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

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Abstract

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 trans-thoracic 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 Amplatzer 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.
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 (Qp : Qs) > 1.5 : 1. Two patients were found to have two ASDs with localization allowing closure with a single device.

Cardiac catheterization, as well as at 1 and 24 months after ASD closure. The diameter of implanted devices ranged from 13 to 32 mm (average: 21.6 ±6.9 mm).

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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 and hemodynamic parameters at peak effort, i.e. maximal heart rate (HRpeak), peak oxygen consumption expressed both in ml/kg/min (VO2peak) and as a percentage of predicted normal VO2max (%N), ventilatory equivalent ratio for oxygen (VE/VO2peak) and carbon dioxide (VE/VCO2peak), and partial pressure of carbon dioxide in expired air (PETCO2peak).

Statistical analysis

SPSS software was used for statistical calculations. The χ² 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.

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 (VO2max) was measured when oxygen uptake remained stable despite workload escalation. Normal VO2max 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 (VO2peak) 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 VO2max (%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 (HRrest), exercise duration (T), oxygen consumption at anaerobic threshold (VO2AT), and several parameters at peak effort, i.e. maximal heart rate (HRpeak), peak oxygen consumption expressed both in ml/kg/min (VO2peak) and as a percentage of predicted normal VO2max (%N), ventilatory equivalent ratio for oxygen (VE/VO2peak) and carbon dioxide (VE/VCO2peak), and partial pressure of carbon dioxide in expired air (PETCO2peak).

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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
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$_{\text{2max}}$ 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$_2$peak 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$_{\text{2max}}$ values differed significantly before and after ASD closure depending on the physical capacity. Mean VO$_{\text{2max}}$ 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$_{\text{2max}}$ 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$_{\text{2max}}$ and VO$_{\text{2AT}}$ levels, and longer time to AT point both before and after ASD closure (Table VI).

### 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.

### 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 ± 4.4 (8–21) | 19.5 ± 7.4 (11–25) | < 0.0001 |
| VO$_{\text{2max}}$ [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$_{\text{2max}}$ – maximal oxygen consumption, peak VO$_2$% – peak oxygen consumption, VE/VCO$_2$ slope – minute ventilation/carbon dioxide production slope.
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 VO₂max 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 exercise duration increased 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-

**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 |
| VO₂AT [ml/kg/min] | 14.1 ±3.8           | 16.1 ±9.2                      | < 0.001 |
| VO₂AT% (%VO₂max) | 43.0 ±8.1           | 50.0 ±9.9                      | < 0.001 |

AT – anaerobic threshold, VO₂AT – oxygen consumption at anaerobic threshold, VO₂AT% – 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 | VO₂max before the procedure [ml/kg/min] | VO₂max 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, VO₂max – maximal oxygen consumption.

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

| Parameter                          | Before the procedure | 24 months after the procedure | P-value | P-value |
|------------------------------------|----------------------|-------------------------------|---------|---------|
|                                   | RVSP < 30 mm Hg      | RVSP > 30 mm Hg               |         |         |
| AT time [s]                        | 489 ±210             | 390 ±199                      | < 0.0001|         |
| VO₂AT [ml/kg/min]                  | 17.3 ±3.2            | 15.1 ±7.1                     | < 0.01  | < 0.01  |
| VO₂AT% (%VO₂max)                  | 46.0 ±4.1            | 41.0 ±7.9                     | < 0.01  | 47 ±8.9 | < 0.001 |
| VO₂max [ml/kg/min]                 | 24 ±7.1              | 21 ±10.4                      | < 0.0001| 33 ±9.1 | < 0.0001|

RVSP – right ventricular systolic pressure, AT – anaerobic threshold, VO₂AT – oxygen consumption at anaerobic threshold, VO₂AT% – oxygen consumption at anaerobic threshold as percentage of maximal oxygen consumption, VO₂max – maximal oxygen consumption.
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$_{2}$max 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 in 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.

References

1. Campbell M. Natural history of atrial septal defect. Br Heart J 1970; 32: 820-6.
2. Tang B, Su F, Sun X, et al. Recent development of transcatheter closure of atrial septal defect and patent foramen ovale with occluders. Biomed Mater Res B Appl Biomater 2016; 106: 433-43.
3. Hoffman J, Kaplan S. The incidence of congenital heart disease. J Am Coll Cardiol 2002; 39: 1890-900.
4. King TD, Mills NL. Secundum atrial septal defects: non-operative closure during cardiac catheterisation. JAMA 1976; 235: 2506-9.
5. Masura J, Gavora P, Formanek A, et al. Transcatheter closure of secundum atrial septal defect using the new self-centering Amplatzer septal occluder: initial human experience. Cathet Cardiovasc Diagn 1997; 42: 388-93.
6. Murphy JG, Bersh BJ, McGoon MD, et al. Long term outcome after surgical repair of isolated atrial septal defect. Follow up at 27 to 32 years. N Engl J Med 1990; 323: 1645-50.
7. Zahn EM, Hellenbrand WE, Latson LA, et al. Transcatheter closure of secundum ASD’s with the CardioSEAL Septal Occlusion System. Early results of the North American Trial. Circulation 1997; 96 Suppl I: 3178.
8. Helber U, Bauman R, Sebold H, et al. Atrial septal defect in adults: cardiopulmonary exercise capacity before and 4 months and 10 years after defect closure. J Am Coll Cardiol 1997; 29: 1345-50.
9. Berger F, Ewert P, Bjornstad PG. Transcatheter closure as standard treatment for most intratral defects: experience in 200 patients treated with Amplatzer Septal Occluder. Cardiol Young 1999; 9: 468-473.
10. Chan KC, Godman MJ, Wilson N, et al. Transcatheter closure of atrial septal defect (ASD) with a new Nitinol double disc device (Amplatzer Septal Occluder, ASO). United Kingdom experience. Eur Heart J 1997; 18 Suppl I: 896.
11. Brochu MC, Barij JF, Dore A, et al. Improvement in exercise capacity in asymptomatic and mildly symptomatic adults after atrial septal defect percutaneous closure. Circulation 2002; 106: 1821-6.
12. Zhong-Dong D, Qi-Ling C, Koening P, et al. Speed of normalization of right ventricular volume overload after transcatheter closure of atrial septal defect in children and adults. Am J Cardiol 2001; 12: 1450-3.
13. Dhillon R, Josen M, Henein M, Redington A. Transcatheter closure of atrial septal defect preserves right ventricular function. Heart 2002; 87: 461-70.
14. Komar M, Przewlocki T, Olszowska M, et al. Is it worth closing the atrial septal defect in patients with insignificant shunt? Postep Kardiol Interw 2014; 10: 78-83.
15. Komar M, Przewlocki T, Olszowska M, et al. The benefit of atrial septal defect closure in elderly patients. Clin Interv Aging 2014; 9: 1101-7.