es basate non solmente super le experientia in le operation de patientes con defeccto ventriculo-septal sed etiam super le experienctia in le operation de patientes con hypertension pulmonar in association con patente dueto arteriose,
defecto atrio-septal, e altere defectos intra-cardiaci.
Le hic-presentate criterio perderia su validitate in le caso del elaboration de methodos pharmacologie pro influeriar favorablemente e perduramente le severmente elevate resistencia pulmonar in patientes qui es currentemente considerate como inoperabile.
Le criterio require ab candidatos pro le intervention chirurgia inter patientes con defecto ventriculo-septal e hypertension pulmonar que lor hypertension resulta de un augmento del fluxo de sanguine pulmonar e non de un augmento del resistencia vascular pulmonar, i.e., in altere parolas, que le fluxo de sanguine pulmonar in illes excede le fluxo de sanguine in le circulation major. Le justification de iste requirimento es que le reparo del defecto ventriculo-septal reduce le fluxo de sanguine pulmonar e ergo pote effectuar un reduction del tension del sanguine pulmonar solmente si isto eseva causate per un augmento del fluxo de sanguine pulmonar e non per un augmento del resistencia vascular pulmonar.

Ben que le criterio es clar, in certe patientes con sever grados de hypertension pulmonar e defecto ventriculo-septal il es difficile in le practica esser certe del magnitudes relative del fluxo de sanguine in le circulation pulmonar e in le circulation major. In casos limine le decision es a vices difficilissime in respecto del utilisation de omne le technicas disponibile pro estimar le operabilitate, inclusive complete catheterisation cardiae. In tal casos limine nos usualmente opta in favor del operation, in plen recognition del faeto que iste decision pote esser erronee.

Un obvio facto final es que le correcte evaluation del operabilitate de casos de defecto ventriculo-septal in association con hypertension pulmonar non suffice pro assecurar unirformemente bon resultatos chirurgie. Le metodo secundo le qual le operation as executate, le perfusion, e le attention postoperatori es etiam factores que contribue a determinar le qualitate del resultato.

References

The case is reported of a 28-year-old laboratory technician who developed pericarditis after he had worked with Coxsackie virus Group B, Type 3. This virus also was recovered from the stool on 2 occasions. Repeated isolation of this virus during the acute phase of the illness and the demonstration of a rise and persistence of antibodies neutralizing the virus indicated the etiologic agent in this case.

Sagall
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JAMES W. DUSHANE and JOHN W. KIRKLIN

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