Incidence of secondary pulmonary hypertension in adults with atrial septal or sinus venosus defects

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Abstract

Objective—To examine the incidence of raised pulmonary artery pressure and resistance in adults with isolated atrial septal defect within the oval fossa (so called secundum defect) or sinus venosus defect.

Design—A historical, retrospective, un-randomised study.

Setting—A tertiary referral centre.

Methods—Cardiac catheterisation was performed in all patients, with measurement of pulmonary artery pressure and resistance. Pulmonary to systemic flow ratio was calculated using the Fick principle. Pulmonary hypertension was defined as mean pulmonary artery pressure > 30 mm Hg, and increased resistance as an Rp/Rs ratio > 0.3.

Patients—All patients with a secundum atrial septal or sinus venosus defect who presented between July 1988 and December 1997 were enrolled in the study.

Results—Pulmonary artery pressure and resistance in the patients with sinus venosus defect (n = 31) was higher than in patients with atrial septal defect (n = 138). Pulmonary hypertension was present in 26% of patients with sinus venosus and in 9% of patients with atrial septal defect. The incidence of raised pulmonary vascular resistance was 16% in patients with sinus venosus and 4% in patients with atrial septal defect. The increase in resistance occurred at a younger age in sinus venosus defect than in atrial septal defect. **Conclusions**—Patients with sinus venosus defect have higher pulmonary pressures and resistances and develop these complications at younger age than patients with atrial septal defects. Thus they should be managed differently than patients with "simple" atrial septal defects.

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Keywords: sinus venosus defect; atrial septal defect; pulmonary hypertension; congenital heart defects

Atrial septal defect is one of the most common congenital heart defects in adults.¹ Recently, there has been some debate about the benefit of closure of atrial septal defects in adulthood.²⁻⁴ Arguments for closure include improvement in quality of life, avoidance of arrhythmias, and prevention of pulmonary vascular disease.^{4, 5} The exact incidence of raised pulmonary artery pressure in adults with atrial septal defect living at low altitude appears variable. Most studies on the natural history or medical management

of atrial septal defects have included some patients with sinus venosus defect,^{3, 4, 6} but to our knowledge a formal study comparing the incidence of pulmonary hypertension evaluated by cardiac catheterisation between patients with sinus venosus and secundum atrial septal defects has not been performed thus far. We therefore examined the incidence and effect on treatment of raised pulmonary artery pressure and resistance in adult patients with atrial septal or sinus venosus defect.

Methods

PATIENT SELECTION

Between January 1988 and December 1997, 169 consecutive patients over the age of 18 years underwent cardiac catheterisation because of an atrial septal or sinus venosus defect at the Deutsches Herzzentrum, Berlin. It has been our policy to assess pulmonary vascular resistance invasively and perform angiography to evaluate coronary artery anatomy in all patients over the age of 40 years with atrial septal or sinus venosus defects. In the 78 patients below the age of 40, cardiac catheterisation was performed as part of evaluation for attempted device closure (n = 55), because of clinical signs of pulmonary hypertension (n = 5), and because of uncertainty regarding pulmonary venous drainage during echocardiographic examination (n = 18). Patients were included in this study on the basis that they had situs solitus, concordant atrioventricular and ventriculoarterial connections, and an atrial septal defect in the oval fossa (so called secundum atrial septal defect) (n = 138) or a sinus venosus defect (n = 31). Thus all patients with such an atrial septal defect who were seen during a 10 year period in our centre were included in the study. Patients with a partial atrioventricular septal defect (so called primum atrial septal defect) or additional anomalies of the tricuspid valve were excluded.

DIAGNOSTIC INVESTIGATIONS

Cardiac catheterisation was performed under sedation with a continuous infusion of 3-5 mg/kg/hour of propofol. Patients with a Pco₂ of > 50 or a pH of < 7.34 during catheterisation were excluded from the study. Pressures were measured with standard fluid filled catheters coupled to a Statham transducer (Statham Inc, Cambridge, Massachusetts, USA). A mean pulmonary artery pressure of > 30 mm Hg was arbitrarily considered to represent pulmonary hypertension. Pulmonary and systemic blood flows were measured by the Fick method.⁷ Mixed venous saturation was obtained from the superior and inferior venae cavae (SVC and

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Table 1 Haemodynamic data in patients with atrial septal defect (ASD) and sinus venosus defect (SVD) in different age groups

	18–40 years		40–60 years		> 60 years	
	ASD (n = 63)	SVD (n = 15)	ASD (n = 50)	SVD (n = 15)	ASD (n = 25)	SVD (n = 1)
Qp/Qs	2.7 (1.1) (1.5 to 6.5)	2.5 (1.0) (1.1 to 5.0)	2.2 (0.7) (1.5 to 4.0)	2.3 (0.6) (1.5 to 3.3)	2.4 (0.8) (1.1 to 4.0)	1.8
Rp/Rs	0.07 (0.04) (0.01 to 0.16)	0.12 (0.20)* (0.07 to 0.76)	0.10 (0.06) (0.01 to 0.30)	0.16 (0.12)* (0.04 to 0.40)	0.13 (0.10) (0.02 to 0.44)	0.4
Mean PA pressure (mm Hg)	16.5 (5.0) (9 to 55)	18.4 (16.0)* (10 to 76)	20.0 (8.1) (8 to 48)	29.0 (17.0)* (12 to 68)	23.6 (8.7) (10 to 45)	58

Values are mean (SD) with range.

*Significant difference ($p < 0.05$) between patients with ASD and SVD.

PA, pulmonary artery; Qp/Qs, ratio of pulmonary to systemic blood flow; Rp/Rs, ratio of pulmonary to systemic vascular resistance.

IVC) and calculated as

$$[(3 \times \text{SVC}) + (1 \times \text{IVC}) \text{ saturation}] / 4.^7$$

Pulmonary and systemic resistances were derived from pressures and flows across the respective vascular beds. The ratio between pulmonary and systemic vascular resistances (resistance index, Rp/Rs) was calculated; we regarded this as the most important indicator of pulmonary vascular resistance because errors in oxygen capacity cancel out⁸ and the use of the ratio avoids the need to index for flows and resistances.⁷ An Rp/Rs ratio greater than 0.3 was arbitrarily considered to represent raised pulmonary vascular resistance.

In all patients a detailed history was taken and symptoms evaluated according to the guidelines of the New York Heart Association (NYHA) to assess functional class. Hospital records were reviewed to obtain information about the outcome, such as the results of surgery.

Patients were arbitrarily divided into three groups according to age: 78 patients were between 18 and 40 years of age, 65 between 40 and 60, and 26 patients over the age of 60 years.

STATISTICAL ANALYSIS

A polynomial regression analysis was performed to relate haemodynamic and functional data and age in the patient groups with atrial septal and sinus venosus defect. Comparison between both groups was performed by using the Wilcoxon rank sum test, with a p value of < 0.05 considered significant.

Results

SINUS VENOSUS VERSUS ATRIAL SEPTAL DEFECT

Among the whole patient cohort of 168 patients, the 31 patients (18.5%) with sinus venosus defect had a significantly higher systolic, diastolic, and mean pulmonary artery pressure, as well as resistance index, than the 138

patients with a defect in the fossa ovalis (table 1). The incidence of pulmonary hypertension (mean pulmonary artery pressure > 30 mm Hg) was 26% in patients with sinus venosus *v* 9% in patients with atrial septal defect. Similarly, the incidence of raised pulmonary vascular resistance (Rp/Rs > 0.3) was 16% (five of 31) in patients with sinus venosus and 4% (five of 138) in patients with atrial septal defect. Female to male ratio in atrial septal defects was 2.5:1 *v* 2.9:1 in sinus venosus defects.

RELATION BETWEEN AGE AND INCREASED PULMONARY ARTERY PRESSURE

An increase in the incidence of raised pulmonary artery pressure and resistance between age groups 18 to 40 and over 40 years was observed, but there was no further increase of incidence in patients over 60 years old (table 2). Using polynomial regression analysis between age and haemodynamic variables, there was a good correlation between age and mean pulmonary artery pressure or resistance index in patients with sinus venosus defect, which was not apparent in patients with atrial septal defect in the oval fossa (table 3). There was a significant correlation between age and NYHA class in both patient groups but only the patients with sinus venosus defect had a significant correlation between NYHA functional class and pulmonary artery pressure and resistance.

EFFECT OF PULMONARY HYPERTENSION ON OUTCOME AND MANAGEMENT

Two patients, one each with superior sinus venosus defect (aged 31 years) and atrial septal defect in the oval fossa (aged 36 years), are listed for a heart–lung transplant. Their mean pulmonary artery pressures were 76 mm Hg (in the patient with sinus venosus defect) and 55 mm Hg, and their Rp/Rs ratios were 0.76 and 0.54, respectively. In neither patient was there a significant fall in mean pulmonary artery pressure or resistance when they were

Table 2 Influence of age group on haemodynamics in patients with atrial septal defect and sinus venosus defect

	Atrial septal defect			Sinus venosus defect	
	18–40 years (n = 63)	40–60 years (n = 50)	> 60 years (n = 25)	18–40 years (n = 15)	40–60 years (n = 15)
Qp/Qs	0.02*	NS		NS	
Rp/Rs	0.005	NS		NS	
Mean PA pressure	0.007	NS		0.02	
NYHA class	0.001	0.007		0.04	

* p values of differences.

NYHA, New York Heart Association functional class; PA, pulmonary artery; Qp/Qs, ratio of pulmonary to systemic blood flow; Rp/Rs, ratio of pulmonary to systemic vascular resistance.

Table 3 Correlation between age and haemodynamic or functional status (NYHA class) in patients with atrial septal defect (ASD) and sinus venosus defect (SVD)

	ASD (n = 138)	SVD (n = 31)
Qp/Qs	$r = 0.19$	$r = 0.30$
Rp/Rs	$r = 0.33$	$r = 0.64$
Mean PA pressure	$r = 0.42$	$r = 0.71$
NYHA class	$r = 0.63$	$r = 0.68$

NYHA, New York Heart Association functional class; PA, pulmonary artery.

given nitric oxide and inhaled prostacyclin in addition to 100% oxygen in the catheterisation laboratory.

The defect was closed in 167 patients: 26 patients with atrial septal defect in the oval fossa were treated with an Amplatzer septal occluder and 141 patients underwent surgery. There was one death in a 58.6 year old patient with a sinus venosus defect and an Rp/Rs ratio of 0.4; this patient had a mean pulmonary artery pressure of 68 mm Hg and a left to right shunt with a ratio of pulmonary to systemic blood flow (Qp/Qs) of 1.8:1. As the left to right shunt increased with administration of oxygen, surgical closure of the defect was attempted but the patient died from a pulmonary hypertensive crisis six hours after surgery.

Discussion

This study shows a difference between sinus venosus and atrial septal defects in the fossa ovalis, with a higher prevalence of pulmonary hypertension and raised pulmonary arteriolar resistance in adult patients with sinus venosus defects. Pulmonary hypertension and increased pulmonary vascular resistance also occurred at an earlier age in patients with a sinus venosus defect than in those with an atrial septal defect, and was clearly related to NYHA functional class. There was also a positive correlation between age and pulmonary vascular resistance in patients with sinus venosus defect, which was not so apparent in patients with atrial septal defect.

PULMONARY HYPERTENSION

To our knowledge a higher incidence of pulmonary hypertension in patients with sinus venosus defect has not been reported before. The development of pulmonary hypertension is considered to be a late complication of untreated atrial septal defect and is rare before the age of 40.^{4 6 9} It seems to be more prevalent in countries at high altitude with decreased oxygen concentrations, than in patients living at sea level.¹⁰ A mild increase in pulmonary arterial pressure and resistance can be well tolerated at rest but may cause symptoms on exercise as it impairs right ventricular systolic function.^{11 12}

Recommendations on management of adult patients with atrial septal defect have been based on data excluding patients with a systolic pulmonary artery pressure of more than 45 mm Hg³ and this could have excluded a significant number of patients who might have fared better with surgery.⁴ Two recent studies^{3 4} with substantial numbers of patients comparing the medical and surgical management of atrial septal defects have included 7% and 8% of patients with sinus venosus defect, respectively, but have not specifically looked for or reported differences between the anatomical groups. As our findings suggest there is a difference in the incidence and evolution of pulmonary hypertension between atrial septal and sinus venosus defects, recommendations regarding medical versus surgical management^{2 4 13} should take the underlying morphology into account, which has not been done up to now. As our

data show, adults with sinus venosus defects are more likely to develop pulmonary hypertension and develop this complication at younger age than patients with atrial septal defect. Thus they should be treated earlier than patients with defects in the oval fossa and it may not be appropriate to manage sinus venosus defects medically. This is also illustrated by the fact that the only death from a pulmonary hypertensive crisis occurred in an adult with a sinus venosus defect.

LIMITATIONS OF THE STUDY

The selection of patients may have been influenced by the fact that ours is a tertiary referral centre. Many of the patients have had diagnostic catheterisation performed elsewhere, and it has been our policy to treat the defect once the diagnosis has been made. Thus we could not follow any patients serially and obtain data on the evolution of increasing pulmonary artery pressure. Because of this, our data cannot reflect the true natural history of either atrial or sinus venosus defects. Our follow up period after surgical correction is rather short, so we could not study the effect of pulmonary hypertension on outcome, particularly in the patients with mild elevation of pulmonary artery pressure and resistance. We did not examine the morphology of lung arterioles as we did not obtain lung biopsies at the time of surgery, and so we cannot say whether this may have been altered by the associated partial anomalous pulmonary venous drainage. As there was no difference in shunt size between the two anatomical types of intra-atrial communication, and as none of the patients with sinus venosus defect had clinical or haemodynamic evidence of pulmonary venous obstruction, we can only speculate on the cause of the higher prevalence of increased pulmonary vascular resistance in sinus venosus defect. Females are more prone than males to develop primary pulmonary hypertension, so the larger number of females in the sinus venosus defect group may have been a contributing factor to the higher incidence of pulmonary hypertension in the sinus venosus defect group. On the other hand we were unable to show any correlation between sex and the incidence of raised pulmonary artery pressure or resistance for the group as a whole. Future studies on sinus venosus defects should involve several centres to ensure that there are enough patients to allow the natural history of the condition to be defined.

CONCLUSIONS

From these data we conclude that raised pulmonary artery pressure and resistance in adults are three times more prevalent in patients with sinus venosus than with atrial septal defect, and occur at a younger age. This implies that adults with sinus venosus defects should be closely monitored for signs of increased pulmonary vascular pressure and resistance, and should be treated at a young age with surgical closure rather than with symptomatic medical treatment.

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