ATRIAL ARRHYTHMIA AFTER SURGICAL CLOSURE OF ATRIAL SEPTAL DEFECTS IN ADULTS

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ABSTRACT

Background Atrial flutter and atrial fibrillation are causes of morbidity in adults with an atrial septal defect. In this study, we attempted to identify risk factors for atrial flutter and fibrillation both before and after the surgical closure of an atrial septal defect.

Methods We searched for preoperative and postoperative atrial flutter or fibrillation in 213 adult patients (82 men and 131 women) who underwent surgical closure of atrial septal defects because of symptoms, a substantial left-to-right shunt (ratio of pulmonary to systemic blood flow, >1.5:1), or both at Toronto Hospital between 1986 and 1997.

Results Forty patients (19 percent) had sustained atrial flutter or fibrillation before surgery. As compared with the patients who did not have atrial flutter or fibrillation before surgery, those who did were older (mean [±SD] age, 59±11 vs. 37±13 years, $P<0.001$) and had higher mean pulmonary arterial pressures (25.0±9.7 vs. 19.7±8.2 mm Hg, $P=0.001$). There were no perioperative deaths. After a mean follow-up period of 3.8±2.5 years, 24 of the 40 patients (60 percent) continued to have atrial flutter or fibrillation. The mean age of these patients was greater than that of the 16 who converted to sinus rhythm ($P=0.02$). New-onset atrial flutter or atrial fibrillation was more likely to have developed at follow-up in patients who were older than 40 years at the time of surgery than in those who were 40 or younger (5 of 67 vs. 0 of 106, $P=0.008$). Late events (those occurring more than one month after surgery) included stroke in six patients (all but one with atrial flutter or fibrillation, one of whom died) and death from noncardiac causes in two patients. Multivariate analysis showed that older age (>40 years) at the time of surgery ($P=0.001$), the presence of preoperative atrial flutter or fibrillation ($P<0.001$), and the presence of postoperative atrial flutter or fibrillation or junctional rhythm ($P=0.02$) were predictive of late postoperative atrial flutter or fibrillation.

Conclusions The risk of atrial flutter or atrial fibrillation in adults with atrial septal defects is related to the age at the time of surgical repair and the pulmonary arterial pressure. To reduce the morbidity associated with atrial flutter and fibrillation, the timely closure of atrial septal defects is warranted. (N Engl J Med 1999;340:839-46.)

ATRIAL flutter and atrial fibrillation are well-documented sequelae of atrial septal defects, associated with substantial morbidity and, occasionally, death.[1-3] The prevention of atrial flutter or fibrillation or the restoration of sinus rhythm in patients with these defects is therefore desirable. The surgical closure of atrial septal defects leads to improved functional status and reduces the risk of right-sided heart failure and progressive or severe pulmonary hypertension.[1,4,5] Atrial flutter or fibrillation, however, has often persisted at late follow-up (>25 years) in patients who have undergone surgical closure after childhood (reported incidence, 41 to 59 percent).[1,4-7]

Evidence suggests that the Cox maze procedure,[8] performed at the time of closure of an atrial septal defect, is feasible and is associated with good short-term and intermediate-term maintenance of sinus rhythm.[9-11] This finding has led several groups to advocate the use of surgical procedures to target atrial flutter and fibrillation at the time of the surgical repair of an atrial septal defect in patients considered to be at high risk for these arrhythmias.[9-12] However, advances in diagnostic and surgical techniques and new guidelines for the management of atrial fibrillation[13] have altered the characteristics of patients with atrial septal defects referred for surgical closure and possibly their outcomes. Data are required to identify patients with atrial septal defects who are currently at risk for atrial flutter or fibrillation despite closure of the defect. We undertook this study to evaluate the incidence and predictors of atrial flutter or fibrillation and the associated outcomes of surgery to close an atrial septal defect in a contemporary cohort of adult patients.

METHODS

Patients and Collection of Data

All patients who underwent surgical closure of atrial septal defects at Toronto Hospital between June 1986 and June 1997 were identified retrospectively from the hospital's cardiovascular surgical data base. The patients were referred for surgery by their cardiologists because they had symptoms, because they had a substantial left-to-right shunt (ratio of pulmonary to systemic blood flow [Qp:Qs], >1.5:1), or because they had both. We excluded

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patients with a persistent foramen ovale or a small atrial septal defect (without evidence of right ventricular volume overload) who were undergoing surgery for episodes of paradoxical embolism. Patients referred for reoperation of previously repaired atrial septal defects and those with complex congenital heart disease were also excluded. Finally, we excluded foreign patients because of the difficulty of obtaining follow-up information. Preoperative and perioperative data, including functional status, the nature of the atrial septal defect, whether cardiac catheterization had been performed, and surgical reports, were obtained from hospital records. The Qp:Qs ratio was determined by oximetry. All surgery was performed by means of cardiopulmonary bypass with the use of bicaval and ascending aortic cannulation. For myocardial protection, moderate systemic hypothermia was used in most cases, with cold potassium-enriched cardioplegia being used when a complicated patch repair was required.

Follow-up for all patients included in the study was conducted between September 1997 and January 1998 and consisted of evaluations at the Toronto Congenital Cardiac Centre for Adults, contact with the patients' physicians, and written questionnaires and telephone interviews with patients. The study protocol was approved by the Toronto Hospital Human Ethics Committee. The patients' physicians were asked to provide additional preoperative information, when such information was required. Information about postoperative death, cardiac rhythm, stroke, heart failure, functional status (as defined by the New York Heart Association [NYHA] classification), the need for reoperation, residual atrial septal defects, systemic hypertension, and type of medical therapy needed was obtained at the time of follow-up. The arrhythmia group comprised all patients presenting with documented sustained atrial flutter or fibrillation and associated symptoms. Patients who had asymptomatic, nonsustained episodes of atrial arrhythmia during Holter monitoring were not included in this group. We did not differentiate between chronic and paroxysmal atrial flutter or fibrillation.

We cross-classified patients according to the presence of atrial flutter or fibrillation before surgery and its presence at the latest follow-up visit after the first postoperative month (defined as late atrial flutter or fibrillation) as follows: group A had atrial flutter or fibrillation both before surgery and at the latest follow-up visit; group B had atrial flutter or fibrillation before surgery but no evidence of recurrence after surgery (i.e., the patient converted to and remained in sinus rhythm); group C was in sinus rhythm before surgery but had atrial flutter or fibrillation at the latest follow-up visit; and group D was in sinus rhythm both before surgery and at the latest follow-up visit.

Statistical Analysis

We analyzed the data using SPSS for Windows (version 7.0, SPSS, Chicago). Descriptive data for continuous variables are presented as means ±SD or as medians with ranges, when appropriate. Discrete variables were analyzed by chi-square or Fisher's exact tests. Continuous data were analyzed by the two-sample t-test or the Wilcoxon rank-sum test; they were analyzed across the four subgroups with the Kruskal–Wallis test. If the result of the Kruskal–Wallis test was significant ($P<0.05$), then pairwise comparisons (group A vs. group B and group C vs. group D) were performed with the Wilcoxon rank-sum test; for pairwise testing, the level of significance was adjusted for multiple comparisons (two-sided test, $P<0.025$). Linear regression analysis of the interaction between the age of the patient at the time of surgical repair and the pulmonary arterial pressure was performed.

The probability of remaining free of late atrial flutter or fibrillation over time was displayed with Kaplan–Meier plots. Univariate analysis of predictors of late atrial flutter or fibrillation was performed with the Cox proportional-hazards model. Univariate predictors with a significance level of <0.20 were entered into a multivariate Cox proportional-hazards model with the use of a backward-elimination algorithm.[14] The level of significance for the multivariate model was set at 0.05. For the purpose of multivariate analysis, univariate predictors that were highly correlated with each other (those with a correlation coefficient of >0.70) were combined into a composite variable. A secondary analysis was performed with the subgroup of 149 patients for whom preoperative cardiac-catheterization data were available.

RESULTS

Preoperative Data

Two hundred eighteen consecutive patients who underwent surgical closure of an isolated atrial septal defect fulfilled the criteria for inclusion in the study (Table 1). An additional 11 patients with a small atrial septal defect who were undergoing surgery for episodes of paradoxical embolism, 4 patients who had had previous repair of an atrial septal defect, and 5 foreign patients were excluded. We were unable to obtain follow-up data on five patients (2.3 percent); information from the provincial death registry indicated that they were alive in 1997. The remaining 213 patients (82 men and 131 women), who made up the study population, underwent closure of an atrial septal defect at a mean (±SD) age of 41±14 years (median, 40; range, 16 to 80). Of the patients referred for surgery by their physicians, 68 percent were referred because of symptoms (exertional dyspnea, with varying degrees of decreasing exercise capacity in 95 percent, heart failure in 3 percent, and presyncope or syncope in 2 percent), and the remaining patients were referred because they had a substantial left-to-right shunt (Qp:Qs, >1.5:1). The NYHA functional class was I or II in 70 percent of the patients, III in 29 percent, and IV in 0.5 percent. The diagnosis was established by echocardiography in 199 patients (93 percent) and at the time of cardiac catheterization in 14 patients. One hundred forty-nine patients (70 percent) underwent cardiac catheterization (Table 1), mainly so that pulmonary arterial pressure could be assessed and coexisting coronary artery disease could be identified. There was a weak correlation between age at the time of surgical repair and mean pulmonary arterial pressure ($r=0.46$, $P<0.001$), but not between the magnitude of the left-to-right shunt and mean pulmonary arterial pressure.

Forty patients (19 percent) had documented sustained atrial flutter or fibrillation before surgery, with exertional dyspnea and decreasing exercise capacity in 32 of these patients, congestive heart failure in 5, and presyncope or syncope in 3. Twenty-one patients had chronic atrial flutter or fibrillation; the remainder had paroxysmal atrial flutter or fibrillation that required one or more electrical or pharmacologic cardioversions. Eleven of the 40 patients had atrial flutter, and 35 had atrial fibrillation (6 of these patients initially presented with atrial flutter but had atrial fibrillation before surgery) (Table 2).

Thirty-nine of the 40 patients were receiving antiarrhythmic-drug therapy at the time of surgical repair. Thirty-three of these patients were taking digoxin,

TABLE 1. CHARACTERISTICS OF THE PATIENTS.*

CHARACTERISTIC	VALUE
Demographic data (n=213)	
Age at repair — yr	
Mean	41±14
Median	40
Range	16–80
Sex — no. (%)	
Male	82 (38)
Female	131 (62)
Type of atrial septal defect — no. (%)	
Secundum	179 (84)
Associated partial anomalous pulmonary venous drainage	2 (1.1)
Sinus venosus	
Superior vena caval	24 (11)
Associated partial anomalous pulmonary venous drainage	19 (79)
Inferior vena caval	3 (1.4)
Primum	7 (3.3)
Data on cardiac catheterization (n=149)	
Age at repair — yr†	
Mean	45.6±15
Range	16–80
Left-to-right shunt — Qp:Qs ratio	
Mean	2.4±0.7
Range	1.5–5.4
Systolic pulmonary arterial pressure — mm Hg	
Mean	35.9±15.2
Range	18–100
Diastolic pulmonary arterial pressure — mm Hg	
Mean	13.3±6.9
Range	4–50
Pulmonary arterial pressure — mm Hg	
Mean	21.4±9.2
Range	8–60
Pulmonary arterial wedge pressure — mm Hg	
Mean	10.5±4.4
Range	4–22
Surgical data (n=213)	
Duration of bypass during surgery — min	
Mean	42.8±24
Median	35
Range	13–141
Duration of cross-clamping of the aorta during surgery — min	
Mean	25.2±17
Median	20
Range	4–90

*Plus–minus values are means ±SD.

†Only the 149 patients who underwent cardiac catheterization are included. The age of the patients who did not undergo cardiac catheterization was 31±8 years.

24 of whom were taking it with other antiarrhythmic drugs. The patients who had atrial flutter or fibrillation were significantly older at the time of surgical repair and had a higher mean pulmonary arterial pressure than those who did not. The magnitude of the left-to-right shunt was similar in the two groups.

Perioperative Data

There were no perioperative deaths. Defects were repaired either by primary suture closure (53 percent) or by autologous pericardial patch (47 percent). Twenty-six patients underwent concomitant cardiac procedures (mitral-valve repair in 8, tricuspid-valve repair in 4, and coronary-artery bypass grafting in 14). The incidence of perioperative complications was 9 percent (pericarditis in 11 patients, bleeding requiring reoperation in 3, congestive heart failure in 2, and tamponade, transient ischemic attack, and deep venous thrombosis in 1 each).

Early postoperative arrhythmia (within 30 days after surgery) occurred in 46 patients (atrial fibrillation in 32, atrial flutter in 6, and junctional rhythm in 8) and was correlated with preoperative atrial flutter or fibrillation ($P<0.001$ by the chi-square test). Twelve of the 40 patients (30 percent) with preoperative atrial flutter or fibrillation had spontaneous conversions to normal sinus rhythm by the time they were discharged from the hospital, with no evidence of recurrence of atrial flutter or fibrillation thereafter. Three patients without atrial arrhythmias required insertion of a pacemaker, two for persistent sinus-node dysfunction and one for complete atrioventricular block.

Follow-up Data

Follow-up data are complete. At a mean duration of follow-up of 3.8±2.5 years from the time of surgical repair (median, 3 years; range, 0.5 to 10), all but three patients were alive. One patient (known to be in atrial fibrillation) died of stroke, and two died of cancer (one of lung cancer and the other of bladder cancer). Three patients underwent reoperation — one for residual atrial septal defect, one for mitral-valve replacement, and one for coronary-artery bypass. One hundred eighty-five patients (87 percent) had functional status of NYHA class I, and 28 (13 percent) had functional status of class II, indicating significant improvement from the preoperative status ($P<0.001$ by the chi-square test).

Twenty-four of the 40 patients (60 percent) with preoperative atrial flutter or fibrillation continued to have these arrhythmias at the latest follow-up visit (Fig. 1 and Table 3). All 24 were older than 40 years at the time of surgical repair, and their mean age was greater than that of the 16 patients who converted to sinus rhythm ($P=0.02$ by the Wilcoxon rank-sum test). In addition, atrial flutter or fibrillation developed in five other patients (all of whom were older than 40 years at the time of surgical repair) by the time the study concluded. All 29 patients with sustained atrial flutter or fibrillation at follow-up were receiving antiarrhythmic-drug therapy. Twenty-five were receiving digoxin, 17 of whom were also taking other antiarrhythmic drugs. For the patients in sinus rhythm preoperatively, those older than 40 years at the time of surgery had an 8 percent risk of late atrial flutter or fibrillation; in contrast, none of the 106 patients 40 years of age or younger at the time of

TABLE 2. PREOPERATIVE ATRIAL FLUTTER OR FIBRILLATION.*

VARIABLE	PATIENTS WITH ATRIAL FLUTTER (N=11)†	PATIENTS WITH ATRIAL FIBRILLATION (N=29)	PATIENTS WITH ATRIAL FLUTTER OR FIBRILLATION (N=40)	PATIENTS WITHOUT ARRHYTHMIA (N=173)	P VALUE‡
Age at repair (yr)	56±9	60±12	59±11	37±13	<0.001
Left-to-right shunt (Qp:Qs ratio)	2.5±0.8	2.4±0.7	2.4±0.7	2.4±0.7	0.78
Pulmonary arterial pressure (mm Hg)	24.9±6.1	25.1±11.5	25.0±9.7	19.7±8.2	<0.001
Pulmonary arterial wedge pressure (mm Hg)	10.6±4.1	12.7±5.1	12.0±4.7	9.6±4.2	0.08
NYHA class (%)§					<0.001¶
I			10.0	35.8	
II			37.5	39.9	
III			50.0	24.3	
IV			2.5	0	

*Plus–minus values are means ±SD. P values are for the comparisons between patients with atrial flutter or fibrillation and patients without arrhythmias. None of the differences between the patients with atrial flutter and the patients with atrial fibrillation were significant.

†Six patients who initially presented with atrial flutter, but who had atrial fibrillation before surgery, are included.

‡Comparisons between groups were calculated with the t-test unless otherwise specified.

§NYHA denotes New York Heart Association.

¶The comparison between groups was calculated with Fisher's exact test.

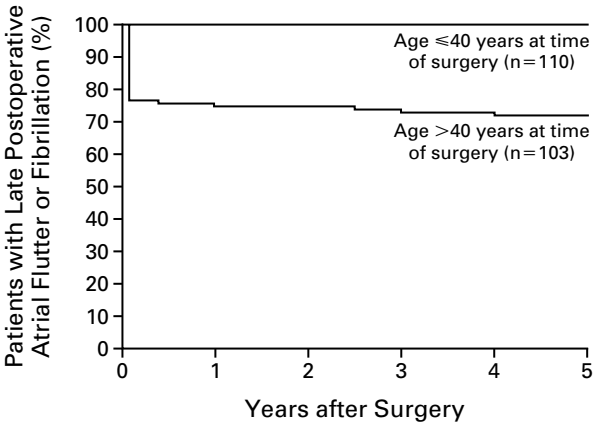

Figure 1. Kaplan–Meier Estimates of Late Postoperative Atrial Flutter or Fibrillation.

The initial downward slope of the curve for the patients older than 40 years at the time of surgery reflects the patients who had atrial flutter or fibrillation one month after surgery. All 24 of these patients had documented atrial flutter or fibrillation before surgery. The average follow-up period was 3.8±2.5 years (for all 213 patients).

surgery had late atrial arrhythmias (P=0.008 by Fisher's exact test).

Six patients had strokes during the follow-up period, one of whom died (Table 4). The NYHA class of all but one improved after surgery. None of the patients had a residual atrial septal defect on echocardiography. Five were known to be in atrial flutter or fibrillation during the follow-up period. Before their strokes, three patients were receiving warfarin, and two were receiving aspirin. All but one were receiving antiarrhythmic-drug therapy. Four patients were receiving additional therapy — two for heart failure and two for systemic hypertension. An additional patient presented with stroke, presumably due to paradoxical embolism, before surgery. This patient had no further embolic episodes after the surgical closure of a large atrial septal defect.

Predictors of Late Postoperative Atrial Flutter or Fibrillation

According to multivariate analysis, an age of more than 40 years at the time of surgical repair, the presence of preoperative and immediate postoperative (within 1 month after surgery) atrial flutter or fibrillation, and the presence of immediate postoperative junctional rhythm were independent predictors of persistent or new atrial flutter or fibrillation by the latest follow-up (Table 5). Secondary analysis in which data on cardiac catheterization were used did not yield additional predictors of late postoperative atrial flutter or fibrillation.

DISCUSSION

This study examined the incidence of and risk factors for atrial flutter or fibrillation in adult patients with atrial septal defects who were referred for surgery because they had symptoms, a substantial left-to-right shunt, or both. The findings of low perioperative morbidity, no perioperative mortality, and

TABLE 3. ATRIAL FLUTTER OR FIBRILLATION AT FOLLOW-UP.*

VARIABLE	GROUP A	GROUP B	GROUP C	GROUP D	P VALUE
All patients					
No. of patients	24	16	5	168	
Age at repair (yr)†	63±9	53±11	69±3	36±12	<0.001
Duration of follow-up (yr)	4.2±2.6	2.3±2.4	4.2±2.6	3.9±2.5	0.10
Age at repair >40/≤40 (no.)	24/0	12/4	5/0	62/106	<0.001‡
Patients who underwent cardiac catheterization					
No. of patients	23	16	5	105	
Left-to-right shunt (Qp:Qs ratio)	2.4±0.6	2.5±0.8	2.2±0.6	2.4±0.7	0.09
Pulmonary arterial pressure (mm Hg)§	24.9±7.4	25.1±12.6	31±4.6	18.7±7.4	<0.001
Pulmonary arterial wedge pressure (mm Hg)	13.5±5.5	9.9±2.4	9±2.8	9.7±4.2	0.19

*Plus–minus values are means ±SD. Group A is made up of the patients with atrial flutter or fibrillation before surgery and at the latest follow-up evaluation; group B those with atrial flutter or fibrillation before surgery but no evidence of recurrence since surgery; group C those in sinus rhythm before surgery with atrial flutter or fibrillation at follow-up; and group D those in sinus rhythm before surgery and at the latest follow-up. Unless otherwise specified, comparisons among all four groups were performed with the Kruskal–Wallis test.

†P=0.02 for the comparison between groups A and B, and P<0.001 for the comparison between groups C and D, both by the Wilcoxon rank-sum test.

‡Fisher's exact test was used to compare groups C and D.

§P=0.34 for the comparison between groups A and B, and P=0.001 for the comparison between groups C and D, both by the Wilcoxon rank-sum test.

TABLE 4. CHARACTERISTICS OF THE SIX PATIENTS WHO HAD STROKES AFTER SURGICAL CLOSURE OF AN ATRIAL SEPTAL DEFECT.*

PATIENT NO./SEX	AGE AT REPAIR	MEAN PULMONARY ARTERIAL PRESSURE	SHUNT	TYPE OF ARRHYTHMIA BEFORE SURGERY	TYPE OF CARDIAC RHYTHM AT HOSPITAL DISCHARGE	DURATION OF FOLLOW-UP	TYPE OF ARRHYTHMIA AT FOLLOW-UP	PRESENCE OF HYPERTENSION	PRESENCE OF HEART FAILURE	USE OF WARFARIN	USE OF ASPIRIN
	yr	mm Hg	Qp:Qs ratio			yr					
1/F	48	24	2.6	None	Junctional rhythm†	0.4	None	No	No	No	No
2/F	66	29	1.7	None	Atrial fibrillation	1	Atrial fibrillation	No	No	No	Yes
3/F	68	34	2.4	Atrial fibrillation	Atrial fibrillation	2	Atrial fibrillation	Yes	No	No	Yes
4/F	58	20	3.4	Atrial fibrillation	Sinus rhythm	3	Atrial fibrillation	No	No	Yes	No
5/F	74	31	3.0	Atrial fibrillation	Atrial fibrillation	2‡	Atrial fibrillation	Yes	Yes	Yes	No
6/F	60	37	1.7	Atrial fibrillation	Atrial fibrillation	8	Atrial fibrillation	No	Yes	Yes	No

*None of the six patients had a residual atrial septal defect.

†Transient junctional rhythm was detected in the immediate postoperative period.

‡The patient died after two years of follow-up.

symptomatic improvement in most of the patients in this series are additional evidence of the beneficial role of surgery. The persistence or development of atrial arrhythmia after surgical repair and its association with important morbidity, however, calls for further modifications in the management of atrial septal defects diagnosed during adulthood.

The age of the patient at the time of the surgical repair of the atrial septal defect was the main predictor of persistent or new arrhythmia after surgery. The explanation for the strength of this prognostic variable is almost certainly multifactorial.[15] Long-standing volume overload, varying degrees of pulmonary hypertension, and ventricular dysfunction have all been implicated in and may contribute to arrhythmogenesis. Atrial stretch,[16] in response to volume overload, prolongs atrial refractoriness in a heterogeneous manner, making the atria vulnerable to

TABLE 5. PREDICTORS OF LATE ATRIAL FLUTTER OR FIBRILLATION.

VARIABLE	RISK RATIO (95% CI)*	P VALUE
Univariate analysis		
Age at repair (per year)	1.1 (1.1–1.2)	<0.001
Male sex	1.3 (0.6–2.6)	0.50
NYHA class, ≥III†	2.6 (1.2–5.3)	0.01
Qp:Qs ratio, >2.5	0.9 (0.4–2.0)	0.74
Mean pulmonary arterial pressure, >20 mm Hg	4.1 (1.6–8.3)	0.003
Hypertension	5.0 (2.3–11.1)	<0.001
Heart failure	11.5 (4.8–27.2)	<0.001
Preoperative atrial flutter or fibrillation	38.1 (12.5–116.4)	<0.001
Atrial septal defect not in ostium secundum	1.4 (0.6–3.5)	0.44
Duration of bypass during surgery, >35 min	2.2 (0.8–6.2)	0.14
Duration of cross-clamping of the aorta during surgery, >20 min	1.9 (0.7–5.1)	0.20
Additional surgery‡	4.1 (1.8–9.1)	<0.001
Postoperative atrial flutter or fibrillation or junctional rhythm	24.8 (8.6–71.4)	<0.001
Multivariate analysis		
Age at repair (per year)	1.1 (1.0–1.1)	0.001
Preoperative atrial flutter or fibrillation	9.9 (2.7–36.7)	<0.001
Postoperative atrial flutter or fibrillation or junctional rhythm	3.9 (1.3–12.6)	0.02
NYHA class, >III†	1.0 (0.4–2.3)	0.09
Mean pulmonary arterial pressure, >20 mm Hg	1.2 (0.1–10.6)	0.64
Hypertension	1.6 (0.7–3.8)	0.43
Heart failure	2.1 (0.8–5.8)	0.13
Duration of bypass during surgery, >35 min	2.0 (0.3–12.1)	0.54
Duration of cross-clamping of the aorta during surgery, >20 min	1.2 (0.5–2.8)	0.98
Additional surgery‡	1.2 (0.5–3.0)	0.41

*CI denotes confidence interval.

†NYHA denotes New York Heart Association.

‡Additional surgery refers to surgery other than closure of an atrial septal defect (e.g., coronary-artery bypass).

the induction of fibrillation. Morillo et al.[17] showed a strong correlation between an increase of 40 percent or more in atrial area and the inducibility of sustained atrial flutter or fibrillation.

Likewise, the persistence of atrial flutter or fibrillation in older patients, found in this and previous studies, may be the result of established enlargement or electrophysiologic derangement of the right atrial wall, which may not resolve completely with closure of the atrial septal defect. Diastolic properties of both ventricles may also be involved in arrhythmogenesis.[18] The elevated pulmonary arterial wedge pressure in patients presenting with arrhythmia may be a reflection of increased left ventricular end-diastolic pressure. A "stiff" left ventricle has the potential to aggravate a preexisting left-to-right intracardiac shunt. Several mechanisms for reduced left ventricular compliance have been proposed, including ventricular–ventricular interaction,[19] abnormal interventricular septal motion,[20,21] and decreased left ventricular preload.[22] Older age may be another contributing factor.

Our data suggest that the relative increase in pulmonary arterial pressure in adult patients with atrial septal defects may be the result of older age. Currently, most patients in whom atrial septal defect is diagnosed do not have pulmonary vascular disease severe enough to preclude closure. This change in patient profile may be due to advances in imaging, facilitating a relatively early diagnosis. Clearly, the risk of pulmonary hypertension in older adults is now lower than previously reported,[2] and it is not one of the main reasons for recommending surgical closure of atrial septal defects in current practice.

In contrast, in this series, as in most previous studies,[1-5,23] the development of symptoms during adulthood was common. Over two thirds of our patients became symptomatic at a mean age of 41 years. Most of them, including the older patients,[7,23] improved clinically after surgery, as was demonstrated by changes in the NYHA class. Despite questions raised by Shah et al.[24] and Ward[25] regarding the prognosis of atrial septal defect in patients who have undergone surgical closure after childhood, the evidence is overwhelming that adult patients with this condition have improved functional status after surgery.[1,4,5,7,23,26] The recent report by Helber et al.[27] on cardiopulmonary testing confirms the previous clinical impression that exercise capacity is limited before the closure of an atrial septal defect in adulthood and improves thereafter. Helber et al. demonstrated restoration of cardiopulmonary function in adults with nonrestrictive atrial septal defects who underwent surgical closure at a mean age of 40 years.

It is a matter of concern that atrial flutter and fibrillation remain important causes of morbidity after surgery to repair an atrial septal defect in adulthood. It has been proposed that atrial flutter and fibrillation may be more responsive to drug therapy if surgery eliminates intracardiac shunting and if the size of the right atrium decreases.[15] However, atrial flutter and fibrillation remain problematic, primarily because of their persistent strong association with stroke, which occurred in six patients in our study, one of whom died. All but one of these six patients had documented atrial fibrillation during follow-up. None of the six patients had residual atrial septal defects that accounted for paradoxical embolism. Two patients were receiving aspirin, whereas three were receiving warfarin. The sixth patient, who had no history of atrial flutter or fibrillation before or after surgery, was known to be in junctional rhythm during the postoperative period. Systemic hypertension was present in two of the patients. The incidence of stroke among the patients in our study, however, appears to exceed the expected annual rates for older patients with chronic atrial flutter or fibrillation, even when corrected for coexisting factors.[28] Other

factors, such as persistently dilated pulmonary veins,[29] may contribute to thrombogenesis in older patients.

Older age and the presence of atrial flutter or fibrillation before or within one month after surgery were strong predictors of late atrial flutter or fibrillation in our study. Our data suggest that modification of the approach to adults with an atrial septal defect is needed. With the operative mortality associated with closure of atrial septal defects approaching zero, it is important to identify the subgroups of patients who can be expected to have long-term sequelae. Our data show that patients older than 40 at the time of surgery are at increased risk for cardiovascular events and, at the very least, need close surveillance. Konstantinides et al.[5] reported better outcomes for patients who underwent surgery than for those who received medical treatment for an atrial septal defect after 40 years of age. These authors emphasized that atrial arrhythmias may persist despite surgery. Data from our study and from previous studies[1,7] show that if we are to prevent atrial flutter and fibrillation and its associated morbidity, the closure of atrial septal defects in adults with evidence of right ventricular volume overload should not be delayed.

Recent reports have shown the safety and efficacy of the modified Cox maze procedure in restoring sinus rhythm in patients undergoing surgery to repair a defect of the mitral valve or the atrial septum.[8-12,30,31] Cox et al.[8] and Sandoval et al.[10] proposed that the maze procedure should be considered for patients with atrial septal defects, although they acknowledged that the selection criteria remained unclear. Our study has identified patients older than 40 years of age who present with atrial flutter or fibrillation as the group at highest risk for late postoperative atrial flutter or fibrillation. The efficacy of procedures (such as the maze procedure) that are performed in addition to surgical closure of the atrial septal defect in preventing late atrial arrhythmia in high-risk patients needs to be evaluated in a randomized clinical trial.

Our study has some limitations. Volumetric data on the right atrium and right ventricle were from different sources and not always available; hence, they were not included in the analysis. The absence of a nonsurgical control group limits the ability of the study to address directly whether the closure of an atrial septal defect should be performed in all adults with a substantial left-to-right shunt. Another limitation was the relatively short follow-up period. In future studies, additional predictors of late atrial arrhythmia might be identified with a larger patient sample and a longer period of observation.

We conclude that in adults with atrial septal defects who are undergoing surgery because they have symptoms or a Qp:Qs ratio greater than 1.5:1, the presence of atrial flutter or fibrillation is related to age and pulmonary arterial pressure. To reduce the morbidity associated with late atrial flutter or fibrillation, the timely closure of atrial septal defects is warranted. For older patients, additional procedures targeting atrial arrhythmia may be required at the time of the surgical closure of the atrial septal defect.

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