OPERATION FOR PARTIAL ATRIOVENTRICULAR SEPTAL DEFECT: A FORTY-YEAR REVIEW

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Background: We describe the long-term outcome of repair of partial atrioventricular septal defect by determining the rates of survival, reoperation, and occurrence of left atrioventricular valve regurgitation, left atrioventricular valve stenosis, left ventricular outflow tract obstruction, and arrhythmia.

Methods: We studied 334 patients who underwent repair of partial atrioventricular septal defect before 1995.

Results: The 30-day and 5-, 10-, 20-, and 40-year survival were 98%, 94%, 93%, 87%, and 76%, respectively. Closure of the left atrioventricular valve cleft ($P = .03$) and age less than 20 years at operation ($P < .001$) were associated with better survival. Reoperation was performed for 38 patients (11%). Repair of residual/recurrent left atrioventricular valve regurgitation or stenosis was the most common reason for reoperation. Left ventricular outflow tract obstruction occurred in 36 patients, and 7 patients underwent reoperation to relieve this obstruction. Supraventricular arrhythmias were observed in 58 patients (16%) after the operation. Supraventricular arrhythmias increased with increasing age at primary operation ($P = .001$). Complete atrioventricular block occurred in 9 patients (3%). Permanent pacemakers were implanted in 11 patients.

Conclusions: Long-term survival after repair of partial atrioventricular septal defect is good. It is important to close the cleft in the left atrioventricular valve. Reoperation for persistent or recurrent left atrioventricular valve malfunction and relief of left ventricular outflow tract obstruction is necessary in approximately 11% of patients. (J Thorac Cardiovasc Surg 2000;119:880-90)

The first surgical correction of partial atrioventricular septal defect (ASD) was reported in 1955,¹ and since then there have been reports of several reasonably large operative series.¹⁻¹⁶ The purpose of this study was to describe the long-term outcome of the largest reported series of patients who underwent surgical repair of partial ASD at one institution. We determined the incidences of survival, reoperation, and occurrence of significant left atrioventricular valve regurgitation, stenosis, left ventricular outflow tract obstruction, and arrhythmia.

Patients and methods

This was a retrospective chart review study of all patients who underwent primary repair of partial ASD at the Mayo Clinic between 1955 and 1995. Some patients in this study were included in previous reports.^{2,5,8,10} The current study, however, includes a considerably longer follow-up period and larger number of patients. This study was approved by the Mayo Foundation Institutional Review Board.

The Mayo medical record of each patient was reviewed, and data were collected regarding the anatomic details of the cardiac defect and details of the operation, especially whether the left atrioventricular valve cleft was closed. Passive follow-up was done with the Mayo medical records to ascertain vital status and outcome events of interest (residual or recurrent ASD, left atrioventricular valve stenosis, and left atrioventricular valve regurgitation, left ventricular outflow tract obstruction, bacterial endocarditis, cardiac reoperation, and arrhythmias). Active follow-up was done with a questionnaire sent to each of the patients not known to be dead and for whom current information regarding the outcome events of interest was not available in the Mayo medical record as of June 1, 1995.⁹ For the few patients lost to follow-up, a nongovernmental index that tracks death information on a national basis (www.ancestry.com) was searched to ascertain vital status.

The presence and severity of left atrioventricular valve regurgitation, stenosis, arrhythmias, and left ventricular out-

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flow obstruction were assessed from clinical evaluations, echocardiographic data, cardiac catheterization data, and operative data contained in the Mayo medical record or obtained from the medical questionnaire sent to the patient or the patient's physician.

Left atrioventricular valve regurgitation was considered to be present if the patient underwent operation for regurgitation or if there was clinical, angiographic, or Doppler echocardiographic evidence for left atrioventricular valve regurgitation. The severity of the regurgitation was based on the severity assigned by the attending physician and recorded in the medical record. The severity assigned was associated with the first recorded observation of regurgitation subsequent to the primary operation.

Left atrioventricular valve stenosis was considered to be present if the patient underwent operation or reoperation for stenosis or if there was a left atrial—left ventricular end-diastolic pressure gradient of more than 3 mm Hg by cardiac catheterization or Doppler echocardiography.

Left ventricular outflow tract obstruction was deemed to be present if there was 5 mm Hg or more pressure gradient across the left ventricular outflow tract measured at cardiac catheterization (peak-to-peak gradient) or Doppler echocardiography (mean gradient) or if operation for relief of obstruction was performed.

A clinically significant arrhythmia was defined as one for which an antiarrhythmia drug (excluding digoxin) treatment or a pacemaker was required.

The date of onset of the event of interest was based on the date of documentation of that event most proximal to the date of the original operation.

Continuous variables are summarized as a median with corresponding 25th (Q1) and 75th (Q3) percentiles, and comparisons between patient groups were based on the Wilcoxon rank sum test. Discrete variables are summarized as a percentage of the total, and comparisons between patient groups were based on the χ^2 test. Incident outcomes of primary interest consisted of all cause deaths, first reoperation, left atrioventricular valve regurgitation and/or stenosis, left ventricular outflow tract obstruction, and arrhythmias. Survival-free events were estimated with the Kaplan-Meier method. Expected survival was estimated with the life tables for the United States white population and observed survival included in hospital deaths. Associations between time to first end point with clinical and surgical findings were investigated within the Cox proportional hazards framework, adjusting for decade of surgery. Independent variables included age at operation, sex, decade of operation, suture closure of cleft, parachute valve malformation, double-orifice valve, and presence of complete or partial cleft. Time of surgery was indicated as 1950s to 1960s, 1970s, and 1980s to 1990s and was used as an adjusting factor to control for the potential changes in referral patterns in the time of this study. Determinants of long-term survival were investigated in subjects with at least 30 days of follow-up and excluded deaths occurring less than 30 days after operation. Events occurring within 30 days of operation are summarized as a percentage of the total cohort. When all-cause deaths were considered, subjects with left

Table I. Demographics by decade of operation

Demographic	Decade of operation		
	1950 through 1969	1970 through 1979	1980 through 1999
Sex (n)			
Male (%)	68 (48)	44 (45)	31 (33)
Female (%)	73 (52)	54 (55)	64 (67)
Total (n)	141	98	95
Down syndrome (n; %)	1 (1)	3 (3)	14 (15)
Median age at operation (y)	9.6 (Q1, 5.4; Q3, 17.6)	6.1 (Q1, 2.7; Q3, 12.3)	7.2 (Q1, 2.9; Q3, 29.6)

atrioventricular valve regurgitation or stenosis and left ventricular outflow tract obstruction as end points were censored at the time of any prior reoperation or last available follow-up date. Censoring was imposed at reoperation because of the potential of altering the risk of the development of subsequent events, which could not be accounted for at baseline.

Results

The study group consisted of 334 consecutive patients (Table I). There were 143 male patients (43%). The median age at operation was 8 years (Q1, 4.1 years; Q3, 18 years). The number of patients who underwent operation during the first, second, third, fourth, and fifth or greater decade of life was 192, 65, 35, 19, and 23, respectively. The distribution of patients who underwent operation during the decades of 1950, 1960, 1970, 1980, and 1990 was 42, 99, 98, 67, and 28, respectively. Eighteen patients (5%) had Down syndrome.

Sufficient information regarding long-term outcome was available from the Mayo medical record (ie, documented follow-up within 6 months before June 1, 1995) for 86 of the 334 patients. For the remaining 248 patients, the outcome events of interest were sought with two different medical questionnaires; one was sent to the patient and the other to the patient's physician.

Follow-up information was obtained for 211 of the 248 patients who were sent questionnaires. Of the 37 patients without follow-up, 13 patients were ascertained to be deceased and 24 patients were lost to follow-up. For these 24 patients, we confirmed that 3 patients had died. The remaining 21 patients were censored for survival analysis at the date they were last known to be alive. Of the 248 patients, 9 patients did not respond to the survey, but their vital status was ascertained.

A complete left atrioventricular valve cleft was present in 247 patients; a partial cleft was present in 74 patients, and 4 patients had no cleft. A double-orifice valve was present in 23 patients, and a parachute valve

Fig 1. Kaplan-Meier curve represents overall survival (**A**) and by the decade of the operation (**B**) in this cohort of patients.

was present in 6 patients. Combination of a double-orifice valve and complete cleft of the valve occurred in 9 patients. Four patients had a complete cleft that was associated with a parachute valve. Ten patients had a double-orifice valve and partial cleft. Some patients had more than one left atrioventricular valve abnormality and were counted more than once.

Surgical procedure. Eight patients (2%) underwent suture closure of the ASD, and 326 patients (98%) underwent patch closure. As part of the initial operation, 283 patients (85%) underwent suture closure of a left atrioventricular valve cleft, 17 patients (5%) underwent left atrioventricular valve annuloplasty, 5 patients (1.5%) underwent atrioventricular valve replacement,

Fig 2. Kaplan-Meier curve represents overall freedom from reoperation (**A**) and by the decade of the operation (**B**).

and 6 patients (1.8%) underwent left ventricular out-flow tract operation for relief of obstruction. The post-operative hospital stay ranged from 5 to 46 days (median, 9 days; Q1, 8 days; Q3, 11 days). The median duration of follow-up for these 334 patients was 19 years (Q1, 10 years; Q3, 29 years).

Survival. There were 41 deaths observed. The esti-

mated survival in the 334 patients was 97% 30 days after operation, 94% at 5 years, 93% at 10 years, 87% at 20 years, 85% at 30 years, and 76% at 40 years, compared with 100%, 99%, 98%, 97%, 94%, and 92% in an age- and sex-matched control population, respectively ($P < .001$; Fig 1). Ten of these deaths occurred less than 30 days after the primary opera-

Fig 3. Kaplan-Meier curve represents overall postoperative freedom from occurrence of left atrioventricular valve regurgitation for patients with greater than mild left atrioventricular valve regurgitation (**A**) and separated by the decade of the operation (**B**).

tion. All of these early deaths occurred before 1980.

There were 31 late deaths. For long-term survival (>30 days), the following variables were associated with longer survival when we controlled for decade of operation: suture closure of the cleft (relative risk [RR],

0.4; 95% confidence interval [95% CI], 0.2-0.9; $P = .026$) and age at operation less than 20 years (RR, 0.2; 95% CI, 0.1-0.4; $P = .001$). The presence of a complete cleft suggested improved survival (RR, 0.5; 95% CI, 0.3-1.1; $P = .07$).

The reported cause of death was determined for 33 of the 41 deaths. There were 24 reported cardiovascular-related deaths. Additionally, there were 3 deaths from drowning, 3 deaths from motor vehicle accidents, 8 deaths from unknown cause, and 3 noncardiac deaths.

There was only 1 death among the 18 patients with Down syndrome. Hence death for patients with or without Down syndrome was similar.

Reoperation. Reoperation was performed for 38 patients (11%; Fig 2). One patient died at reoperation, and 1 additional patient died within 30 days of reoperation. The median interval between the primary repair and the subsequent reoperation was 17.8 years (Q1, 7.6 years; Q3, 28.2 years). The estimated incidence of reoperation was 3% at 1 year after initial operation, 6% at 5 years, 8% at 10 years, 12% at 20 years, 17% at 30 years, and 22% at 40 years. At reoperation, there were 7 incidents of residual ASD closure, 5 of which were at the first reoperation and 2 were at subsequent reoperation. There were 5 incidents of closure of a left atrioventricular valve cleft, 6 incidents of atrioventricular valve annuloplasty, 14 incidents of atrioventricular valve replacement, and 8 incidents for the relief of left ventricular outflow tract obstruction. Some patients had combinations of these procedures as part of one operation. After we controlled for the decade of the operation, patients who had closure of the cleft of the left atrioventricular valve at their primary operation had a suggested lower need for reoperation (RR, 0.5; 95% CI, 0.3-1.1; $P = .068$).

Left atrioventricular valve regurgitation. Postoperative left atrioventricular valve regurgitation was documented in 230 patients (69%; Fig 3, A). Clinical, Doppler echocardiographic, or angiographic evidence of left atrioventricular valve regurgitation was present in 141, 128, and 26 patients, respectively. The severity of the left atrioventricular valve regurgitation was moderate in 21 patients and moderate-severe in 21 patients (Table II). Left atrioventricular valve regurgitation developed in 6 patients after the first reoperation. For the purpose of the Kaplan-Meier survival estimates, these patients were censored at reoperation. Of the 224 patients with regurgitation before reoperation, the median interval from primary operation to the diagnosis of left atrioventricular valve regurgitation was 0.1 years (Q1, 0.02 years; Q3, 6.6 years). The estimated incidence for diagnosis of regurgitation was 34% at 30 days after operation, 41% at 1 year, 51% at 5 years, 57% at 10 years, 66% at 20 years, 74% at 30 years, and 89% at 40 years.

After we controlled for the decade of the operation, increased age at operation was associated with lower occurrence of left atrioventricular valve regurgitation

Table II. Severity of left atrioventricular valve regurgitation on the basis of clinical, Doppler echocardiographic, or angiographic findings

Severity	No. of patients (%)
Unknown	35 (15)
Trivial	17 (7)
Mild	128 (56)
Mild-moderate	8 (4)
Moderate	21 (9)
Moderate-severe	2 (1)
Severe	19 (8)

(Fig 3, B). Patients who underwent operation and who were older than 20 years showed a lower risk of left atrioventricular valve regurgitation (RR, 0.6; 95% CI, 0.4-0.9; $P = .01$).

Of the 31 patients who underwent reoperation after diagnosis of left atrioventricular valve regurgitation, 25 patients had some type of atrioventricular valve repair during reoperation, including atrioventricular valve replacement (11 patients), atrioventricular valvuloplasty (6 patients), atrioventricular valve annuloplasty (6 patients), and closure of atrioventricular valve cleft (4 patients). Some patients had combinations of these procedures during their first reoperation.

Left atrioventricular valve stenosis. Left atrioventricular valve stenosis was identified in 19 patients (6%) after operation. For 15 of these 19 patients, the mean transvalvular gradient was 7 mm Hg (Q1, 4 mm Hg; Q3, 10 mm Hg). A complete cleft, partial cleft, or parachute valve was present in 13, 3, and 1 patients, respectively. In 2 patients the anatomy was unclear. Three of these patients were identified after their first reoperation and were censored at reoperation. Of the remaining 16 patients in whom the diagnosis of left atrioventricular valve stenosis was made before any reoperation, the median interval from their primary operation to the diagnosis of left atrioventricular valve stenosis was 7.3 days (Q1, 3.6 days; Q3, 4.1 days). The estimated incidence of diagnosis of left atrioventricular valve stenosis was 3% 30 days after reoperation, 4% at 5 years, 5% at 10 years, 5% at 20 years, and 6% at 30 years. After we controlled for the decade of the operation, increased age at operation was associated with a greater occurrence of left atrioventricular valve stenosis. Specifically, patients more than 40 years of age who had undergone primary repair demonstrated an increased risk for the development of left atrioventricular valve stenosis (RR, 4.26; 95% CI, 1.5-12.4; $P = .01$).

Three patients underwent left atrioventricular valve replacement after the diagnosis of left atrioventricular valve stenosis.

Table III. Distribution of perioperative and long-term arrhythmias

Arrhythmia type	No. of perioperative arrhythmias* (%)	No. of long-term arrhythmias† (%)	Total arrhythmias (%)
PSVT	18 (5)	12 (4)	24 (7)
Atrial fibrillation	7 (2)	21 (6)	25 (8)
Atrial flutter	7 (2)	6 (2)	13 (4)
Complete AV block	5 (2)	4 (1)	9 (3)
Premature atrial contractions	1 (<1)	1 (<1)	2 (1)
Premature ventricular contractions	1 (<1)	2 (1)	3 (1)

PSVT, Paroxysmal supraventricular tachycardia; AV, atrioventricular.

*Less than 30 days after operation.

†More than 30 days after operation.

Left atrioventricular valve regurgitation or stenosis. There were 228 patients who were diagnosed with either left atrioventricular valve regurgitation or left atrioventricular valve stenosis before any reoperation. The estimated incidence of left atrioventricular valve regurgitation or stenosis was 36% 30 days after the operation, 43% at 1 year, 52% at 5 years, 58% at 10 years, 67% at 20 years, 75% at 30 years, and 89% at 40 years.

Left ventricular outflow tract obstruction. Left ventricular outflow tract obstruction was identified in 36 patients (11%). In 4 of these patients the diagnosis of obstruction was made after their first reoperation, and they were censored at reoperation. Of the 32 patients with obstruction before reoperation, the median interval from primary operation to diagnosis of obstruction was 4.9 years (Q1, 0.18 years; Q3, 15.88 years). The estimated incidence for diagnosis of obstruction was 3% 30 days after operation, 6% at 5 years, 7% at 10 years, 10% at 20 years, 13% at 30 years, and 16% at 40 years. After we controlled for the decade of the operation, there were no variables associated with the occurrence of left ventricular outflow obstruction.

Of the 32 patients who were diagnosed with left ventricular outflow tract obstruction subsequent to their primary operation, 10 patients underwent reoperation. Seven of these 10 patients received left ventricular outflow tract reconstruction at reoperation. Of these 7, 6 patients underwent reoperation at the Mayo Clinic, and details of the anatomy of and the relief of the obstruction are available. All 6 patients had a subaortic fibrous (5 patients) or fibromuscular (1 patient) ring. Three of the 6 patients also had septal hypertrophy that con-

tributed to the obstruction. One patient had vegetation on the noncoronary cusp of the aortic valve and obstruction at the midmuscular level because of the anomalous location of the anterior papillary muscle of the left atrioventricular valve. All 6 underwent resection of the subaortic membrane and septal myectomy. In addition, 1 patient underwent excision of some papillary muscle tissue. One year after the reoperation, 1 patient required a modified Konno procedure for persistent/recurrent left ventricular outflow tract obstruction.

Residual or recurrent ASD. Residual or recurrent ASD was identified in 12 patients during follow-up. Seven of these patients had closure of the ASD during reoperation, and 5 patients had no surgical intervention. The median interval from primary surgery to the diagnosis of residual or recurrent ASD was 10.6 years (Q1, 2.8 years; Q2, 22.6 years).

Arrhythmia. Early postoperative arrhythmias (<30 days) were identified in 37 patients. These arrhythmias included paroxysmal supraventricular tachycardia (18 patients), atrial fibrillation (7 patients), atrial flutter (7 patients), complete atrioventricular dissociation (5 patients), and premature atrial (1 patient) and ventricular contractions (1 patient). Some patients may have experienced more than one type of arrhythmia within 30 days of the primary operation.

Arrhythmias occurring more than 30 days after operation that required treatment developed in 46 patients (14%). These arrhythmias included paroxysmal supraventricular tachycardia (12 patients), atrial fibrillation (21 patients), atrial flutter (6 patients), complete atrioventricular dissociation (4 patients), premature atrial contractions (1 patient), and ventricular contractions (2 patients). Some patients may have experienced more than one type of arrhythmia. The median interval from primary repair to the onset of arrhythmia (long-term) was 11.1 years (Q1, 6.7 years; Q3, 23.9 years; Table III). The occurrence of arrhythmias increased with increasing age at primary operation (RR, 1.05; 95% CI, 1.03-1.07; $P = .0001$).

Postoperative supraventricular arrhythmias (atrial flutter, fibrillation, or paroxysmal supraventricular tachycardia) were observed in 42 patients (14%). The occurrence of supraventricular arrhythmias, adjusted for the decade of the operation, increased with increasing age at operation (RR, 1.05 years; 95% CI, 1.03-1.07; $P = .0001$). The percentage of patients who exhibited supraventricular arrhythmias and who underwent operation in the first, second, third, fourth, and fifth or greater decade of life was 9%, 16%, 20%, 26%, and 47%, respectively. In addition, patients who had suture closure of the left atrioventricular valve cleft

were less likely to have postoperative arrhythmias than patients who did not have closure of the cleft (RR, 0.4; 95% CI, 0.2-0.9; $P = .0174$).

Complete atrioventricular block occurred in 9 patients (2.7%), 5 patients after operation and 4 patients late. There were no cases of complete atrioventricular block in patients who had primary repair after 1979. Permanent pacemakers were implanted in 11 patients between 1967 and 1997, whose primary repairs occurred before 1987.

Bacterial endocarditis. Bacterial endocarditis was documented in 7 patients (2%). The median interval from the primary operation to this diagnosis was 8 years (Q1, 0.26 years; Q3, 23 years; range, 0.16-27 years).

Discussion

In a study of 144 patients with uncorrected partial atrioventricular septal defect, Weyn and colleagues⁷ found only 8 patients older than 30 years of age, suggesting an important effect of this lesion on long-term survival. Somerville¹¹ reviewed the factors responsible for the disability and death in 27 of 122 patients with partial ASD who were not treated surgically. Arrhythmia was the most common cause of deterioration and occurred in 25% by age 30 years and in 80% by age 45 years. Arrhythmia or atrioventricular block was responsible for 11 of 14 deaths that occurred after age 30 years. Except for rare cases in which the ASD is quite small, this defect should be repaired.^{5,6}

Survival. Hospital or 30-day mortalities have ranged from 5.5% to 10%. In the current study, it was 3%. The variables associated with operative or 30-day deaths have been inconsistent from study to study.

Losay and colleagues¹² reported 5- and 10-year survival of 86% and 81%, respectively, for a cohort of 92 patients who underwent operation between 1955 and 1975. Burke and colleagues,¹⁴ studying 33 patients who underwent operation between 1972 and 1994, reported a 5-year survival of 89%. These investigators did not analyze the determinants of late death.

In the current study, the long-term survival at 5, 10, 20, and 40 years were 94%, 93%, 87%, and 76%, respectively. Age less than 20 years at operation and suture approximation of the left atrioventricular valve cleft were associated with better long-term survival. It is possible that, for those patients in whom the cleft was not sutured, there were associated anatomic abnormalities that precluded suture closure. Hence for patients in whom the cleft could not be closed, increased surveillance with the expectation of increased risk of late morbidity and death seems appropriate.

Reoperation. Reoperation was necessary for 11% of the patients. Others have reported reoperation rates of 8.6%,¹² 7.6%,¹³ 6%,¹⁴ and 22.6%.¹⁵ These studies, however, had shorter follow-up times than the present study. Considering the spectrum of abnormalities of the left atrioventricular valve in this condition, it is not surprising that left atrioventricular valve regurgitation was the most common reason for reoperation. Although we found no predictors of reoperation, there was a suggestion that failure to suture the left atrioventricular valve cleft at the original operation was predictive of reoperation.

Left atrioventricular valve stenosis and regurgitation. Assessing the presence, absence, degree, and importance of left atrioventricular valve regurgitation in a study spanning 40 years is difficult because of the changes in technology of assessment of left atrioventricular valve regurgitation. With the advent of Doppler echocardiographic technology, it has become easier to detect left atrioventricular valve regurgitation. Hence it is impossible to know whether the presence, absence, degree, and importance of left atrioventricular valve regurgitation have changed over the years with changes in patient selection for operation, timing of operation, and operative techniques. Although we found a progressively higher occurrence of left atrioventricular valve regurgitation with an increasing length of follow-up, this simply may reflect greater sensitivity of the techniques (Doppler echocardiography) available to measure regurgitation. We did find that patients who had initial repair at more than 20 years of age had a lower incidence of postoperative left atrioventricular valve regurgitation than those whose initial repair occurred at less than 20 years of age. This probably reflects the fact that patients who undergo operation at younger ages have more severe malformation of the left atrioventricular valve than patients who reach an older age before operation. Alternatively, it may reflect a more aggressive approach to the elimination of the valve regurgitation in older patients. Others¹⁵ have observed that the degree of preoperative left atrioventricular valve regurgitation predicts postoperative valve regurgitation.

The rarity of late occurrence of significant left atrioventricular valve stenosis is reassuring in view of past concerns that suture closure of the cleft of the left atrioventricular valve would lead to a high incidence of postoperative stenosis.

Left ventricular outflow tract obstruction. Subaortic stenosis after repair of partial ASD is an uncommon but recognized problem. The reported incidence is 3% to 7%.^{15,17-25} We found an incidence of 11%. With the availability of Doppler echocardi-

graphic techniques, left ventricular outflow tract obstruction may be diagnosed more readily than it was before Doppler echocardiographic techniques were available. The presence of left ventricular outflow tract does not always warrant reoperation. Because of the elongated left ventricular tract in patients with endocardial cushion defects, adequate relief of the obstruction may be challenging.

Arrhythmia. It is generally accepted that patients with significant left-to-right shunt from an ASD have an increasing risk of the development of atrial arrhythmias with increasing age. This was true for patients with secundum ASD.²⁶ In the current study, we also found that the occurrence of supraventricular arrhythmias was related to older age at operation. These data support the argument for younger rather than older age at primary repair.

Complete atrioventricular block is not purely a surgical complication. Six of the 27 patients with ostium primum defect in Somerville's series¹¹ manifested clinical deterioration because of the atrioventricular block without undergoing surgical repair.

Conclusions

This study defines the expected occurrence rates for left atrioventricular valve dysfunction, left ventricular outflow tract obstruction, and arrhythmias. This information is important for the counseling of patients about the expected outcome and possible adverse outcome events after this operation. In addition, it provides guidance for clinicians as to appropriate follow-up evaluation of these patients.

Outcomes studies such as this rely on data acquisition that is dependent on scheduled follow-up visits. This, of course, makes it difficult to know the actual time that a specific event developed and introduces difficulty in timed event analysis.

The following conclusions can be drawn from this study: (1) although long-term survival is good, it is lower than that of the general population; (2) reoperation was necessary for 11% of the patients; (3) postoperative left atrioventricular valve regurgitation is common and is the most frequent reason for reoperation; (4) it is important to close the left atrioventricular valve cleft at primary operation; (5) left ventricular outflow tract obstruction occurred in 36 patients (11%) but required operation in only 7 patients; and (6) postoperative supraventricular arrhythmias are more common for older patients.

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Commentary

The in-depth and careful study of outcomes related to congenital heart disease and its management is of increasing importance, given the growing population of adult survivors. Studies of outcomes in adult patients who received follow-up in specialized clinics can be misleading, because the denominator or cohort from which these patients are derived is usually not defined. Likewise, outcomes studies from pediatric institutions tend to terminate near the age of 18 years. Studies such as that by El-Najdawi and associates, in which an entire inception cohort is carefully traced and followed to the present, are difficult but necessary to provide accurate information about prognosis and to identify potentially higher risk subgroups that may require altered surveillance and preventative management.

Nonetheless, the article is largely descriptive, with some important flaws in the data analysis that limit ready acceptance of some of their findings. The "Users Guides to the Medical Literature" series of articles succinctly highlights the key issues in the critical appraisal of an article concerning prognosis.¹ The study population is well defined and likely representative of patients who have undergone repair of partial atrioventricular canal defects. Because significant changes in diagnosis and management are likely to have occurred over the 40-year period, a more detailed analysis of outcomes and associated factors over time should have been included. Also, outcomes from smaller case series from a single institution are less likely to be generalizable to any other institution than outcomes from a larger case

series pooled from a representative sample of institutions. The follow-up is sufficiently complete, given the limitations of tracing and contacting patients no longer being followed at the originating institution. Although the outcomes of death and reoperation are objective, left atrioventricular valve regurgitation and stenosis, left ventricular outflow obstruction, and supraventricular arrhythmias were mainly assessed in a subjective manner with evolving technologies and varying degrees of accuracy, completeness, and interpretation as recorded by multiple levels of providers in the medical record. The definitions for these latter outcomes are thus necessarily vague. More details about the medical questionnaire should be given, particularly regarding content, validity, and reliability as completed by the patients and nonstudy providers. In addition, the analysis of some of the morbidity outcomes as discretely timed events is erroneous, because these outcomes more accurately take on varying grades of severity that evolve over time. The patients (usually) do not suddenly experience the development of a threshold grade of left atrioventricular valve regurgitation or stenosis at a given date. Also, the dates used to define these outcome events (date of first notation in the medical record) are largely dependent on the providers' schedule of follow-up assessment. The error in this method for analyzing the data is clearly illustrated in Fig 3, *B*, of the article, in which it might appear that there is a significant trend toward earlier development of left atrioventricular valve regurgitation with the more recent experience, when, in fact, this probably represents improved detection with the advent of echocardiography.

An important aspect of an article about prognosis is the analysis of associated factors of prognostic importance; otherwise, the study is purely descriptive and of limited value. In the analysis of prognostic factors, the authors arbitrarily divided the cohort into 3 groups on the basis of the patients' date of repair procedure and entered this variable into models that assumed discretely timed events and presupposed that this provided adequate adjustment for changes that may have occurred over a 40-year period. The arbitrary categorization of continuously measured variables is rarely justified and diminishes both statistical power and the ability to elucidate more complex associations. Age at repair procedure, another potentially important prognostic factor, was also arbitrarily categorized. When exploring potential prognostic factors in multivariable analysis, it is very simplistic and often erroneous to assume that entering the date of repair into the model adequately adjusts for unmeasured trends over time in prognostic factors and outcomes. This is in addition to the fact that, before prognostic factors were examined,

the appropriate method of modeling of the outcome should have been performed (not a timed-event analysis), and the relationships between potential prognostic factors should have been explored.

How might the authors have improved the quantity and quality of evidence provided by their study? It would have been ideal if all surviving patients had undergone a standardized assessment in the same manner within a defined end-point interval, preferably performed at the study institutions by the dedicated investigators. This would supplement the study with important and more valid cross-sectional information about current outcomes in a defined cohort. A more detailed analysis of trends in patient characteristics and outcomes over time should have been performed. From the patients' perspective, outcomes begin at birth (and maybe even before birth), not at repair. Perhaps an analysis by birth cohorts (grouping the patients by their date of birth) should also have been performed, recognizing that the study results are relevant only to those patients with partial atrioventricular canal defects who underwent repair procedures. Other than survival and reoperation, the longitudinal aspects of this study are weak, given the limitations of the definitions. Statistical methods for the analysis of repeated or serial measurements are currently available for the modeling of evolving longitudinal outcomes and the testing of associated prognostic factors. The study should have collected more quantitative data longitudinally over all available assessments (particularly grade of valve regurgitation or stenosis and severity of left ventricular outflow obstruction) and used these analytic techniques. This was likely not feasible or sufficiently valid over the long period of the study. A less optimal but more feasible alternative would have been to improve the analysis of reoperation, particularly by identifying freedom from

reoperation for particular causes. Although the definition of left atrioventricular valve residual or recurrent defects and left ventricular outflow obstruction may be subjective and problematic, one measure of the significance of these defects is the need for reoperation, an end point that is discrete and subject to less debate. The number of potential prognostic factors reported in this study is small; perhaps a more detailed and enriched data set might have been created. Health status and quality of life are important outcomes to patients; perhaps patients might have completed one of the currently available validated questionnaires, especially because most of the subjects were either seen at the study institution or were contacted to complete a medical questionnaire.

Despite these missed opportunities, the study by El-Najdawi and associates represents an excellent attempt at a more valid and comprehensive assessment of outcomes, and the authors are to be commended on the excellent follow-up of a well-defined patient series. Nonetheless, the reported results related to medical morbidity must be viewed in light of important threats to validity. It should also be recognized that if only perfect studies were published, much of the available evidence currently guiding medical practice would not exist.

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