Original paper

Improvement of physical capacity in patients undergoing transcatheter closure of atrial septal defects

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A b s t r a c t

Introduction: Atrial septal defect (ASD) is the most common congenital cardiac anomaly diagnosed in adults. It often remains asymptomatic until the fourth or fifth decade of life. Significant left-to-right interatrial shunting is associated with the risk of heart failure, pulmonary hypertension and atrial fibrillation. Percutaneous ASD closure is a recognized method of treatment.

Aim: To evaluate the clinical outcomes and physical capacity in patients undergoing transcatheter closure of ostium secundum ASD.

Material and methods: One hundred and twenty adult patients (75 females and 45 males) with a mean age of 43.1 ±13.3 (17–78) years who underwent transcatheter device closure of ostium secundum ASD were analyzed. Clinical evaluation and transthoracic color Doppler echocardiographic study were repeated in all patients before as well as 1 and 24 months after the procedure. To assess the physical capacity symptom-limited treadmill exercise tests with respiratory gas-exchange analysis were performed in all patients before the procedure and after 24 months of follow-up.

Results: The devices were successfully implanted in all patients. During 24 months of follow-up all patients showed significant clinical and spiroergometric improvement of exercise capacity, and a significant decrease of right heart chamber overload features on echocardiography.

Conclusions: Transcatheter closure of ASD in patients with significant shunt resulted in significant clinical and hemodynamic improvement regardless of the baseline functional class.

Key words: atrial septal defect, transcatheter closure, echocardiography, cardiopulmonary exercise test.

Introduction

Atrial septal defect (ASD) is the most common congenital cardiac anomaly diagnosed in adults (22–25% of all cases). Atrial septal defect constitutes 7–11% of all cardiac defects and occurs twice as often in women [1, 2].

Atrial septal defect frequently remains asymptomatic until the fourth or fifth decade of life, when patients start to complain of reduced exercise capacity, dyspnea, and nonspecific chest pain. Atrial fibrillation occurs in approximately 10–15% of patients and its incidence tends to increase with age [1, 3]. Pulmonary hypertension develops in 10% of ASD patients, especially in the presence of relevant left-to-right shunt (pulmonary to systemic blood flow ratio ≥ 2 : 1).

Until the 1970s surgical management of ASDs had been the only treatment available. The first catheter occlusion of ASD was performed by King and Mills in 1976 [4]. Since then there has been dynamic progress and refinement of transcatheter closure techniques. In the 1990s several new devices were introduced, including the Sideris buttoned device, Das Angel Wings, ASDOS, CardioSeal, and Amplatzer Septal Occluder (first used by J. Masura in Bratislava in 1995 [5]). Over the last couple of years the use of CardioSeal and Amplatz devices has yielded the most promising results. At present the percutaneous method is an accepted treatment of ostium secundum ASDs.

Aim

The aim of this study was to explore hemodynamic effects and clinical outcomes in patients undergoing transcatheter closure of ostium secundum ASDs based on self-collected data.

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Material and methods

We enrolled 120 consecutive adult patients with ostium secundum ASD in the study (75 females and 45 males). All patients underwent transcatheter closure of ASD. The mean age of enrolled patients was 43.1 ±13.3 (17–78) years.

The diagnosis of ASD was based on clinical examination and transthoracic echocardiography (TTE). The patients were qualified for the procedure depending on the results of transesophageal echocardiographic study (TEE). The diagnosis and feasibility were confirmed by heart catheterization directly before device implantation.

Principal qualification criteria for transcatheter closure were: single central ostium secundum ASD, maximal defect diameter of 38 mm, minimal surrounding tissue margin of 5 mm, and hemodynamically significant left-to-right shunting (pulmonary to systemic blood flow ratio (Qp : Qs) > 1.5 : 1). Two patients were found to have two ASDs with localization allowing closure with a single device.

Devices were implanted in a typical way as described above.

The procedures were performed under local anesthesia after oral premedication with lorazepam and antiemetic administration. During the procedure every patient received an IV bolus of unfractionated heparin (UFH, 100 U/kg) which was either continued as an IV drip up to 12 h after ASD closure or exchanged for two SC injections of enoxaparin (1 mg/kg) every 12 h. In addition, for 6 months following the procedure patients received aspirin.

Cardiac functional capacity assessment (according to New York Heart Association (NYHA) classification) and TTE studies were performed before the device implantation, as well as at 1 and 24 months after ASD closure.

Transthoracic echocardiograms were obtained using Toshiba Power Vision 6000 and Aloka 550 ultrasound machines (cardiac transducers with frequency range of 2–3.7 MHz) according to the Standards of the Polish Cardiac Society Section of Echocardiography. The TTE examination comprised evaluation of dimensions of cardiac chambers, valvular pathologies, pulmonary artery systolic pressure (PASP) estimated by tricuspid regurgitation pressure gradient, and calculation of pulmonary (Qp) to systemic (Qs) blood flow ratio. Size of the right atrium (RA) was assessed in apical-four-chamber view by measuring its short axis dimension in ventricular end-systole. The right ventricle (RV) analysis consisted of measuring its end-diastolic diameter in parasternal long-axis view using M-mode presentation. Post-procedural TTE study included evaluation of the aforementioned features, position of the occluder, possible residual interatrial shunting, and presence and degree of valvular regurgitations. In one case residual shunting was evaluated by TEE due to equivocal results of the TTE study.

As an integral part of comprehensive physical capacity evaluation, clinical assessment and echocardiography were complemented with cardiopulmonary exercise testing (CPET) performed prior to and 24 months after the procedure. The CPET was performed with the Sensor Medicus 229 system and Market type treadmill using the modified Bruce protocol.

Maximal oxygen consumption (VO_{2max}) was measured when oxygen uptake remained stable despite workload escalation. Normal VO_{2max} values were predicted according to the Wasserman equation taking into account age, sex and weight of the patients. When achieved CPET results did not reach 85% of predicted normal values, decreased physical capacity was recognized. Peak oxygen consumption (VO_{2peak}) was estimated as an average of measurements taken during the last 30 s of exercise. The values were presented with respect to body weight in kilograms (ml/kg/min) and as a percentage of predicted normal VO_{2max} (VO_{2peak}%N).

Anaerobic threshold (AT) was established according to Wasserman's criteria by noninvasive gas exchange analysis. Other measured CPET parameters included: heart rate at rest (HR_{rest}), exercise duration (T), oxygen consumption at anaerobic threshold (VO_{2AT}), and several parameters at peak effort, i.e. maximal heart rate (HR_{peak}), peak oxygen consumption expressed both in ml/kg/min (VO_{2peak}) and as percentage of predicted normal VO_{2max} (VO_{2peak} %N), ventilatory equivalent ratio for oxygen (VE/VO_{2peak}) and carbon dioxide (VE/VCO_{2peak}), and partial pressure of carbon dioxide in expired air ($PETCO_{2peak}$).

Statistical analysis

SPSS software was used for statistical calculations. The χ^2 test was used for statistical analysis of the collected data. Qualitative variables were compared by Fisher's exact test for contingency tables. Differences between groups were assessed with paired Student's *t*-test. Multiple comparison analysis was conducted with the analysis of variance (ANOVA) test.

Results

Baseline echocardiographic studies showed enlargement of the right atrium (> 36 mm) and ventricle (> 25 mm) in 106 (88.3%) patients, and paradoxical septal motion in 72 (60%) individuals. Baseline mean PASP on cardiac catheterization was 30.7 ±8.7 (24–45) mm Hg, and mean Qp : Qs ratio was 1.8 (1.5–3.1). Mean ASD diameter measured by TEE was 14.2 ±4.3 (7–24) mm, while the stretched diameter determined with a balloon sizing catheter was 16.2 ±5.9 (13–28) mm.

The diameter of implanted devices ranged from 13 to 32 mm (average: 21.6 ±6.9 mm).

During the first 24 h following the device closure there was a small, insignificant residual shunting on echocardiography in 4 (3.3%) patients which disappeared over a 30-day follow-up period. Multifactor analysis taking into account the degree of shunting before the procedure

Table I. Dimensions of the right heart chambers before and after ASD closure

Variable	Right ventricle – PLAX, M-mode [mm]	Right atrium – A4C, lateromedial diameter [mm]
Before procedure	32.3 ±8.2	46 ±6.4
1 month after the procedure	24.0 ±3.3	41 ±4.6
24 months after the procedure	23.0 ±2.8	37 ±4.3
P-value (before vs. 1 month after the procedure)	< 0.001	< 0.01
P-value (before vs. 24 months after the procedure)	< 0.001	< 0.002

ASD – atrial septal defect, PLAX – parasternal long-axis view, A4C – apical four-chamber view.

and the size of the used occluders proved them unrelated to the residual leak.

Paradoxical septal motion observed in 78 (65%) individuals prior to ASD closure normalized in all cases within a month after the procedure ($p < 0.0001$).

During a 30-day follow-up RV diastolic diameter decreased by a mean of 5.0 ±3.4 (1.5–8) mm in 84 (70%) patients, while in 87 (72.5%) patients RA diameter decreased on average by 8.65 ±4.3 (2–20) mm. Moreover, 33 (27.5%) individuals presented a decrease of the left atrium dimension by 6.2 ±3.6 (1–18) mm on average. The TTE studies performed after 24 months mainly showed further reduction of RA size. In 88 (73.3%) cases the size of the right heart chambers returned to normal. The comparison of echocardiographic findings is depicted in Table I.

Within 30 days of observation there were no remarkable changes regarding physical capacity assessed by NYHA classification. On the other hand, after 24 months 114 (95%) patients experienced improvement in NYHA class ≥ 1 (Table II).

Before device implantation all patients underwent CPET, which confirmed impaired exercise tolerance in 108 (90%) subjects. Mean VO_{2max} ranged from 19 to 27 (22.5 ±7.9) ml/kg/min, and the average exercise duration was 12.0 ±5.9 (6–20) min. There was a significant improvement of physical capacity after 24 months following the procedure. Subsequent CPETs demonstrated longer exercise time, increased peak and maximal oxygen consumption and lower VE/VCO_{2peak} values (Table III).

Spiroergometric parameters at anaerobic threshold (AT) before and after ASD closure differed considerably. At baseline average time to AT was 420 ±165 s with mean oxygen consumption of 14.1 ±3.8 ml/kg/min. Following device implantation patients reached AT on average after 501 ±192 s with oxygen uptake of 16.1 ±9.2 ml/kg/min (Table IV).

Measured VO_2max values differed significantly before and after ASD closure depending on the physical capacity. Mean VO_{2max} achieved by patients in NYHA class I–II was considerably higher than those in NYHA class III (24.3 ±7.9 vs. 21.6 ±5.5; $p < 0.002$). Within 24 months of observation there was improvement in VO_{2max} regardless of the baseline NYHA functional class (Table V).

Moreover, there were statistically significant differences in spiroergometric results between patients with normal (< 30 mm Hg) and elevated (> 30 mm Hg) right ventricular systolic pressure (RVSP). The group with normal RVSP had higher VO_{2max} and VO_2AT levels, and longer time to AT point both before and after ASD closure (Table VI).

Table II. Functional capacity of patients according to NYHA classification

Variable	Before the procedure (n = 120)	1 month after the procedure (n = 120)	24 months after the procedure (n = 120)
No heart failure symptoms	0 (0%)	0 (0%)	87 (72.5%)
NYHA I	48 (40%)	64 (53.3%)	33 (27.5%)
NYHA II	53 (44.2%)	55 (45.8%)	0 (0%)
NYHA III	19 (15.8%)	1 (0.8%)	0 (0%)
NYHA IV	0 (0%)	0 (0%)	0 (0%)

NYHA – New York Heart Association.

Table III. Physical capacity assessed by cardiopulmonary exercise test

Parameter	Before the procedure	24 months after the procedure	*P*-value
Exercise duration [min]	12.5 ±5.4 (8–21)	19.5 ±7.4 (11–25)	< 0.0001
VO_{2max} [ml/kg/min]	22.5 ±7.3 (18–27)	30.5 ±10.4 (24–34)	< 0.0001
Peak VO_2%	77.5 ±12.4 (70–81)	86.7 ±11.2 (76–90)	< 0.0002
VE/VCO_2 slope	26.9 ±7.9 (24–33.1)	24.1 ±6.8 (25–8.1)	< 0.003

VO_{2max} – maximal oxygen consumption, peak VO_2% – peak oxygen consumption, VE/VCO_2 slope – minute ventilation/carbon dioxide production slope.

Table IV. Spiroergometric parameters at the point of the anaerobic threshold

Parameter	Before the procedure	24 months after the procedure	*P*-value
Time to AT [s]	420 ±165	501 ±192	< 0.001
VO_2AT [ml/kg/min]	14.1 ±3.8	16.1 ±9.2	< 0.001
VO_2AT% (%VO_{2max})	43.0 ±8.1	50.0 ±9.9	< 0.001

AT – anaerobic threshold, VO_2AT – oxygen consumption at anaerobic threshold, VO_2AT% – oxygen consumption at anaerobic threshold as percentage of maximal oxygen consumption.

Table V. Maximal oxygen uptake according to NYHA functional class

NYHA class before the procedure	VO_{2max} before the procedure [ml/kg/min]	VO_{2max} 24 months after the procedure [ml/kg/min]	*P*-value
NYHA I	25.3 ±6.2	31.0 ±8.7	< 0.002
NYHA II	23.3 ±4.5	29.1 ±4.2	< 0.002
NYHA III	21.6 ±5.5	26.4 ±5.3	< 0.001

NYHA – New York Heart Association, VO_{2max} – maximal oxygen consumption.

Table VI. Spiroergometric results depending on estimated right ventricular systolic pressure

Parameter	Before the procedure			24 months after the procedure		
	RVSP < 30 mm Hg	RVSP > 30 mm Hg	*P*-value	RVSP < 30 mm Hg	RVSP > 30 mm Hg	*P*-value
AT time [s]	489 ±210	390 ±199	< 0.0001	590 ±230	470 ±187	< 0.001
VO_2AT [ml/kg/min]	17.3 ±3.2	15.1 ±7.1	< 0.01	20 ±4.2	18 ±7.3	< 0.01
VO_2AT% (%VO_{2max})	46.0 ±4.1	41.0 ±7.9	< 0.01	51.0 ±5.1	47 ±8.9	< 0.001
VO_{2max} [ml/kg/min]	24 ±7.1	21 ±10.4	< 0.0001	33 ±9.1	27 ±9.4	< 0.0001

RVSP – right ventricular systolic pressure, AT – anaerobic threshold, VO_2AT – oxygen consumption at anaerobic threshold, VO_2AT% – oxygen consumption at anaerobic threshold as percentage of maximal oxygen consumption, VO_{2max} – maximal oxygen consumption.

However, there were no notable differences regarding the extent of improvement of CPET results against RVSP values.

Spiroergometric parameters were also analyzed according to the age of the subjects. The patients were subdivided into two groups: group I comprised individuals aged ≤ 40 years (68, 56.7%), and group II comprised 52 individuals aged 41–65 years (43.3%). The mean VO_{2max} increase in group I was higher and equaled 8.4 ±6.2 (3–11) ml/kg/min, whereas in group II it was 3.0 ±2.3 (2–6.1) (p < 0.001). General excercise duration icreased from baseline 12.5 ±5.4 (8–21) min to 19.5 ±7.4 (11–25) min 24 months after the procedure (p < 0.0001) (Table III).

Discussion

Almost half a century has passed since the first transcatheter ASD occlusion. Nevertheless, the literature provides discrepant opinions regarding the controversial subject of ASD closure in adults with mild or no clinical symptoms. Some authors call into question the benefits of such a procedure, emphasizing its irrelevant effect on the lifespan and quality of life [6]. On the other hand, data published in 1970 by Campbell *et al.* hinted at significantly lower life expectancy in patients with significant interatrial shunting [1]. Within the analyzed population with hemodynamically relevant ASD only 10–15% of patients lived past 60 years of age despite being asymptomatic during the first decades of life. At present, the majority of opinions advocate ASD closure in the case of relevant left-to-right shunt despite the lack of clinical symptoms [7, 8].

In our experience the results of transcatheter ASD device closure are encouraging. The fact that the device implantation was successful in all patients enrolled in the study indicates that with proper selection of candidates and careful qualification the procedure is safe and effective.

In all cases the procedure was performed under local anesthesia preceded by mild premedication. Conversely, most of the cited authors used general anesthesia [9, 10]. From our experience the majority of patients comply well during peri-procedural TEE, and avoiding general anesthesia adds to simplification and shorter total time of the procedure.

According to the available literature residual shunting is observed in 1–4% of patients during 3–4 months of observation and tends to disappear within a year after device implantation [7, 8]. Our study corroborated these observa-

tions – post-procedural residual shunting was detected in 6 (5%) cases and receded in the subsequent 30 days.

We established that significant improvement of physical capacity, expressed by longer exercise duration and higher maximal oxygen consumption, was already evident after 24 months following percutaneous ASD occlusion. In contrast, Helber *et al.* following up patients after surgical ASD closure observed an increase in VO_{2max} only after 10 years, and no notable effects within the first 4 months [8]. The authors explained this delayed improvement by operative trauma and lack of exercise due to sedentary lifestyle immediately after surgery – which is not a factor in the case of the transcatheter techniques.

In our group even patients with initially normal or mildly impaired physical capacity (NYHA I–II class) presented clinical improvement and achieved better results in CPET later on. These data prove ASD closure in asymptomatic patients to be both justifiable and beneficial. Brochu *et al.*, likewise, studied a group of ASD patients aged on average 49.4 (19–76) years, either with mild or without clinical symptoms (NYHA I–II) before and after device closure [11]. They observed significant improvement of physical capacity as well, despite its slight baseline impairment.

In our study exercise capacity after ASD closure tended to increase remarkably in patients younger than 40 years. These observations are borne out by other authors such as Brochu *et al.*, who established that CPET parameters after 6 months following the procedure were significantly better in younger individuals [11].

Although subjective clinical improvement is reported only after 24 months of observation, objective echocardiographic features of right heart volume overload (i.e. decrease of RA and RV size, normalization of intraventricular septal motion) decreased already after a month. In most patients the size of right heart chambers returned to normal in a 24-month follow-up, which was consistent with the findings of Zhong-Dong *et al.* [12]. Furthermore, Dhillon *et al.* observed improvement of right ventricular systolic and diastolic function 6–12-months after ASD closure [13–15].

To sum up, there is beyond doubt a need for extended follow-up as well as determination of long-term outcomes of transcatheter ASD closure and possible adverse effects associated with the use of large occluders.

Conclusions

Transcatheter ostium secundum ASD closure is a safe and effective method which can be performed without general anesthesia. Improvement of hemodynamic parameters was observed already after 1 month following the procedure (decrease in the size of right heart chambers and normalization of intraventricular septal motion). Within a 24-month follow-up the majority of patients demonstrated improvement of physical capacity, especially those younger than 40 years of age. Exercise tolerance improved regardless of the baseline functional impairment.

Conflict of interest

The authors declare no conflict of interest.

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