

# Natural history of secundum atrial septal defect in adults after medical or surgical treatment: a historical prospective study

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## Abstract

**Objective**—To compare outcome in patients with medically treated secundum atrial septal defect (ASD) first diagnosed after the age of 25 with the long-term outcome in a similar group of patients after surgical closure.

**Design**—A historical, prospective, unrandomised study.

**Setting**—A tertiary referral centre.

**Patients**—All patients with ASD followed up since 1955 who fulfilled the entry criteria and had reached a current age of over 45 years—that is, 34 medical and 48 surgical patients with a mean follow up of 25 years.

**Main outcome measures**—Survival, symptoms, and complications.

**Results**—There was no difference in survival or symptoms between the two groups and no difference in the incidence of new arrhythmias, stroke or other embolic phenomena, or cardiac failure. No patient in either group developed progressive pulmonary vascular disease.

**Conclusion**—Outcome in adults with ASD was not improved by surgical closure. Because progressive pulmonary vascular disease did not develop in any of these patients its prevention is not a reason for advising closure of ASD in adults.

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Atrial septal defect (ASD) was first described by Rokitsky in 1875 (cited by Edwards *et al.*<sup>1</sup> Its clinical features were described in 1941 by Bedford *et al.*<sup>2</sup> and became well known with the writings of Barber *et al.*, Wood and Leatham and Gray,<sup>3-5</sup> in the 1950s. After bicuspid aortic valve it is the most common congenital defect in adults. Fuster *et al* reported an incidence of 22%

among adults with congenital heart disease,<sup>6</sup> but the true incidence is unknown as it is often not recognised until comparatively late in life or not at all.<sup>7</sup> The defect is compatible with a normal life span<sup>8</sup>—survival up to 94 years has been reported<sup>9</sup>—and ASD was well represented in a large necropsy series in the aged.<sup>10</sup>

Early studies of patients with ASD suggested high morbidity and reduced survival,<sup>11-14</sup> but these patients were highly selected because at that time florid clinical signs of abnormality were needed before cardiac catheterisation was considered. The earliest open heart surgery was practised on such patients.<sup>15,16</sup> Widespread modern medical screening and the availability of echocardiography has greatly increased detection of ASD<sup>17,18</sup> and made it even more important to know the natural history of this common defect.

The low mortality of surgical closure, even in older patients has been stressed.<sup>19</sup> Patients have usually been advised to have their defects closed because their prognosis with an untreated defect was thought to be poor.<sup>12-15,20</sup> This approach meant that the long-term results of surgery were never compared with those of medical treatment.

We have compared the long-term outcome after surgical closure with the natural history of the uncorrected defect in a historical prospective study.

## Patients and methods

All patients with uncomplicated ASD followed up at the Hammersmith Hospital since 1955 who were over 25 at presentation and had a current age of > 45 years were entered into the study. We studied only patients with ostium secundum or sinus venosus defects (partial anomalous pulmonary venous drainage was not regarded as a complication), without severe pulmonary vascular disease (mean pulmonary artery systolic pressure < 45 mm Hg), without partial atrioventricular canal defects (ostium primum defects), and without any other cardiac abnormalities.

All the patients were seen again at the Hammersmith Hospital between October 1989 and March 1991.

## Results

Table 1 shows the clinical and haemodynamic data of the 82 patients with complete follow up. There were 34 in the medical

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Table 1 Clinical features of patients with complete follow up

Feature	At presentation (n = 82)		At last follow up (n = 82)	
	Medical	Surgical	Medical	Surgical
No	34	48	34	48
Age (yr) (range)	38.6 (25-54)	36.2 (26-51)	63 (46-83)	62 (48-81)
NYHA (%):				
I	25 (74)	34 (71)	19 (56)	26 (54)
II	9 (26)	14 (29)	15 (44)	22 (46)
III	0	0	0 (0)	0
Mean Qp/Qs shunts (range)	2.5 (1.8-4.0)	2.5 (1.6-3.5)	—	—
Mean PAP (range)	34 (22-42)	30 (20-44)	—	—
On diuretics (%)	7 (20)	12 (25)	New 8 (24) Total 15 (44)	New 13 (27) Total 25 (52)

PAP, pulmonary arterial pressure.

Table 2 Clinical features of patients lost to follow up

At presentation	Medical	Surgical
No	7	15
Age (yr) (range)	30 (25-36)	37 (27-51)
NYHA:		
I	5	12
II	2	5
III	0	0
Atrial fibrillation	0	0
Mean Qp/Qs shunts (range)	2.4 (2.0-3.4)	2.6 (2.1-3.2)
Mean PAP (range)	24 (20-34)	30 (22-38)
On diuretics	0	1

PAP, pulmonary arterial pressure.

group and 48 in the surgical group. Their mean (range) ages when first seen or operated on were 39 (range 25-54) for the medical and 36 (26-51) years for the surgical patients.

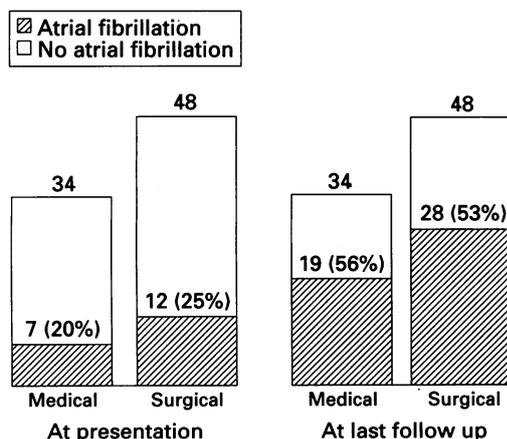
One hundred and five patients met the inclusion criteria. Follow up was complete in 82 patients (78%). Of the 25 patients lost to follow up, six had emigrated and 12 had returned overseas. The remaining seven could not be traced but their names did not appear in the Home Office Register of Deaths. Their clinical and haemodynamic variables at presentation were similar to the rest of the patient population (table 2).

CLINICAL FEATURES AT PRESENTATION

More than 70% of patients in both groups were symptom free when first seen and had been identified at routine medical examinations but 10 (29%) in the medical group and 17 (35%) in the surgical group mentioned palpitation. Shortness of breath on exertion was described by nine (26%) of the medical and 14 (29%) of the surgical groups. Atrial fibrillation was most prevalent in older patients and was present in seven (20%) in the medical and 12 (25%) in the surgical group when they were first seen.

HAEMODYNAMIC VARIABLES AT PRESENTATION

The mean (range) pulmonary artery pressure was 34 (22-42) mm Hg in the medical group and 30 (20-44) mm Hg in the surgical group (NS). The mean shunt flows were 2.5:1 in each group and the ranges were comparable (medical 1.8-4.0:1, surgical 1.6-3.5:1, NS).



Distribution of atrial fibrillation

All patients had normal arterial oxygen saturations at rest but most showed small right to left shunts on indicator dilution curves.

SURVIVAL AND DEATHS

There were no operative or perioperative deaths. Early postoperative morbidity such as chest or wound infection is not considered in this comparison of the long-term health and wellbeing of operated and unoperated adults with ASD.

Eight patients died during follow up. Two patients in the surgical group and one in the medical group died from cardiovascular causes (fig 1). The duration of follow up (mean 25 years), the current mean ages (medical 63 years and surgical 62 years, NS), and the ranges for both groups were similar (NS). The oldest patient is in the medical group and is 83 years old.

CLINICAL AND HAEMODYNAMIC VARIABLES AT THE LAST FOLLOW UP

More than 50% of all the patients were symptomatic at the last follow up. Fourteen (41%) of the medical and 22 (44%) of the surgical group complained of shortness of breath on effort; 19 (56%) of the medical and 26 (54%) of the surgical groups complained of palpitation, all of them were in chronic atrial fibrillation. The symptoms in the two groups showed no differences (NS).

In 12 (35%) medical and 16 (33%) surgical patients chronic atrial fibrillation developed during follow up. Nine (26%) in the medical and 10 (21%) in the surgical groups had episodes of supraventricular arrhythmia. Again there was no difference between the groups.

Fifteen (44%) in the medical and 24 (50%) in the surgical group were taking diuretics (NS) when last seen. The doses did not exceed 40 mg frusemide or an equivalent in any patient.

RE-EVALUATION

Haemodynamic studies

Three patients in the medical group had repeat haemodynamic studies because of worsening symptoms—shortness of breath in two and fatigue in one. The new data were unchanged. All these patients continued medical follow up and are alive and well.

Four patients in the surgical group had repeat cardiac catheterisation, three for shortness of breath and one for fatigue. Only one patient showed incomplete closure of the defect. Repeat haemodynamic study in this patient showed a shunt size of 1.3:1 with a mean pulmonary artery pressure of 26 mm Hg.

ECHOCARDIOGRAPHY

During the follow up period patients underwent a comprehensive cross sectional echocardiographic examination by Doppler, with a Toshiba SSH 65A and SSH 160A or General Electric Pass C cardiac ultrasound equipment. A 3.7 or 3.75 M Hz phased array transducer was used for optimal cross sectional imaging and 2 or 2.5 M Hz phased

array transducers for Doppler calculations. Colour flow imaging was also used.

Of 30 patients in the non-surgical group, 13 (43%) had tricuspid regurgitation that was mild in seven and moderate in six patients and thought to be secondary to a stretched tricuspid annulus. The average (SD) peak tricuspid regurgitant flow velocity was 3.1(0.6) m/s and the average peak systolic gradient between the right atrium and ventricle was 39.04(14.3) mm Hg. Conversely, of the 48 patients who had had their ASD closed only eight (17%) had mild functional tricuspid regurgitation ( $p < 0.05$ ). The average peak tricuspid regurgitant flow velocity was 2.7(0.6) m/s with an average peak systolic pressure gradient of 29.5(13.2) mm Hg (NS).

It was not possible to estimate right ventricular pressure in the other patients because they had no tricuspid regurgitation detected. Detected tricuspid reflux was more common in the medical group but there was no significant difference in the estimated right ventricular pressure and therefore no evidence of progressive pulmonary hypertension in the unoperated patients studied.

### Discussion

This study included all our adult patients with asymptomatic or minimally symptomatic ASD at presentation. Because the reported complications of ASD tend to be higher after the fifth decade<sup>12-14,21</sup> we decided on a minimum age of 45 years at last follow up to increase the likelihood of detecting a difference between the groups. Clinical and haemodynamic characteristics at presentation in those not operated on were similar to those whose defects were closed surgically. The 25 patients lost to follow up had similar clinical and haemodynamic variables to the 82 patients reported here and there is no reason to think that outcome was different in these patients. Most had been referred from abroad.

Both our medical group and surgical group had similar long-term survival to that reported by Murphy *et al* for surgically treated patients<sup>20</sup> but the 91% survival in our medical group is much better than in previously reported series of unoperated ASDs.<sup>12-14</sup> This is not surprising because these early studies, when echocardiography was not available, selectively identified patients with obvious symptoms. We know now that symptoms are usually absent and clinical, electrocardiographic, and radiological signs are often unimpressive. Our ability to diagnose ASD improved considerably with experience of echocardiography and subsequent confirmation of a large shunt at catheterisation. Yet figures for natural history obtained from these early papers are still quoted.<sup>22</sup> There are no other figures because routine closure of ASD has been practised since the early days of open heart surgery. Campbell *et al* suggested that 75% of patients are dead by the age of 50 years and 90% by 60,<sup>11</sup> but this was in 1957 when patients were only likely to have been

referred because of symptoms, and therefore usually with heart failure and often with severe pulmonary hypertension. Many of the patients described in this paper would then have been regarded as having functional murmurs or mild pulmonary stenosis with a good prognosis and would not have been included in early series such as that of Campbell *et al*<sup>11</sup> as they would not have been thought to warrant catheterisation. Though the longevity of our surgical group compares well with other reported series,<sup>19,23</sup> our medical group shares the same longevity and shows no greater morbidity.

### ATRIAL FIBRILLATION

Comparison of the incidence of development of atrial fibrillation, embolic episodes, and cardiac failure provided information on possible reduction of complications of ASD by surgical closure. At presentation seven (20%) of the medical group and 12 (25%) of the surgical group were in atrial fibrillation. At the last follow up 19 (56%) of the medical group and 28 (53%) of the surgical group were in atrial fibrillation. Thus 47 (57%) out of 82 of all our patients were in atrial fibrillation and though their mean age at the last follow up was  $> 60$  years, this incidence is high compared with a control population.<sup>24</sup> When the two groups were compared, however, the development of new atrial fibrillation in the medical and surgical patients was no different. Information on the prevalence of atrial fibrillation in unoperated patients with ASD is provided by preoperative data from operated series.<sup>20,21</sup> In our medical group the rate of atrial fibrillation was 45% in patients over the age of 40, which is comparable with 51% in the series of Murphy *et al* for the same age group.<sup>20</sup> In a population undergoing surgical closure in their sixties, St John Sutton *et al* reported a 58% preoperative rate of atrial fibrillation, which is comparable with 52% in our medical group of the same age. The rate of atrial fibrillation in our surgical group was 40% for patients in their 40s and 58% for patients in their 60s. This compares well with published series after closure of ASD.<sup>19-23</sup> Thus in our study the development of atrial fibrillation was neither reduced nor delayed by closure of ASD.

### SYSTEMIC EMBOLISM

All the embolic episodes occurred in patients who had been in atrial fibrillation when last seen. The incidence of embolisation was similar in the two groups. The number of embolic complications in operated patients was similar to that in published series that also stressed the presence of atrial fibrillation.<sup>20-25</sup> Though paradoxical embolism has been reported in patients with ASD (and also in those with only a patent foramen ovale), it is rare and was not recognised in our series. All patients with paroxysmal or established atrial fibrillation were treated with warfarin.

### CONGESTIVE FEATURES

A high jugular venous pressure with tricuspid

regurgitation may develop in patients with ASD who are in atrial fibrillation.<sup>10 26 27</sup> Forty five per cent of our medical and 50% of our surgical patients were receiving diuretics at the last follow up. All of them were in atrial fibrillation. The development of cardiac failure is reported to be multifactorial in patients with ASD<sup>20 28-31</sup> and it has been proposed that left ventricular dysfunction contributes to its development.<sup>29 31</sup> Left ventricular dysfunction was not detected by echocardiographic assessment performed in our patients at the last follow up. Though right ventricular dilatation was noted in both operated and unoperated patients, overall function remained good in both groups. Right ventricular thickness was within the normal range in both the medical and surgical groups at last follow up and cardiac failure in these patients was attributable to tricuspid regurgitation associated with atrial fibrillation as suggested by Wood.<sup>27 28</sup> The frequency of raised venous pressure was not influenced by surgical treatment, though tricuspid regurgitation was detected more often by Doppler echocardiography in the unoperated group.

#### PULMONARY VASCULAR DISEASE

That we included patients both with dynamic pulmonary hypertension and moderate pulmonary vascular disease (resistance up to 11 Wood units) may be a cause for surprise; but we did not find clinical or Doppler echocardiographic evidence of progression of pulmonary vascular disease in any of our medical patients.

Patients with more severe pulmonary vascular disease had the pulmonary hypertension when they were first seen and were not included in this survey because all those with left to right shunts had their defects closed. Other patients with severe pulmonary vascular disease who had no significant shunts and small hearts at the time of presentation looked and behaved like patients with primary pulmonary hypertension with an ASD that was almost incidental.

In conclusion, with the increased detection rate of congenital heart disease in adults, which has resulted from more medical examinations and the availability of modern echocardiography, it has become even more important to know the likely natural history in order to offer the best treatment. Many benign abnormalities are now detected. Surgical intervention in people with few or no symptoms must be proved to be of benefit. Such benefit has never been shown in a randomised prospective series of adults with ASD and our experience suggests that delayed closure of ASD in adult life does not alter the natural history. Neither survival nor the incidence or timing of development of atrial arrhythmias, embolic stroke, pulmonary vascular disease, or heart failure were affected by surgery in our patients whose defects had not been detected until adulthood. The main problems were the development of atrial fibrillation and embolic stroke. These should be preventable by anticoagulant treatment. Both medically and surgically treated patients had

similar morbidity though this was higher than in the normal population. We suggest that routine surgical closure of ASD in adults is not justified because it does not influence future morbidity, which remains higher than in the normal population. Atrial septal defects should of course be detected and closed during childhood when it is believed (but has not been shown) that subsequent differential growth and remodelling improves the long-term outlook for retention of sinus rhythm.

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**Comment**

The decision whether or not to close an atrial septal defect in adults is a difficult one. The paper from Hammersmith that appears on pages 224 to 228 is based on Celia Oakley's conservative approach over the past 25 years and provides a breath of fresh air.

In people with an atrial septal defect pulmonary vascular resistance is actually reduced (possibly because of pulsatile flow). High pulmonary vascular resistance rarely or only coincidentally develops. It is useful to see this confirmed. Over the years many cardiologists will have wondered whether a rise of venous pressure with the onset of atrial fibrillation in elderly people with an atrial septal defect indicates that they should have been referred for surgery earlier. It is reassuring to read that atrial fibrillation and heart failure were as common in the operated

group as in the non-operated group. The question that remains is whether or not there is a haemodynamic benefit from closure of the atrial septal defect. Many of us have probably recommended that closure is advisable in physically active people but not worthwhile in those who are sedentary and it is unfortunate that cardiac output on exertion was not compared in the operated and non-operated groups in the Hammersmith paper. A hint in favour of the concept of recommending closure for physically active patients is that tricuspid regurgitation (presumably judged by a dominant systolic wave in the neck) was found in 43% of the non-operated group but in only 17% of the operated group. Another argument in favour of surgery is eradication of the threat of paradoxical embolism.

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