Atrial septal defect in adults: the influence of age and haemodynamic parameters on the results of surgical repair

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Abstract

Introduction: Indications for closure of atrial septal defect (ASD) are well established in children but still unclear in adult patients. There is also a discrepancy regarding the natural history of the defect and benefits of ASD closure and long-term prognosis.

Aim: The aim of the study was to evaluate the outcome of surgical closure of atrial septal defect (ASD) with respect to age and selected haemodynamic parameters.

Methods: The study involved 52 patients with ASD, aged 38.6±15 years. All patients had a clinical examination, echocardiography, Holter ECG monitoring and cardiopulmonary exercise test (CPX) prior to and at least one year after the surgery. The results were analysed for the entire group of patients and then for the following subgroups of pts.: aged <40 and ≥40 years; with right ventricular systolic blood pressure (RVSP) ≤30 and >30 mmHg; and with shunt volume ratio (Qp/Qs) <2.5 and ≥2.5.

Results: After repair of ASD, a significant improvement of the clinical status, as defined by NYHA class, was observed. At the same time, a constant or even increased incidence of arrhythmias was found. Repair of the defect resulted in a significant reduction of the right ventricular diameters in all studied subgroups. Among all evaluated parameters, only age at time of the operation was significantly associated with right ventricular diameter after surgery (β=0.598; p <0.001). Exercise capacity was found to have significantly increased after surgery, regardless of age, RVSP and Qp/Qs, but it remained significantly reduced in patients with pulmonary arterial hypertension compared to subjects with normal RVSP before ASD repair. A significant correlation was shown between peak oxygen consumption and RVSP both before (r=–0.68; p <0.001) and after (r=–0.38; p=0.01) surgery.

Conclusions: Patients benefit from surgical closure of ASD regardless of age and previous RVSP and Qp/Qs. Age at the time of surgery and pulmonary arterial pressure determine long-term results and improvement of echocardiographic and ETT parameters.

Key words: atrial septal defect, surgical repair, age

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Introduction

Atrial septal defect (ASD) makes up about 10% of all congenital heart diseases diagnosed after delivery and up to 30–40% of heart defects diagnosed in patients aged over 40 years. ASD is the most common congenital heart anomaly together with bicuspid aortic valve and mitral prolapse.

The surgical or percutaneous closure of ASD in children with a haemodynamically significant shunt is currently a widely accepted therapeutic standard. Early repair of the defect prevents arrhythmias, pulmonary arterial hypertension and heart failure. Indications for closure of ASD are well validated in children; in adults however, according to many authors, they are

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ambiguous. The most controversial is the issue of qualification of patients older than 40 years with normal pulmonary pressure and minor clinical symptoms for defect closure. Inconsistencies also include the assessment of the natural history of the defect, benefits of ASD closure and long-term outcomes [1, 2].

In the light of diverse views on the necessity of repair of the defect in adult patients, this study attempted to comprehensively evaluate cardiovascular function in adults with ASD prior to and after repair of atrial septal defect in the context of clinical data and selected haemodynamic parameters.

The aim of the study was to evaluate the results of surgical closure of ASD in adults with respect to their age and selected haemodynamic parameters.

Methods

The study group consisted of 52 patients operated on due to ASD type 2 (45 subjects) or sinus venosus (7 subjects) aged from 17 to 68 years, mean 38.6±15.0 years. The cardiovascular status of all patients was assessed using NYHA functional class and the following examinations were performed by up to 7 days before and between 12 and 18 months post ASD repair (mean 14.2±1.4 months): transthoracic echocardiography, cardiopulmonary exercise test (CPX) and Holter ECG monitoring.

Echocardiography performed before and after surgery was used to determine right ventricular systolic pressure (RVSP) using the modified Bernoulli equation and pulmonary-to-systemic flow ratio (Qp/Qs).

Before CPX patients underwent resting spirometry which determined the forced vital capacity (FVC) [1] and forced vital capacity in 1 second – (FEV_1) [1]. The results of FVC and FEV_1 were also expressed as a percentage of the established normal age- and sex-adjusted values (FVC%; FEV_1%). Values equal to 100±20% of reference ones were found normal.

A cardiopulmonary exercise test was performed on a treadmill according to the modified Bruce protocol. Anaerobic threshold (AT) was determined using the V-slope method. The analysis included the following CPX parameters: exercise duration (D), peak oxygen uptake (VO_{2peak} – ml/kg/min), oxygen uptake expressed as a percentage of predicted normal VO_{2max} – (VO_{2peak}%), ventilation/carbon dioxide production ratio (VE/VCO_2) and oxygen uptake at the anaerobic threshold (AT) expressed as a percentage of predicted normal VO_{2max}.

The analysis of examination results prior to and after surgery was performed in the entire study group and subsequently the results were compared between the groups with respect to age at surgery <40 and ≥40 years, RVSP ≤30 and >30 mmHg, and Qp/Qs <2.5 and ≥2.5. Clinical characteristics of the groups are presented in Table I.

Statistical analysis

The results of preoperative and postoperative examinations were compared using Student's t-test. Nonparametric u-Mann-Whitney test for independent samples was applied to compare the distribution of results between groups. An evaluation of the relationships between parameters was performed by drawing regression lines with 95% confidence interval and calculating the coefficient of regression. Moreover, multiple linear regression analysis was used to determine the influence of age, RVSP and Qp/Qs on the outcomes of ETT and spirometry. A statistical analysis was performed with Statistica software. The value of $p < 0.05$ was assumed significant.

Results

Following ASD repair, a significant improvement of clinical symptoms as assessed with NYHA classification was observed in patients operated on before (2±0.35 *vs* 1.1±0.33, $p < 0.001$) and after the age of 40 years

Table I. Clinical and echocardiographic data in analysed patients

Parameter	Mean ±SD (range)		Number of patients	Mean ±SD
Age [years]	38.6±15(17–68)	<40	25	25±6.4
		≥40	27	51.3±7.6
RVSP* [mmHg]	36.7±10.5(24–85)	≤30	21	27.7±2.1
		>30	27	43.7±8.9
Qp/Qs	2.7±0.7(1.5–4.3)	<2.5	25	2.1±0.31
		>2.5	27	3.2±0.45

Abbreviations: RVSP – right ventricular systolic pressure; Qp/Qs – pulmonary-to-systemic flow ratio
** – parameter determined in 48 (92%) patients*

Table II. Number of patients with arrhythmias recorded before and after surgical closure of ASD

	Before surgery	After surgery	
	Number of patients	Number of patients	p
Persistent atrial fibrillation	1 (2%)	3 (6%)	ns
Paroxysmal atrial fibrillation	7 (13%)	10 (19%)	ns
Paroxysmal supraventricular tachycardia	3 (6%)	3 (6%)	ns

Table III. Resting spirometry results before and after repair of ASD

Parameter	Before surgery	After surgery	p
FVC (l)	3.77±1.01	3.85±1.04	ns
FVC%	95.9±15.2	98.5±15.5	ns
FEV1 (l)	3.08±0.86	3.17±0.93	ns
FEV1%	93.3±15.7	97.2±18.2	ns

Abbreviations: FVC – forced vital capacity, FVC% – forced vital capacity expressed as a percentage of normal value, FEV_1 – forced vital capacity in 1 second, FEV_1% – forced vital capacity in 1 s expressed as a percentage of the normal value

(2.4±0.49 *vs* 1.4±0.5, p <0.001). The incidence of arrhythmias increased in study patients after the operation, but the difference was statistically insignificant (Table II). Atrial fibrillation was observed particularly often in patients older than 40 years (87% patients with recorded arrhythmias), both before and after repair of the defect; these patients also had pulmonary hypertension. A correlation between shunt volume and incidence of arrhythmias was not confirmed. The arrhythmias persisted in all patients experiencing them prior to surgery.

After surgical closure of ASD, RV diameter was found to diminish from 39.3±7.8 to 28±5.3 mm (p <0.001). Multiple linear regression analysis showed that of all the analysed parameters (age, RVSP and Qp/Qs), only Qp/Qs significantly influenced RV diameter before surgery (β=0.587; p <0.001). Right ventricular size after repair of ASD was associated only with age at the time of surgery (β=0.598; p <0.001).

Mean RVSP before surgery was 36.7±10.5 mmHg (range: 24–85 mmHg) and decreased after closure of the defect to 26.7±17.0 mmHg (17–42 mmHg, p <0.001).

No significant differences were noted regarding the analysed parameters of resting spirometry parameters before and after surgical closure of ASD. Values of FVC% and FEV_1% expressed as means of the predicted normal values remained within normal ranges when tested prior to and after surgery (Table III). However, some deflections from normal values of certain parameters were observed in a few patients, both before and after repair of the defect. Decreased FVC% and FEV_1% levels (both pre- and post-surgical closure of ASD) were only found in individuals with increased preoperative RVSPs.

Multiple linear regression analysis showed that of all the analysed parameters preoperatively assessed FVC% (β=–0.35; p=0.03) and FEV_1% (β=–0.35; p=0.03) were only dependent on RVSP. A negative correlation was found between RVSP and FVC% (r=–0.43; p=0.002) and FEV_1% (r=–0.42; p=0.003). After closure of ASD in patients with elevated RVSP, a significant increase in FEV_1% was observed (Table IV).

Repair of the defect was associated with an extremely significant improvement in exercise capacity in patients assessed with CPX. Oxygen uptake at peak exercise (VO_2 peak) in the entire group increased from 23.4±8.9 to 29.3±10.2 ml/kg/min, i.e. from 63.6±18.4 % to 82.6% of the normal value (p <0.001). Furthermore, significant prolongation of exercise duration (D) (723±308 vs 896±241 s, p <0.001) and an increase of the anaerobic threshold (AT) from 40±7.9 to 49.1±10.3 (p <0.001) were observed. The VE/VCO_2 ratio decreased from 28.5±5.5 to 27.1±4.2 (p <0.01).

The results (adjusted for age and RVSP) of CPX carried out before and after closure of ASD are shown in Tables V and VI, respectively. Before surgery, significantly lower VO_{2peak} was reported in patients over 40 years compared to younger ones and subjects with RVSP >30 mmHg. However, after expressing oxygen uptake as VO_{2peak}% only the difference between patients with normal and increased RVSP reached statistical significance.

Multiple linear regression analysis showed that of all the analysed parameters only RVSP significantly correlated with VO_{2peak}% before surgery (β=–0.68; p <0.001). A negative correlation was found between resting RVSP and VO_{2peak}% in examinations performed both prior to (r=–0.68; p <0.001; Figure 1) and after surgery (r=–0.38; p=0.01).

Preoperative VE/VCO_2 was significantly higher in patients aged >40 years (30.9±5.7 *vs*. 26±4.1; p <0.01) and subjects with RVSP >30 mmHg (30.6±5.9 *vs* 26±4.2, p <0.01). After closure of ASD, no significant differences were observed between the groups.

An analysis of CPX parameters with respect to shunt volume showed no significant differences between patients with Qp/Qs ≥2.5 and Qp/Qs <2.5. Also no correlation was found between Qp/Qs and VO_{2peak}.

Discussion

Respiratory function in patients with ASD has been relatively rarely assessed. Both normal and decreased

Table IV. Resting spirometry results before and after repair of ASD with respect to RVSP values ≤30 mm Hg and >30 mm Hg

	Before surgery			After surgery		
	RVSP ≤30	RVSP >30	p	RVSP ≤30	RVSP >30	p
FVC (1)	4.24±0.86	3.39±0.97	0.001	4.36±0.88	3.50±1.07	<0.01
FVC %	100.9±12.9	92.0±16.0	<0.05	100.3±12.7	98.4±18.1	ns
FEV_1 (1)	3.6±0.64	2.71±0.88	<0.001	3.58±0.72	2.86±1.02	<0.01
FEV_1 %	99.7±11.0	88.4±15.7	0.01	97.4±14.6	96.5±21.5*	ns

Abbreviations: as in Tables I and III
** – p <0.05; ** – p <0.01; *** – p <0.001 compared to preoperative examination*

Table V. Results of CPX before and after surgical closure of ASD with respect to patients' age: <40 and ≥40 years

	Before surgery			After surgery		
	<40 years	≥40 years	p	<40 years	≥40 years	p
AT[%VO_{2max}]	39.2±7.9	40.6±7.8	ns	49.6±11.2***	48.1±9.8**	ns
D [s]	871±272	585±278	<0.001	1021±193***	779±223***	<0.001
VO_{2peak} [ml/kg/min]	28.0±8.5	19.0±6.0	<0.001	34.7±9.9***	24.3±7.6***	<0.001
VO_{2peak}%	67.9±18.1	59.7±18.2	ns	85.2±20.8***	80.1±19.7***	ns
VE/VCO_2	26.0±4.1	30.9±5.7	<0.01	26.1±3.1	28.1±4.8**	ns

Abbreviations: T – exercise phase duration; VE/VCO_2 – ventilation/carbon dioxide production ratio; VO_{2peak}% – peak oxygen consumption expressed as a percentage of predicted normal; VO_{2peak} – peak oxygen consumption expressed in ml/kg/min, AT – anaerobic threshold
** p <0.05 ** p <0.01 ***p <0.001 compared to preoperative examination*

values of basic parameters of resting spirometry have been reported [3-5]. The published data suggest that there is a relationship between functional respiratory disorders and pulmonary artery pressure. De Troyer et al. [3] found a significant reduction of vital capacity (VC) and FEV_1 in patients with mean pulmonary artery pressure exceeding 25 mmHg. Similar results were reported by Schofield et al. [4], who additionally showed a significant correlation between mean pulmonary artery pressure and both VC and FEV_1. Our spirometric results remain consistent with the published data. A detailed analysis of preoperative parameters revealed significantly decreased values of FEV_1% and FVC% before surgery in patients with pulmonary hypertension. These parameters correlated significantly with RVSP.

Causes of compromised respiratory function in patients with ASD include primarily pulmonary fibrosis. Enhanced blood flow and pressure in the pulmonary circulation increasing vascular wall tension may lead to vascular hypertrophy, extensive production of connective tissue and adverse fibrosis. Furthermore, bronchial compression by dilated pulmonary arteries and enlarged cardiac chambers may result in obstructive lesions in these patients [5]. A specific fight for space takes place between the pulmonary vessels and small bronchioles. Extensive filling of blood vessels may thus result in the narrowing of bronchioles and an increase of respiratory pathways resistance [6].

Despite increased pulmonary flow and RV volume overload, patients with uncomplicated ASD commonly report no significant complaints, although objective evaluations of their exercise capacity show a significant

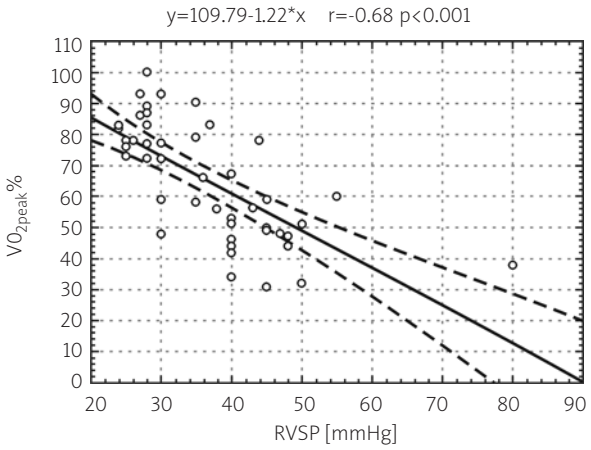

Figure 1. Negative correlation between peak oxygen consumption VO_{2peak}% and pulmonary artery systolic pressure (RVSP) before surgery (r=–0.68; p <0.001).

Table VI. Results of CPX before and after repair of ASD with respect to RVSP values ≤30 and >30 mmHg

	Before surgery			After surgery		
	RVSP ≤30 mmHg	RVSP >30 mmHg	p	RVSP ≤30 mmHg	RVSP >30 mmHg	p
AT [%VO_{2max}]	43.0±8.0	38.2±7.5	<0.05	52.4±10.9***	45.7±8.5***	<0.05
T (s)	962±171	542±274	<0.001	1036±161*	753.7±216***	<0.001
VO_{2peak} [ml/kg/min]	31.2±6.2	17.8±6.2	<0.001	34.7±8.6*	23.8±6.2***	<0.001
VO_{2peak}%	79.0±11.4	54.2±15.1	<0.001	89.3±21.2*	76.0±16.6***	<0.05
VE/VCO_2	26.0±4.2	30.6±5.9	<0.01	26.9±4.5	27.3±4.2**	ns

Abbreviations: as in Table V
** – p <0.05, ** – p <0.01, ***– p <0.001 compared to preoperative examinatio*

reduction of exercise tolerance. Impairment of exercise capacity was also confirmed with the results of this study. Mean VO_{2peak}% was 63.6±18.4% of the normal value, which is consistent with the results reported by other investigators [6-9].

An analysis of ETT parameters with respect to age, RVSP and shunt volume showed that pulmonary hypertension was the strongest predictor of preoperative exercise capacity.

Patients with pulmonary hypertension had their exercise capacity most impaired. In this group of patients the lowest VO_{2peak} values were found and they reached the anaerobic threshold (AT) at the lowest oxygen uptake levels. These results are similar to those of Oelberg at al. [8], who suggested that impairment of exercise capacity in patients with ASD was associated with elevated pulmonary arterial pressure and its further increase during exercise. Decreased exercise capacity in patients with ASD may thus result from the inability to increase cardiac output enough to meet the increased demand. It is caused by impairment of the effectiveness of pulmonary circulation and reduced pulmonary venous return, possibly leading to diminished left ventricular output.

An analysis of ETT parameters with respect to the age of patients (expressed as a percentage of age-matched predicted normal values) showed no significant differences between patients below and above 40 years both before and after surgery. Also, no significant correlation was found between age and VO_{2peak}%. These outcomes remain consistent with the studies of Brochu et al. [9], who failed to demonstrate any significant differences in VO_{2peak} between patients aged below and above 40 years.

The results of ETT revealed that VE/VCO_2 at peak exercise was significantly higher in older patients and patients with elevated RVSP. This parameter describes the respiratory response to exercise. In healthy individuals, there is a linear increase of ventilation along with the increase of CO_2 production during exercise of increasing intensity. There is no unequivocal explanation of why patients with chronic cardiac disorders respond with enhanced ventilation to physical exertion. In heart failure patients explanations of this phenomenon include elevated pulmonary dead volume, disturbed pulmonary circulation, impaired pulmonary perfusion-ventilation balance, reduced lung diffusion capacity and abnormal mechanisms of reflex breathing control resulting from overreactive reflexes from intramuscular chemoreceptors and ergoreceptors [10]. There is no study available on this issue in patients with ASD. However, it seems that elevated VE/VCO_2 in patients aged above 40 years and subjects with pulmonary hypertension may indicate more extensive impairment of cardiopulmonary capacity in these patients.

An analysis of ETT parameters with respect to shunt volume showed no significant differences between patients with Qp/Qs ≥2.5 and Qp/Qs <2.5. Similar results were published by Helber et al. [6] and Oelberg et al. [8], whereas Giardini et al. [11] showed an association between VO_{2peak} and Qp/Qs.

A major improvement was observed after closure of ASD. An improvement of ETT parameters after surgery was most prominent in the subgroup with preoperatively known elevated pulmonary arterial pressure. Nonetheless, exercise capacity remained at lower levels in this subgroup compared to patients with normal RVSP. Some authors suggest that chronic pulmonary hypertension prompts the development of irreversible changes in the pulmonary circulation, which could explain the lack of improvement in exercise capacity in these patients.

The improvement of exercise capacity was independent of age of patients at the time of surgery. Following closure of ASD, the exercise capacity of patients aged over 40 years at repair was considerably lower than that of subjects operated on at a younger age. However, the differences between subgroups were statistically insignificant after adjusting for the effect of age on exercise capacity and expressing oxygen uptake

at the anaerobic threshold and at peak exercise as a percentage of the normal value. Similar results were obtained by Brochu et al. [9], who showed that an improvement of exercise capacity in patients undergoing percutaneous closure of ASD occurred regardless of age at the time of repair of the defect.

After closure of ASD, despite an evident improvement of exercise tolerance, some of the patients did not show normalisation of their exercise capacity. The results of our study remain consistent with the conclusions of Reybrouk et al. [12] and Perrault et al. [13], who found that recovery of full exercise capacity may be expected in children operated on before the age of 5 years.

Conclusions

Patients benefit from closure of haemodynamically significant ASD regardless of their age at operation, pulmonary artery pressure and shunt volume, which was confirmed with the results of a clinical work-up test, including echocardiography and cardiopulmonary exercise test. Age at the time of surgery and pulmonary arterial pressure predict the long-term outcome of treatment and an improvement of echocardiographic and ETT parameters. Therefore, the defect should be repaired as early as possible to prevent haemodynamic complications, including the development of pulmonary hypertension and cardiac arrhythmias.

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Ubytek przegrody międzyprzedsionkowej u dorosłych: wpływ wieku i parametrów hemodynamicznych na wyniki leczenia operacyjnego

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Streszczenie

Wstęp: Wskazania do zamknięcia ubytku w przegrodzie międzyprzedsionkowej (ASD) są jasno określone u dzieci, jednak u dorosłych są one niejednoznaczne. Istnieje również rozbieżność co do naturalnego przebiegu wady jak i korzyści wynikających z zamknięcia ubytku oraz odległego rokowania.

Cel: Celem badania była ocena wyników leczenia operacyjnego u dorosłych z ASD w zależności od wieku chorych oraz wybranych parametrów hemodynamicznych.

Metodyka: Do badania włączono 52 chorych z ASD w wieku 38,6±15 lat. U wszystkich chorych przed operacją i co najmniej 1 rok po niej wykonano badanie kliniczne, echokardiograficzne, holterowskie oraz wysiłkowy test spiroergometryczny (CPX). Przeanalizowano wyniki badań całej grupy chorych, a następnie z uwzględnieniem wieku: <40 i ≥40 lat, wysokości skurczowego ciśnienia w prawej komorze (RVSP): ≤30 i >30 mmHg oraz wielkości przecieku (Qp/Qs): <2,5 i ≥2,5.

Wyniki: Po operacji zamknięcia ASD stwierdzono istotną poprawę stanu klinicznego ocenianego według klasyfikacji NYHA. Jednocześnie obserwowano utrzymywanie się, a nawet nasilanie zaburzeń rytmu serca. Korekcja wady spowodowała istotne zmniejszenie wymiarów prawej komory we wszystkich analizowanych podgrupach. Spośród ocenianych parametrów jedynym istotnie wpływającym na wymiar prawej komory po operacji okazał się wiek chorego w chwili operacji (β=0,598; p <0,001). Po operacji wykazano istotną poprawę wydolności wysiłkowej chorych niezależnie od wieku, RVSP i Qp/Qs, niemniej jednak w grupie chorych z nadciśnieniem płucnym wydolność wysiłkowa pozostała istotnie niższa w porównaniu do chorych z prawidłowym RVSP przed operacją. Stwierdzono istotną korelację pomiędzy szczytowym zużyciem tlenu a RVSP zarówno przed (r=–0,68; p <0,001), jak i po operacji (r=–0,38; p=0,01).

Wnioski: Chorzy odnoszą korzyści z chirurgicznego zamknięciu ASD bez względu na wiek i przedoperacyjne wartości RVSP i Qp/Qs. Wiek w chwili operacji oraz wysokość ciśnienia w tętnicy płucnej są czynnikami determinującymi odległe wyniki leczenia oraz poprawę parametrów echokardiograficznych i CPX.

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