Ventricular Septal Defects in Adults

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Because congenital ventricular septal defects are of different sizes and locations, their clinical presentation, natural history, and treatment vary greatly. This review discusses the different types of ventricular septal defects commonly seen in adults in the authors' experience and in published literature. Ventricular septal defects are either isolated small defects or larger defects associated with pulmonary stenosis, pulmonary hypertension, or aortic regurgitation. These associations play an important role in the pathophysiologic consequences of the defect, its long-term complications, and treatment options. Knowledge of the different clinical presentations in adulthood and the specific features pertinent to these defects will help in the assessment and the care of adult patients with one of the most common congenital cardiac malformations.

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Ventricular septal defects (VSDs), first described by Dalrymple in 1847 (1), account for 20% of congenital cardiovascular malformations and 10% of those diagnosed in adults (2, 3). Its prevalence is estimated at 1.17 per 1000 live births and at 0.5 per 1000 adults and has increased lately because of improved detection (4, 5). With one exception (subarterial defect), VSDs have no sex preference. They can be associated with atrial septal defect (35%), patent ductus arteriosus (22%), right aortic arch (13%), and, less often, pulmonary stenosis (6). Multiple VSDs (4% to 18% of isolated defects) are more prevalent in association with double-outlet right ventricle and tetralogy of Fallot and play an important role in these complex congenital malformations (7–9). This review, however, focuses on isolated defects.

Anatomy

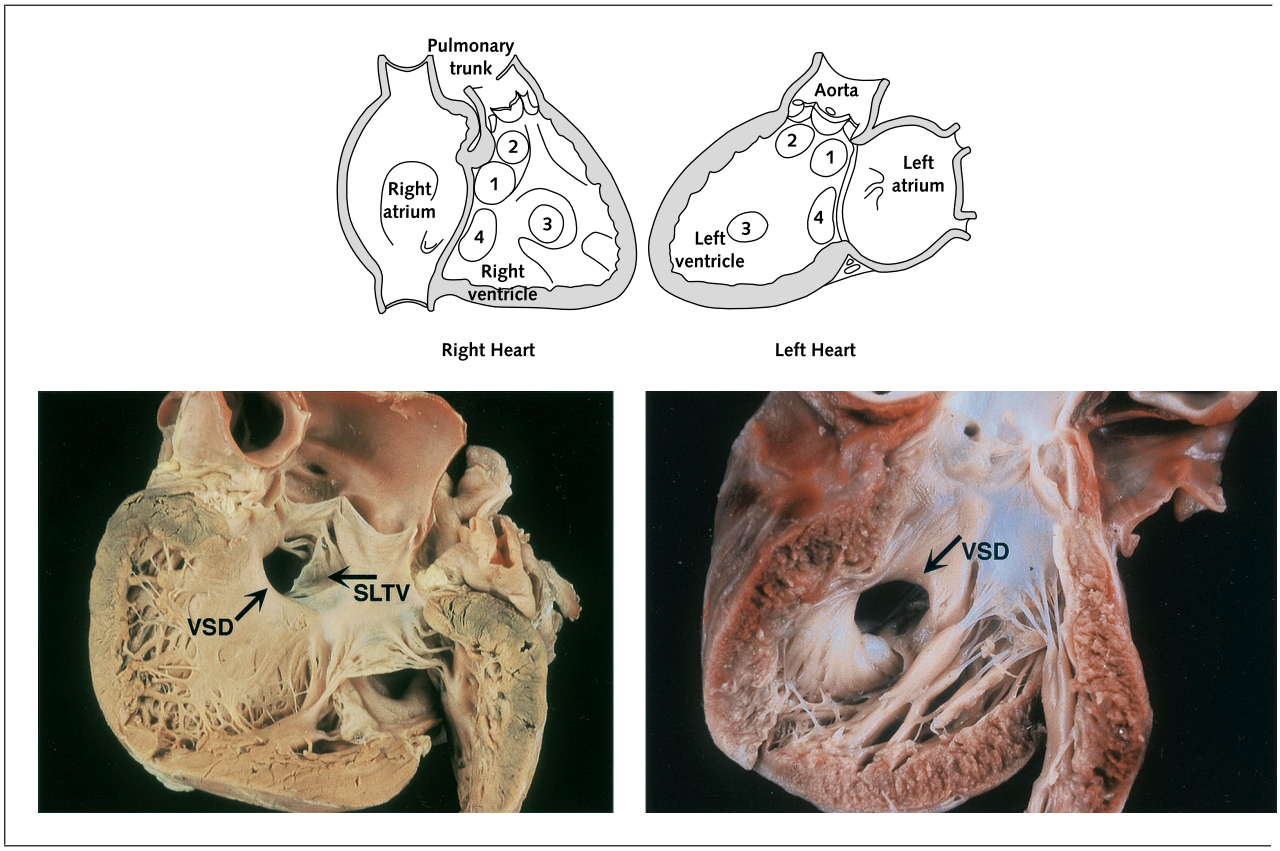
The ventricular septum is a three-dimensional structure with five components: the membranous septum, the trabecular or muscular septum, the infundibular septum, the atrioventricular septum, and the inlet septum. Ventricular septal defects resulting from deficient growth or failure of fusion of these components vary in size from tiny defects to virtual absence of the septum (10). Understanding of the morphologic characteristics of VSD has been complicated by the plethora of existing classification schemes (1, 11–13). Capelli and colleagues (14) described these defects in relation to universally recognized structures: the cardiac valves (**Figure 1**, *top*). The most common membranous defects (75% to 80%) result from a defect in the membranous septum inferior to the crista supraventricularis and can extend into the muscular septum (perimembranous) (**Figure 1**, *bottom left*). Canal or inlet defects are less frequent (8%), are typically large, and lie beneath both atrioventricular valves, primarily the septal leaflet of the tricuspid valve. This defect, often seen in patients with Down syndrome, rarely presents in adulthood without pulmonary hypertension. Muscular or trabecular defects (5% to 20%) are bordered by muscle within the apical, central (**Figure 1**, *bottom right*), or outlet portion of the septum and can be small or large, single or multiple, and occasionally oblique with multiple exits resembling Swiss cheese (2, 15). Subarterial defect, also called outlet, infundibular, conoseptal, or supracristal, is the least common (5% to 7%), except in Asia (30%) (2, 3, 16, 17). It results from deficiency in the septum beneath the semilunar valve but above and anterior to the crista supraventricularis. The resultant loss of support of the right or the noncoronary cusp (or both) causes secondary aortic valve prolapse and regurgitation (18, 19).

Pathophysiology

The direction and volume of the shunt in isolated VSDs are determined primarily by the size of the defect rather than by its location and the ratio of pulmonary to systemic vascular resistance. In adults, the shunt is left to right in the absence of pulmonary stenosis and pulmonary hypertension, resulting in volume overload of the left atrium, both ventricles, and pulmonary arteries. The volume of the shunt dictates the clinical presentation and ultimately the natural history of the patient.

The association between aortic regurgitation and VSD, first reported in 1921 (20), is more common in young men (21, 22). Aortic regurgitation is an acquired

Figure 1. **Septal defects.**



Top. Positions of different ventricular septal defects. 1 = membranous; 2 = subarterial or supracristal; 3 = muscular or trabecular; 4 = inlet or canal. (Modified from Capelli and colleagues [14] with permission of Excerpta Medica.) **Bottom left.** Membranous ventricular septal defect (*VSD*), as seen from the left ventricle, partially obliterated by the septal leaflet of the tricuspid valve (*SLTV*). **Bottom right.** Muscular VSD as seen from the left ventricle. (Photographs courtesy of Dr. William D. Edwards, Division of Anatomic Pathology, Mayo Clinic Rochester.)

lesion seen more with subarterial defects than with perimembranous defects. It results from deficiency or hypoplasia of the conal septum that leads to abnormal apposition in diastole and prolapse of the poorly supported noncoronary or right coronary cusp through the VSD into the right ventricle (18, 19). This results in distortion of the aortic valve and progressive aortic regurgitation (**Figure 2**) (23). Aortic regurgitation often increases in severity with age and indicates a worse prognosis (3, 24).

Clinical Presentation

At presentation in adults, VSD is a small, medium, or large defect with or without pulmonary stenosis, pulmonary hypertension, or aortic regurgitation (2, 15, 25). Small defects are asymptomatic and could represent a larger defect that became smaller because of incomplete spontaneous closure. Medium defects are uncommon unless associated with protective valvular or subvalvular pulmonary stenosis (25% to 30%) (26). Patients often present with dyspnea. Large VSDs present in infancy with heart failure and require surgery unless they spontaneously become smaller. They can also present in association with pulmonary stenosis or can be complicated by pulmonary hypertension (the Eisenmenger complex). The latter group most commonly presents in adolescence with cyanosis, dyspnea, and syncope (27). Patients with VSD and aortic regurgitation most commonly present with a new diastolic murmur of aortic regurgitation, syncope secondary to right ventricular outflow tract obstruction caused by the prolapsing coronary cusp, or heart failure due to progressive left ventricular volume overload.

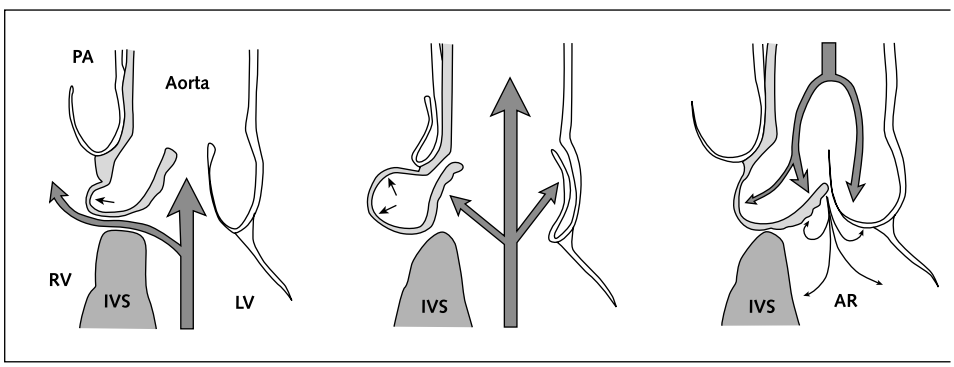
PHYSICAL EXAMINATION

Most VSDs can be identified by auscultation (**Figure 3**). This varies depending on the size of the defect; its location; and associated pulmonary stenosis, hypertension, and aortic regurgitation. Small defects are associated with a palpable thrill in the third or fourth intercostal space. The aortic closure sound may be normal or masked by the systolic murmur. A systolic click can be heard in the presence of a septal aneurysm. The defect murmur is a typical harsh holosystolic plateau-shaped murmur of relatively high frequency best heard in the left third and fourth intercostal spaces. If the defect is subarterial, the blood is shunted directly into the pulmonary artery and therefore the murmur is heard maximally in the second intercostal space and may become "diamond-shaped" (crescendo–decrescendo) or simply consist of a systolic ejection component. If the defect is muscular, the murmur may stop well before the second sound because the defect decreases in size or obliterates in the later part of systole. The physical examination of patients with VSD and pulmonary stenosis depends on the degree of right ventricular outflow obstruction. If it is mild, then the VSD murmur is holosystolic but the pulmonary closure sound is delayed. However, if the pulmonary stenosis is moderately severe, then the VSD murmur gets shorter as the left-to-right shunt diminishes, and the pulmonary sound is soft and delayed. If the pulmonary stenosis is severe, the VSD murmur is replaced by a long systolic ejection murmur typical of pulmonary stenosis.

Patients with the Eisenmenger syndrome are often cyanotic, with clubbed fingers and toes. Most have increased venous pressure, predominantly an "A" wave due to right ventricular hypertrophy and decreased compliance. A "V" wave is seen in association with a failing right ventricle and tricuspid regurgitation. The right ventricular impulse is prominent secondary to hypertrophy accompanied by a palpable single and loud pulmonary closure sound. A midsystolic pulmonary ejection click is often heard from a dilated pulmonary artery. The systemic pulmonary artery pressure abolishes the left-to-right shunt, and the holosystolic murmur therefore vanishes. A diastolic blowing murmur of pulmonary regurgitation may be heard in the left upper sternal border. Later in life, an additional systolic murmur of tricuspid regurgitation may be heard at the left lower sternal border in association with the onset of right-sided heart failure.

Patients with VSD and aortic regurgitation often demonstrate a wide pulse pressure as well as other features of aortic regurgitation. The murmur is to-and-fro, best heard in the upper sternal border, and composed of a systolic VSD murmur that can be plateau-shaped or "diamond-shaped" and a separate, high-frequency diastolic murmur of aortic regurgitation. This may simulate murmurs of a coronary artery fistula, a ruptured sinus of Valsalva aneurysm, or a patent ductus. However, in patients with VSD and aortic regurgitation, the systolic component stops at or before the second heart sound and does not envelop it as continuous murmurs do (2).

Figure 2. **Pathophysiology of aortic regurgitation.**



In early systole (*left*), ejected blood from the left ventricle (*LV*) will be shunted through the ventricular septal defect. As a result, the anatomically unsupported coronary cusp and aortic sinus are driven into the right ventricle (*RV*) (*middle*); this is known as the Venturi effect. In diastole (*right*), the intra-aortic pressure forces the aortic valve leaflet to close, but the unsupported cusp (right or noncoronary) is pushed down into the left ventricular outflow tract away from the opposed coronary cusp, resulting in regurgitation. AR = aortic regurgitation; IVS = interventricular septum; PA = pulmonary artery. (Reproduced from Tatsuno and colleagues [23] with permission of the American Heart Association.)

ELECTROCARDIOGRAPHY

Various electrocardiographic abnormalities have been observed, depending on the size and location of the defect; however, up to 66% of patients can have normal results on electrocardiography (28) and up to 85% are in sinus rhythm (25). One of the most common abnormalities is intraventricular conduction delay or right bundle-branch block. Patients with the Eisenmenger complex often have right-axis deviation, right atrial enlargement, and ventricular hypertrophy (**Figure** 4). In the presence of pulmonary stenosis, the electrocardiogram would be similar to that of a patient with tetralogy of Fallot, depending on the severity of the stenosis. Finally, signs of left ventricular enlargement and hypertrophy are often noted in patients with VSD and aortic regurgitation.

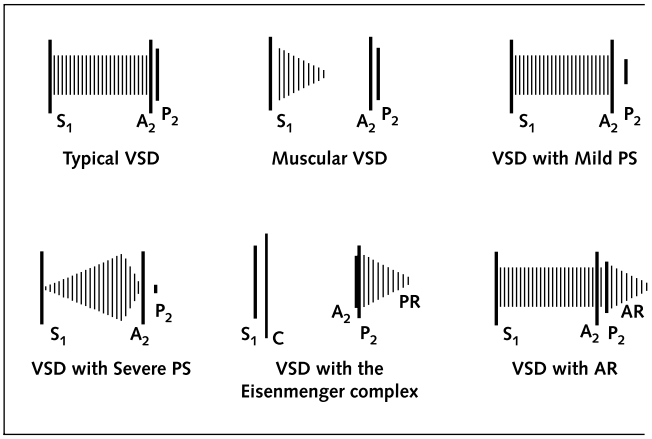
CHEST RADIOGRAPHY

Patients with a small VSD have a normal cardiac silhouette and pulmonary vascularity. The presence of mild cardiomegaly secondary to volume overload is directly related to the magnitude of the shunt (ratio of pulmonary to systemic flow [QP/QS] > 2) (2). In patients with the Eisenmenger complex, the likelihood of cardiomegaly increases to 48% as a result of enlargement of the right heart and of the pulmonary artery, with pruning of outer pulmonary vessels (**Figure 5**) (2, 15, 28, 29). Patients with pulmonary stenosis often have a boot-shaped heart, with right ventricular contour and decreased pulmonary vascularity. Finally, in patients with VSD and aortic regurgitation, the severity of the latter determines the findings on chest radiography. Chest radiography commonly shows left atrial and ventricular enlargement that is disproportionate to the shunt severity (30, 31).

ECHOCARDIOGRAPHY

Echocardiography is the noninvasive method of choice for evaluation of VSD. It is a sensitive, descriptive tool with an excellent detection rate (88% to 95%), depending on the size and location of the defect and on technician experience (32–37). A thorough echocardiographic examination is best achieved by imaging the intraventricular septum in multiple planes using color-flow and spectral Doppler echocardiography (**Figure 6**). Echocardiography is most sensitive for defects larger than 5 mm that are located in the membranous, inlet, or outlet portion of the septum. It is least sensitive for apical muscular defects.

Figure 3. **The cardiac examination in ventricular septal defect (*VSD*).**



Top left. Holosystolic murmur of VSD. **Top middle.** Shortened systolic murmur of muscular VSD. **Top right.** Typical murmur of VSD with mild pulmonary stenosis (*PS*) showing the delayed pulmonary closure sound (P_2). **Bottom left.** Systolic ejection murmur of severe pulmonary stenosis with delayed and reduced P_2. **Bottom middle.** Eisenmenger complex with absence of the holosystolic murmur of VSD, a loud P_2 secondary to pulmonary hypertension, and pulmonary regurgitation (*PR*) diastolic murmur. **Bottom right.** VSD murmur followed by diastolic murmur of aortic regurgitation (*AR*); A_2 = aortic closure sound; C = ejection click; S_1 = first heart sound.

Echocardiography can confidently identify the morphologic features of the defect, including its size and borders and associated defects (32). It also provides an accurate hemodynamic assessment of the shunt, severity, volume overload, subpulmonic (double-chambered right ventricle) or pulmonic stenosis, and pulmonary hypertension (38, 39). In addition, echocardiography can assess the degree of aortic valve distortion and prolapse (right and noncoronary cusp) in patients with subarterial VSD and evaluate the severity of aortic regurgitation and right ventricular outflow tract obstruction caused by the prolapsing coronary cusp (2, 30, 32, 40). Yearly echocardiographic assessment of aortic regurgitation has important prognostic implications, especially with regard to timing of surgical treatment.

CARDIAC CATHETERIZATION

Angiography is an important diagnostic tool used to assess pulmonary vascular resistance of complicated VSDs, such as those that are multiple and especially

apical or those associated with pulmonary stenosis, aortic regurgitation, and pulmonary hypertension (15, 30, 36, 41, 42).

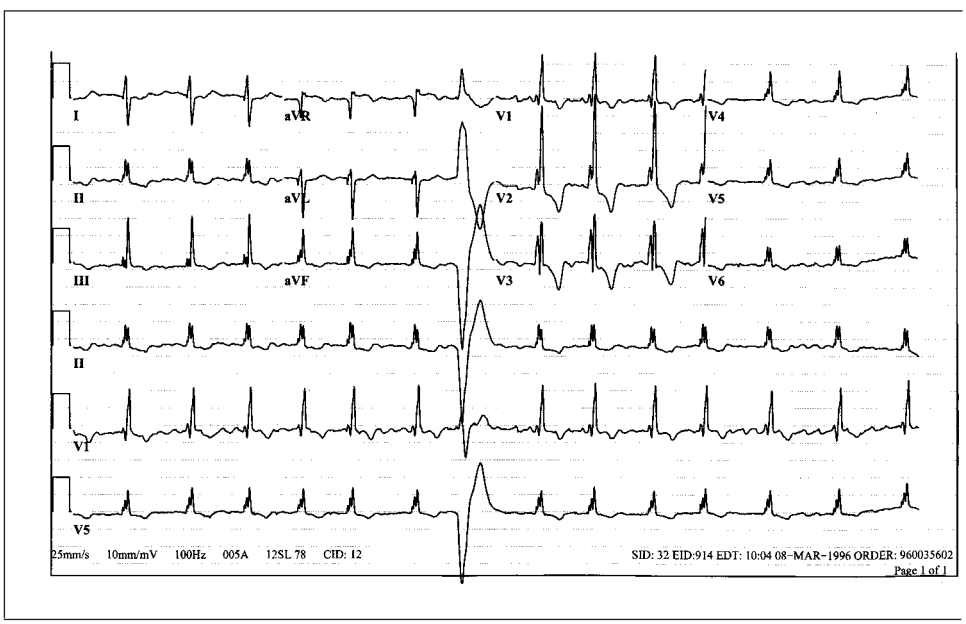
Left ventriculography is best performed by using a large-volume contrast bolus over a short time. An optimal radiographic projection makes the portion of the septum suspected of containing the defect tangent to the x-ray beam. Although findings on angiography correlate well with anatomic findings at surgery, a complementary shunt study, using oximetry or the indicator dilution curves, improves the diagnostic accuracy of cardiac catheterization. In patients with suspected aortic regurgitation, additional aortography allows detection of aortic valve prolapse even before the appearance of its clinical feature and helps grade the severity of aortic regurgitation (43).

NATURAL HISTORY

The natural history of isolated VSD depends on the type of defect, its size, and associated anomalies. Defects can close spontaneously (some incompletely). Persistent defects, however, may predispose patients to endocarditis, arrhythmias, heart failure, aortic regurgitation, and pulmonary hypertension. Therefore, periodic clinical and laboratory evaluations with electrocardiography, chest radiography, and echocardiography are recommended, depending on the presence of these complications or associated lesions.

Spontaneous closure occurs in 40% to 60% of patients, mostly in preschoolers (2, 8, 44–46). Thereafter, it is uncommon. However, it has been reported to occur in young adults (5, 46). Closure occurs as a result of muscular growth around the defect; ingrowth of border-forming proliferative fibrous tissue; or, in the case of membranous defects, an aneurysm of the tricuspid valve leaflet adhering to the edge of the defect. Spontaneous closure is more common in women with small muscular or membranous defects and normal pulmonary artery pressure (2, 25, 44–48). Inlet and subarterial defects seldom close spontaneously because of their close proximity to the valves (49). However, subarterial defects can decrease in size or functionally close by the prolapsing aortic valve at the expense of leaflet distortion and regurgitation and occasionally right ventricular outflow tract obstruction (19, 22, 50). Patients who experience spontaneous closure often remain asymptomatic, with a residual click, and can lead normal lives. However, impaired atrioventricular conduction can occur, including complete heart block and late right ventricular outflow tract obstruction (2, 51).

Figure 4. **Electrocardiogram of a 42-year-old woman with Eisenmenger complex, demonstrating atrial fibrillation with right axis deviation, right ventricular hypertrophy, right bundle-branch block, and premature ventricular beat.**

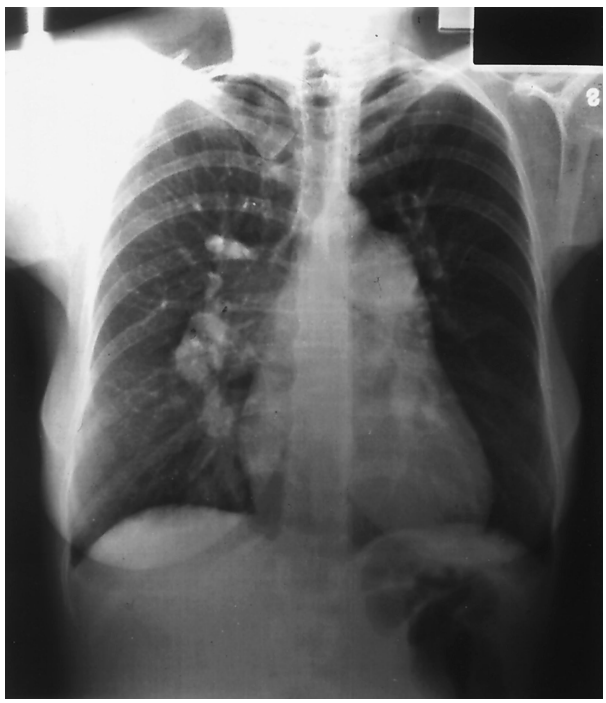


Patients with VSD have a high incidence of arrhythmia compared with historical controls. The incidence of ventricular arrhythmias, defined as ventricular couplets, multiform ventricular ectopics, and ventricular tachycardias, is 22.2% in medically treated patients, whereas the incidence of ventricular tachycardia is 5.7% and the incidence of sudden death is 4.0% (28, 52). Wolfe and associates (52) demonstrated that age and pulmonary artery pressure are the best predictors of arrhythmias. The odds ratio of serious arrhythmias increases to 1.51 for every 10-year increase in age and to 1.49 for any increase in mean pulmonary artery pressure of 10 mm Hg (52). This is especially true in patients with the Eisenmenger complex, whose hypertrophied right ventricles represent an ideal substrate (28). In this group of patients, the risk for ventricular tachycardia is 19% (52). Supraventricular tachycardia, mostly atrial fibrillation, is also prevalent, especially with increasing age. The treatment options for arrhythmias associated with VSD include observation, antiarrhythmic medications, ablation, and implantable devices. Treatment should be individualized, depending on the severity and frequency of such arrhythmia, associated symptoms (such as syncope), presence of conduction delay, or ventricular dysfunction. Annual Holter monitoring is recommended in high-risk patients, such as those with the Eisenmenger syndrome.

Patients who have small VSDs and patients whose VSDs are associated with aortic regurgitation are at high risk for endocarditis because of the highly turbulent jet (53–55). The incidence is reported at 15.0 to 24.0 per 10 000 patient-years and increases with age (54, 55). Gersony and Hayes (55) have shown that endocarditis is more common in older men. Transesophageal echocardiography remains the diagnostic procedure of choice in the evaluation of patients with suspected or proven endocarditis. It is an excellent technique for the detection of vegetations around the borders of the defect or on adjacent valves and for the assessment of potential complications, such as abscess formation (56).

Congestive heart failure due to chronic volume overload of the ventricles occurs in patients with isolated medium or large VSDs (2, 28). It is rarely seen in adults because most patients present and undergo repair before adulthood (15). However, right-sided heart failure can occur in adults when the defect is associated with significant pulmonary stenosis or acquired subpulmonic stenosis (double-chambered right ventricle); it can also occur at advanced stages of the Eisenmenger complex. However, left-sided failure can occur secondary to significant aortic regurgitation in patients with aortic valve prolapse.

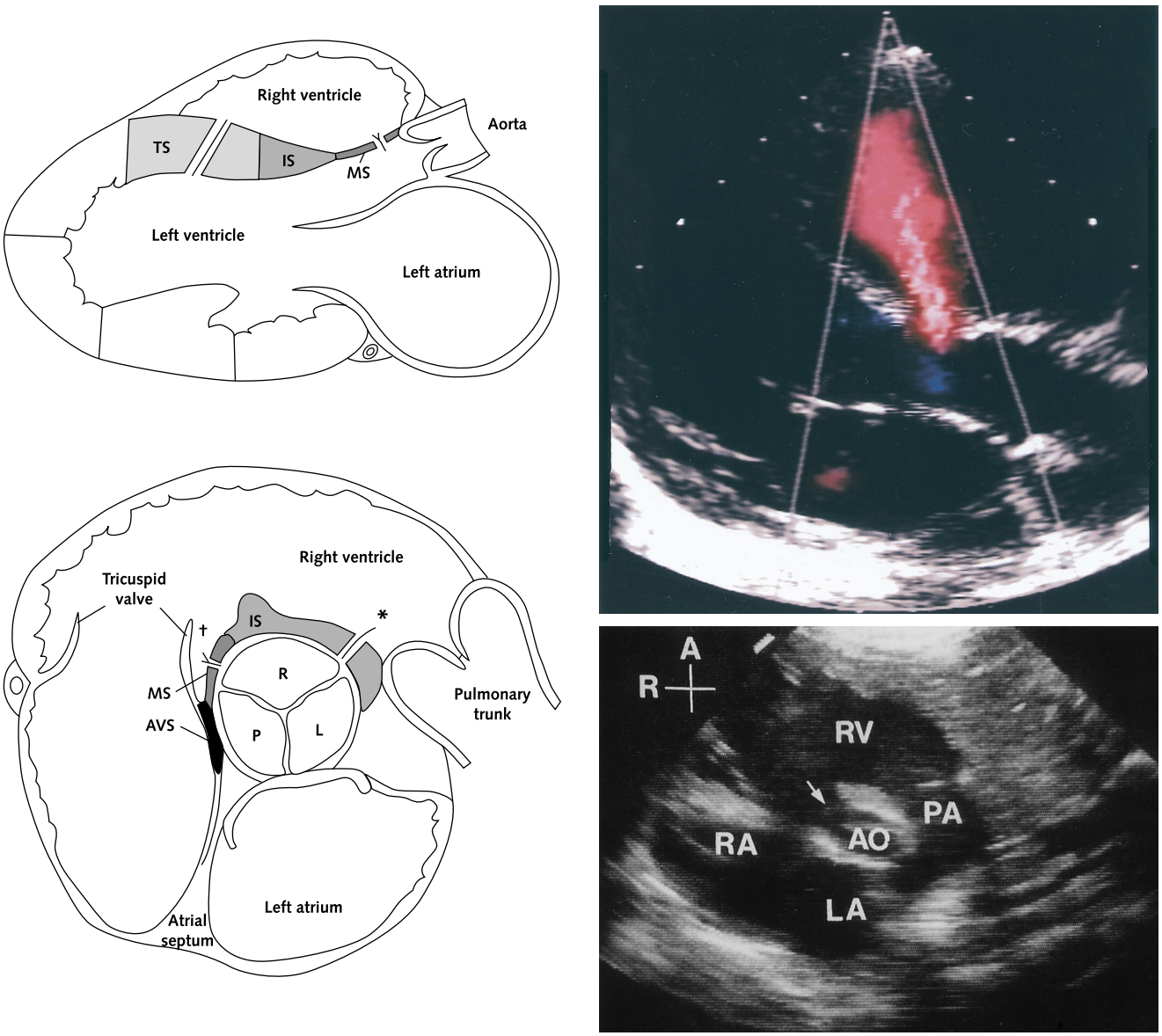
Figure 5. **Chest radiograph in a patient with the Eisenmenger complex, showing cardiomegaly with severe enlargement of the proximal pulmonary arteries and pruning of the outer pulmonary vessels.**



Eisenmenger Complex

Irreversible pulmonary vascular obstructive disease, or the Eisenmenger complex, develops in 10% to 15% of patients with VSD, most commonly in the second and third decades of life (2, 57, 58). The Eisenmenger complex results from long-standing left-to-right shunt leading to progressive pulmonary hypertension that ultimately becomes irreversible, leading to reversal of the intracardiac shunt and systemic desaturation. Systemic desaturation results in cyanosis, and secondary erythrocytosis occurs because of the release of erythropoietin (59). This can be complicated by the hyperviscosity syndrome and by cerebrovascular events (59, 60). The in-

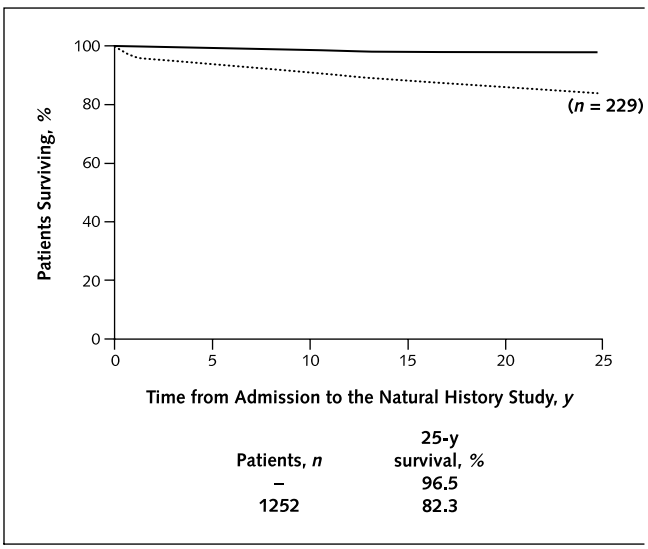
Figure 6. **Echocardiographic examination of ventricular septal defects (VSDs).**



Top left. Standard parasternal long-axis echocardiographic views show the membranous septum (*MS*), the infundibular septum (*IS*), and the trabecular muscular septum (*TS*). (Reproduced from Hagler and colleagues [13] with permission of the Mayo Foundation). **Top right.** Color-flow Doppler echocardiogram demonstrating a membranous VSD with a left-to-right shunt (red flow from left ventricle to right ventricle). **Bottom left.** Parasternal short-axis view. The asterisk indicates supracristal or subarterial ventricular septal defect in the right ventricular outflow tract. In the same basal view, the dagger indicates membranous ventricular septal defect in proximity to the tricuspid valve. **Bottom right.** Freeze-frame image of a membranous VSD (*arrow*), as seen on parasternal short-axis view. AO = aorta; AVS = atrioventricular septum; L = left coronary cusp; LA = left atrium; P = posterior noncoronary cusp; PA = pulmonary artery; R = right coronary cusp; RA = right atrium; RV = right ventricle.

cidence of cerebrovascular events has been reported to be approximately 1/100 patient-years (60). The identified risk factors include atrial fibrillation, iron-deficiency anemia, and previous phlebotomy. Iron-deficient erythrocytes are spherical and therefore do not circulate as readily as iron-replete cells. Patients with the Eisen-

Figure 7. **Kaplan–Meier survival curve of all patients with ventricular septal defects (n = 1252) from the Natural History Study (*dashed line*) compared with the expected survival curve (*solid line*) for a sex- and age-matched population.**



The number in parentheses indicates the number of patients remaining under observation 25 years after admission. (Reproduced from Kidd and colleagues [28] with permission of the American Heart Association.)

menger complex often present with dyspnea, chest pain, hemoptysis, syncope, and tachyarrhythmias and have mild renal insufficiency caused by tubular atrophy, hyperuricemia with gout due to increased erythrocyte turnover, and increased risk for calcium bilirubinate stones.

The prognosis of patients with the Eisenmenger complex is poor, especially after onset of serious arrhythmia, hemoptysis, congestive heart failure, and significant tricuspid regurgitation. Most patients succumb by their fourth decade. However, survival has been reported into the seventh decade (2, 61). Increased survival is best achieved by a conservative approach that includes avoidance of smoking and aspirin products in patients who have platelet dysfunction; avoidance of contraceptive pills, which can increase the risk for thromboembolic events; avoidance of dehydration and iron-deficiency anemia, which increase the risk for hyperviscosity syndrome and cerebrovascular events; and practice of good oral hygiene and skin care to decrease the risk for infective endocarditis (62). Periodic referral to a tertiary care facility that offers specialized expertise in the care of adult patients with congenital heart disease is suggested, preferably before heart failure develops.

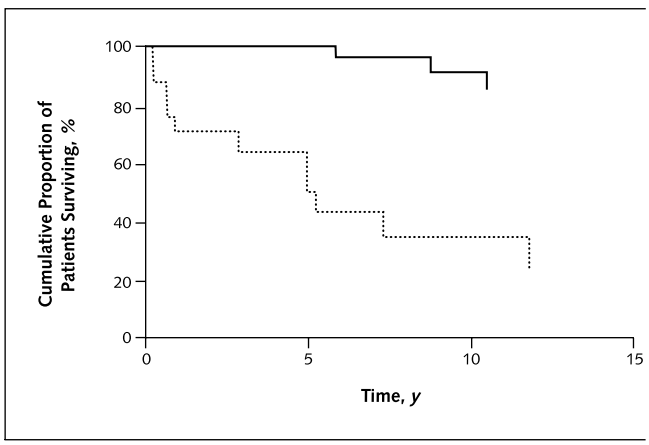
Pregnancy

Ventricular septal defect is uncommon in women of reproductive age. Patients who have small defects with a shunt ratio less than 2.0, normal pulmonary pressure, and preserved functional aerobic capacity can undergo pregnancy with little or no risk. However, pregnancy is contraindicated in patients with the Eisenmenger complex because of the significant risk for maternal death, up to 50% (63). First-trimester spontaneous abortions and small-for-date babies are also common, and offspring are at increased risk for congenital heart disease (6% to 10%) (63–65).

Late Death

The early natural history study by Campbell (45) showed mortality rates of 27% by 20 years of age and 69% by 60 years of age in patients with VSD. More recent data by Kidd and colleagues (28) demonstrated a 25-year survival rate of 82.3% (**Figure 7**). Multivariate proportional hazards assessment showed that survival was affected by age and pulmonary artery pressure. The 25-year survival rate was 85.2% for patients younger than 20 years of age and 63.2% for those older than 21 years of age. Patients with the Eisenmenger complex

Figure 8. **Survival rate for patients with ventricular septal defects by pulmonary artery systolic pressure.**



The solid line indicates a pressure less than 50 mm Hg (n = 36); the dashed line indicates a pressure of 50 mm Hg or greater (n = 17). (Reproduced from Ellis and colleagues [25] with permission of the CV Mosby Company.)

have a 10- to 12-fold higher risk for death (28) and a 25-year survival rate of 41.7%, compared with 95.9% for patients with small VSDs. Gersony and colleagues (66) reported that more than 85% of patients treated medically or surgically were in good or excellent health while continuing to lead a productive life. Only 13% felt restricted, and 4.8% were classified as having New York Heart Association (NYHA) functional class III or IV disease. Ellis and associates (25) demonstrated that survival was affected by functional capacity (10-year survival rate, 90% for NYHA class I and 58% for NYHA classes II to IV), cardiomegaly (10-year survival rate, 90% without cardiomegaly and 58% with cardiomegaly), and pulmonary artery pressure (**Figure 8**). A mean pressure less than 20 mm Hg carries an excellent prognosis. However, the two most common causes of death in medically treated patients are heart failure (35%) and sudden death (35%), followed by pulmonary embolism, myocardial infarction, and endocarditis.

Ventricular Septal Defect and Aortic Regurgitation

The risk for aortic valve prolapse and regurgitation in patients with membranous or subarterial defects increases with age (22, 24, 40, 67). Aortic regurgitation is believed to be 2.5 times more frequent in patients with subarterial VSDs. Momma and coworkers (22) reported on 395 patients with subarterial defects; aortic regurgitation was seen in 50% of patients by 8 years and in 87% of patients by 20 years. As the aortic valve prolapse progresses, the intraventricular shunting decreases at the expense of aortic valve distortion and regurgitation. This increases risk for endocarditis, left ventricular volume overload, and, less commonly, right ventricular outflow tract obstruction and sinus of Valsalva aneurysm (2, 3, 15, 22, 43, 68). The progressive nature of the aortic regurgitation and the associated increased morbidity have led to the recommendation of early surgical intervention (23, 24, 67, 69, 70). However, unless endocarditis supervenes, the rate of progression is often slow and variable. Therefore, the proper timing and type of operation are still controversial.

TREATMENT

The treatment of isolated VSD depends on the type of defect; its size; shunt severity; pulmonary vascular resistance; functional capacity; and associated acquired anomalies, such as aortic regurgitation, subpulmonary stenosis, or pulmonary hypertension. Surgical closure decreases the risk for endocarditis by at least 50%, reduces pulmonary artery pressure, improves functional classification, and increases long-term survival (25, 28, 54, 66, 70).

Adult patients with small defects and normal pulmonary pressure have an excellent prognosis and need only endocarditis prophylaxis (3, 15, 71). However, surgical repair should be considered after a second episode of endocarditis. In addition, it has been our experience that in adults with small defects, volume overload of the left ventricle can occur late because of a long-standing shunt. Surgical intervention should be considered.

Medium to large defects with a QP/QS value greater than 1.5/1.0 and pulmonary vascular resistance less than 7 units/m^2 are not common in adults. Most defects of this type require closure during infancy and childhood, and long-term results are good (28, 45, 70, 72). Surgical repair of medium to large defects associated with pulmonary stenosis or hypertension depends on the degree of right ventricular outflow tract obstruction in the former and on pulmonary vascular resistance in the latter (15). In patients with pulmonary hypertension, cardiac catheterization is crucial in decision making. Surgery can be considered with low risk for postoperative persistent pulmonary hypertension if the pulmonary artery pressure is only 50% to 75% of systemic pressure; if pulmonary vascular resistance is less than 7 to 8 units/m^2; and if pulmonary hypertension is reversible by oxygen, vasodilators, or nitrous oxide (15, 57). When surgery is performed in adults with irreversible elevated pulmonary vascular resistance (>8 units/m^2), the operative mortality rate and the risk for postoperative pulmonary hypertension are increased (15, 70, 72–74). Persistent pulmonary hypertension is an independent determinant of postoperative cardiac performance and prognosis. Approximately 25% of patients with preoperative pulmonary hypertension and pulmonary vascular resistance of greater than 10 units/m^2 die within 5 years of surgery (75). Patients with irreversible pulmonary hypertension should be managed conservatively until signs of right-sided heart failure develop. At that time, heart–lung transplantation can be considered. Prostacyclin and its analogues hold some promise for some of these patients.

Successful surgical repair is characterized by absence

of residual shunt, resolution of symptoms, and normalization of pulmonary artery pressure. The improved surgical techniques, especially with regard to cardioplegia and surgical approach, have substantially decreased perioperative morbidity and mortality (70, 76).

The operative mortality rate for repair of uncomplicated VSD is less than 2% (15). This rate increases with more than one defect, with moderate pulmonary hypertension (>50% of systemic pressure), and in the presence of aortic regurgitation (8, 28, 70). The second natural history study by Kidd and colleagues (28) showed that the 1-month mortality rate in 1280 surgically treated patients was 6%; 89.9% of deaths were from cardiac causes (heart failure and sudden death).

Although the prognosis after surgical repair of uncomplicated VSD is excellent, late complications, often of little clinical significance, are not uncommon. When evaluating patients who had reparative surgery for VSD as a child, clinicians should focus on the presence of these complications. Complications include decreased aerobic capacity (71, 77, 78) and conduction defects, such as right bundle-branch block with (18% to 100%) or without (30%) left anterior hemiblock, especially after ventriculotomy and patch closure of the defect (70, 72, 79–81). Late sinus node dysfunction, including complete heart block requiring pacemaker placement, is infrequent (≤2%) (70, 72, 82, 83). Blake and associates (84) observed an association between postoperative conduction defect and late, sudden death and ventricular arrhythmia.

The risk for serious tachyarrhythmia continues even after surgery (52, 70, 72, 82). The incidence increases with higher functional classification, cardiomegaly, and increased pulmonary artery pressure (52). Cardiomegaly, for example, increases the risk threefold. The overall risk in surgically treated patients is 36.4%, compared with 22.2% in medically treated patients. Most of these arrhythmias are only premature ventricular beats (20% to 34%) (72). Ventricular tachycardia has been documented in up to 14.8% of surgical patients, and sudden death has accounted for as many as 39% of all cardiac deaths after surgery (52).

Residual VSDs occur in up to 34% of cases, regardless of surgical approach, but are often small and hemodynamically insignificant (28, 70, 72, 85, 86). Patients with residual VSDs, however, need continued endocarditis prophylaxis and periodic follow-up to determine the need for repeated surgery (70).

The risk for infective endocarditis after surgical repair is approximately half that in medically treated patients. The reported incidence varies from 0.8 to 1.7 per 1000 patient-years (54, 70). Infective endocarditis occurs more often in patients with residual defect or aortic regurgitation (54, 84, 87). In the absence of significant residua, endocarditis prophylaxis is not recommended for more than 6 months after surgery (88).

Long-standing volume overload may increase cardiac mass and can precipitate ventricular dysfunction (89). Reparative surgery promotes normalization of left ventricular mass and function. However, ventricular dysfunction with congestive heart failure may persist or even worsen after repair (70, 72, 90, 91), especially in patients with residual ventricular septal defect, aortic regurgitation, and abnormal septal wall motion (70). Acquired cardiovascular disease, such as hypertension and ischemic coronary disease, adds to the burden.

Natural history studies have demonstrated that the 25-year survival rate after surgical repair of ventricular septal defect is 89% (28, 92). Late death depends on the patient's age at surgery and on pulmonary vascular resistance. Otterstad and coworkers (70) demonstrated that survival is improved when surgery is done at an earlier age and that late mortality rates are similar to those of a normal population matched for age, sex, and observation time (15, 28, 72).

The optimal surgical treatment and timing of surgery in patients who have VSD and aortic regurgitation are controversial, especially after the discouraging early surgical results (93, 94). However, recent studies have suggested that earlier intervention is feasible and indicated, depending on the defect (subarterial or membranous) and the degree of valve distortion and aortic regurgitation (31, 50, 67, 68, 95, 96). The surgical approach, introduced by Spencer and colleagues (31) and Trusler and associates (96), consists of defect closure with or without aortic valve valvuloplasty, depending on the severity of aortic valve distortion (24, 31, 50, 67). Aortic regurgitation resolves or improves in up to 84% of patients (68). Younger patients have better results (70, 97). Ohkita and coworkers (97) reported a 5.3% incidence of significant aortic regurgitation necessitating repeated surgery. The mean interval between the first and second surgery was 7 years. In patients in whom

aortic valve repair is not feasible because of extensive distortion, fenestration, or significant fibrosis or calcification (10% to 15% of cases), valve replacement should be considered (21, 23).

CONCLUSION

Ventricular septal defects are of different sizes and shapes, are located in different areas, and can be associated with many types of congenital and acquired heart disease. To understand the ways in which these different defects affect cardiovascular hemodynamics and performance, clinicians must have knowledge of congenital and acquired heart disease. Surgical and medical expertise is essential and helps in the understanding and care of adult patients with congenital cardiac malformations, whose numbers are constantly increasing. These patients, even those with the Eisenmenger complex, can lead productive lives when cared for appropriately.

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