Pediatr Cardiol (2018) 39:329–334
https://doi.org/10.1007/s00246-017-1759-6

ORIGINAL ARTICLE

# Rapid Improvement of Pulmonary Functions in Children After Transcatheter Closure of an Atrial Septal Defect

**Serkan F. Çelik[1] · Cemşit Karakurt[1] · Nurdan Yıldırım Acar[2] · Elif Çelik[3]**

Received: 8 June 2017 / Accepted: 24 October 2017 / Published online: 31 October 2017
© Springer Science+Business Media, LLC 2017

**Abstract** There are very few studies in the literature on respiratory system functions and complications of children with an atrial septal defect (ASD). The aim of this study is to investigate the pulmonary functions and pulmonary complications before and after transcatheter closure in children with an ASD. In this study, pulmonary function test parameters of 30 ASD patients between 5 and 18 years of age who were eligible to be treated by transcatheter ASD closure were compared with 30 healthy children. The patients undergoing transcatheter ASD closure received pulmonary function tests (PFT) at baseline (1 day before ASD closure), and 3 months after the procedure. Forced vital capacity (FVC), forced expired volume in 1 s (FEV1), peak expiratory flow, and mean forced expiratory flow during the middle half of FVC were measured. The mean age of the 30 ASD patients was 9.59 ± 3.1 years; and 20 (66.6%) were female and 10 (33.3%) were male. The mean age of the control group was 10.15 ± 2.21 years, and 19 (63.3%) were girls and 11 (36.6%) were males. ASD patients had significantly reduced FVC (73.11 ± 24.6%; 86.05 ± 26.1; $p = 0.001$, respectively), and FEV1 (81.34 ± 26.2% and 99.2 ± 19.6%; $p = 0.001$; respectively) at baseline. But significant improvement was observed in FVC values in the 3rd-month post-closure comparison of the patient group with the control group (73.11 ± 24.6%; and 88.36 ± 14.5%; $p = 0.01$, respectively); FEV1 values (81.34 ± 26% and 99.54 ± 18.2%; $p = 0.005$, respectively) and mean forced expiratory flow between 25 and 75% of vital capacity (MEF25–75) values (94.6 ± 33.4% and 124.2 ± −24.1%; $p = 0.01$, respectively) were also improved. There was no statistically significant relationship between the PFT measurements at baseline and after closure of the defect and age at transcatheter closure, gender, body height, body weight, ASD diameter, $Q_p/Q_s$, right ventricle systolic pressure, or mean pulmonary artery pressure values. At the 3rd month of ASD closure, there was no significant difference in the comparison of the PFT values of the patient and control group. Disturbance in the significant flow limitation of the peripheral airway of ASD patients was observed with PFT. Better pulmonary outcomes were observed in ASD patients after transcatheter closure.

**Keywords** Atrial septal defect · Pulmonary function · Spirometry

## Introduction

Atrial septal defects (ASD) are common among children with congenital heart diseases (CHD) [1]. According to different anatomical levels, ASD can be classified as secundum, primum, and sinus venosus types. In ASD, the left-to-right blood shunting causes right heart volume overload. Long-period exposure to right heart volume overload may cause right atrium and ventricle dilatations and increase pulmonary blood flow. Pulmonary hypertension (PH) and right heart failure occur in untreated ASD patients [2].

Although we very often encounter ASD in children, there is not enough published data regarding the changes of

✉ Serkan F. Çelik
docser2003@yahoo.com

[1] Department of Pediatric Cardiology, Faculty of Medicine, Inonu University, Malatya, Turkey

[2] Department of Pediatrics, Faculty of Medicine, Inonu University, Malatya, Turkey

[3] Department of Pediatrics, Magnet Hospital, Kayseri, Turkey

pulmonary functions after transcatheter closure in pediatric ASD patients, and the results of past studies are contradictory [3, 4]. In this study, we aimed to assess the early changes in pulmonary outcomes in pediatric patients before and after transcatheter closure of an ASD.

## Materials and Methods

Thirty children between the ages of 5 and 18 with an ASD were included in this study. The demographic and clinical characteristics of the participants were recorded. Thirty age- and sex-matched healthy children constituted the control group. The demographic and clinical characteristics of healthy children were recorded from the same computerized database. All patients' parents signed individual informed consent forms before enrollment, and all procedures were in accordance with the ethical guidelines of our institution.

The Vivid 7 Pro Ultrasound System (GE Medical Systems, Norway) was used for two-dimensional, M-mode, and colour-flow Doppler imaging echocardiography before and after successful transcatheter closure. Echocardiographic examinations were performed after vital signs, blood pressures, oxygen saturations, and echocardiograms (ECG) of the patient and control groups were evaluated. The general conditions of the ASD patients, age and weight, presence of clinical symptoms related to ASD, ASD diameters, presence of adequate rim, and distances of the defects from the atrioventricular valves were recorded.

Thirty of the 40 ASD patients were found to be transcatheter closure-compatible. Ten patients were excluded from the study because they were not suitable for transcatheter closure or had PH. Respiratory function tests were performed according to the American Thoracic Society and European Respiratory Society child criteria [5, 6]. ASD closure was performed under general anaesthesia, fluoroscopy, and transesophageal echocardiography (TEE). Left and right heart catheterization was performed to measure the pulmonary artery pressure during transcatheter ASD closure and to calculate pulmonary vascular resistance with left–right shunt volume. Mean pulmonary artery pressure (MPAP) and right ventricular systolic pressure (RVSP) were recorded. Pulmonary flow-to-systemic flow ($Q_p/Q_s$) ratios were calculated by oximetry according to Fick's principles. The size, location, and relation of the ASD to surrounding tissues were assessed by TEE. An Amplatzer septal occluder (ASO, St. Jude Medical, Plymouth, MN, USA) was implanted using previously reported techniques [7]. The pulmonary function test (PFT) values of the patients before and 3 months after transcatheter ASD closure were compared again. The same equipment (ZAN100 USB spirometer, nSpire Health GmbH, Oberthulba, Germany) was used to conduct the PFT in all ASD patients. Pulmonary outcomes were assessed individually based on the PFT data. The ASD patients at baseline and 3 months after percutaneous transcatheter ASD closure were classified as either normal [forced vital capacity (FVC) and forced expired volume in 1 s (FEV1) $\geq$ 80% of the predicted value with normal FEV1/FVC], obstructive (FEV1/FVC $<$ 80%), or restrictive (FVC $<$ 80% of the predicted value with normal FEV1/FVC).

## Statistical Analysis

Data for quantitative variables are given as mean ± standard deviation (mean ± SD) or median (minimum–maximum). Data on qualitative variables were presented in terms of number and percentage. Quantitative variables were tested with the Shapiro–Wilk normality test. Unpaired *t* tests, Mann–Whitney U tests and Pearson chi-squared analysis were used to compare the values between groups. The PFT parameters between baseline and 3 months after the procedure were compared by repeated and measured one-way analysis of variance (ANOVA). $p < 0.05$ was considered statistically significant. SPSS 18.0 (SPSS Inc., Chicago, IL, USA) was used for data management and analysis.

## Results

### Simple Statistical Calculations

Between January 2011 and February 2017, 30 pediatric ASD patients, 20 (66.6%) females and 10 (33.4%) males, were enrolled in this study. The mean age of the ASD patients was 9.47 ± 3.59 years. There was no statistically difference between the groups in terms of height, age, and weight ($p > 0.05$; Table 1). Before ASD closure, compared with the healthy group, the ASD patients had reduced mean FVC, FEV1, FEV1/FVC, peak expiratory flow (PEF), and mean forced expiratory flow between 25 and 75% of vital capacity (MEF25–75) values but only FVC (73.11 ± 24.6% vs. 86.05 ± 26.1%; $p = 0.001$), FEV1 (81.34 ± 26.2% vs. 99.2 ± 19.6%; $p = 0.001$) were significantly lower ($p < 0.05$). The baseline PFT of the ASD patients and controls included in the study are summarized in Table 2. When control PFT were performed 3 months after the transcatheter ASD closure, FVC (73.11 ± 24.6% vs. 88.36 ± 14.5%; $p = 0.010$), FEV1 (81.34 ± 26.2% vs. 99.54 ± 18.2%; $p = 0.005$), and MEF25–75 (94.6 ± 33.4% vs. 124.2 ± 24.1%; $p = 0.010$) values of the ASD patients were significantly improved (Table 3).

**Table 1** Baseline clinical, echocardiographic, and hemodynamic characteristics of the groups

| | ASD patients ($n$ = 30) | Controls ($n$ = 30) | $p$ |
|---|---|---|---|
| Age (years) | 9.59 ± 3.1 | 10.15 ± 2.21 | 0.35 |
| Body height (cm) | 136.1 ± 20.0 | 137.5 ± 20.4 | 0.39 |
| Body weight (kg) | 34.5 ± 11.7 | 35.1 ± 12.6 | 0.60 |
| Gender (M: male, F: female) | 20F/10M | 19F/11M | 0.40 |
| Secundum ASD diameter, TTE (mm) | 10.57 ± 4.05 | – | – |
| $Q_p/Q_s$ | 1.94 ± 0.79 | – | – |
| Right ventricle systolic pressure (mmHg) | 28.2 ± 5.3 | – | – |
| Mean pulmonary artery pressure (mmHg) | 18.1 ± 3.9 | – | – |

Values are expressed as mean ± SD

*TTE* transthoracic echocardiography; $Q_p/Q_s$ the ratio of pulmonary-to-systemic flow

* $p < 0.05$

**Table 2** Comparison of PFT parameters in ASD patients and controls at baseline

| | ASD patients ($n$ = 30) | Controls ($n$ = 30) | $p$ |
|---|---|---|---|
| FVC (%)[a] | 73.11 ± 24.6 | 86.05 ± 26.1 | **0.001*** |
| FEV1 (%)[a] | 81.34 ± 26.2 | 99.2 ± 19.6 | **0.001*** |
| PEF (%)[a] | 83.52 ± 21.5 | 89.24 ± 16.4 | 0.22 |
| MEF25–75 (%)[a] | 94.6 ± 33.4 | 109.47 ± 26.3 | 0.60 |
| FEV1/FVC[b] | 114 (80–121) | 118 (95–128) | 0.32 |

$p < 0.05$ indicates statistically significant, and $p < 0.05$ are given in bold

*FVC* forced vital capacity; *FEV1* forced expired volume in 1 s; *FEV1/FVC* FEV1 to FVC ratio; *PEF* peak expiratory flow; *MEF25–75* mean forced expiratory flow between 25 and 75% of vital capacity

* $p < 0.05$

[a]Values are expressed as mean ± SD

[b]Or median (min–max)

**Table 3** Comparison of PFT parameters in ASD patients at baseline and 3 months after transcatheter ASD closure

| | Baseline | Three months after | $p$ |
|---|---|---|---|
| FVC (%)[a] | 73.11 ± 24.6 | 88.36 ± 14.5 | **0.01*** |
| FEV1 (%)[a] | 81.34 ± 26.2 | 99.54 ± 18.2 | **0.005*** |
| PEF (%)[a] | 83.52 ± 21.5 | 92.31 ± 18.4 | 0.07 |
| MEF25–75 (%)[a] | 94.6 ± 33.4 | 124.2 ± 24.1 | **0.01*** |
| FEV1/FVC[b] | 114 (80–121) | 115 (107–124) | 0.52 |

$p < 0.05$ indicates statistically significant, and $p < 0.05$ are given in bold

*FVC* forced vital capacity; *FEV1* forced expired volume in 1 s; *FEV1/FVC* FEV1 to FVC ratio; *PEF* peak expiratory flow; *MEF25–75* mean forced expiratory flow between 25 and 75% of vital capacity

* $p < 0.05$

[a]Values are expressed as mean ± SD

[b]Or median (min–max)

There was an increase in FEV1/FVC and PEF values, but this increase was not statistically significant ($p > 0.05$). In the 3rd month of the ASD closure, there was no significant difference between PFT values of the patient and control groups (Table 4). Of the 30 children completing spirometry tests, 16 (53.3%) had normal PFT, 5 (16.6%) had an obstructive defect, and 9 (30%) had a restrictive defect before the transcatheter closure. Three months after the transcatheter closure of ASD, patients with normal PFT increased from 16 (53.3%) at baseline to 22 (73.3%), and 3 of 5 patients with air flow obstruction and 3 of 9 with a restrictive defect at baseline were reclassified as normal (Table 5).

## Multiple Linear Regression Analysis

Clinical and echocardiographic variables which could be correlated with PFT values in the Student's $t$ test [secundum ASD diameter (mm) with echocardiography and TTE, $Q_p/Q_s$, RVSP (mmHg), MPAP (mmHg), gender, age (years), body height (cm), and body weight (kg)] were included in multiple linear regression analysis to detect the determinants of possible pulmonary dysfunction in the patient group. There was no statistically significant relationship between the PFT measurements at baseline and after the closure of the defect and age at transcatheter

**Table 4** Comparison of PFT parameters in ASD patients after transcatheter ASD closure and controls

| | Three months after ASD patients ($n$ = 30) | Controls ($n$ = 30 | $p$ |
|---|---|---|---|
| FVC (%)[a] | 88.36 ± 14.2 | 86.05 ± 26.1 | 0.88 |
| FEV1 (%)[a] | 99.54 ± 18.2 | 99.2 ± 19.6 | 0.92 |
| PEF (%)[a] | 92.31 ± 18.4 | 89.24 ± 16.4 | 0.64 |
| MEF25–75 (%)[a] | 124.2 ± 24.1 | 109.47 ± 26.3 | 0.24 |
| FEV1/FVC[b] | 115 (107–124) | 118 (95–128) | 0.74 |

*FVC* forced vital capacity; *FEV1* forced expired volume in 1 s; *FEV1/FVC* FEV1 to FVC ratio; *PEF* peak expiratory flow; *MEF25–75* mean forced expiratory flow between 25 and 75% of vital capacity

* $p < 0.05$

[a]Values are expressed as mean ± SD

[b]Or median (min–max)

**Table 5** Pulmonary classification in ASD patients at baseline and 3 months after percutaneous transcatheter ASD closure

| PFT classification | Baseline $n$ (%) | Three months after $n$ (%) |
|---|---|---|
| Normal | 16 (53.3%) | 22 (73.3%) |
| Obstructive | 5 (16.6%) | 2 (6.6%) |
| Restrictive | 9 (30%) | 6 (20%) |
| Total | 30 | 30 |

closure, gender, body height, body weight, ASD diameter, $Q_p/Q_s$, MPAP and RVSP.

## Discussion

To our knowledge, this is the first study to compare the PFT parameters after transcatheter closure of ASD in pediatric patients and healthy controls. Pediatric patients with secundum ASD had significant reduction in FVC, FEV1, PEF and MEF25–75 at baseline, and FVC and FEV1 were significantly lower when compared with controls. There was significant improvement in mean FVC, FEV1, and MEF25–75 values after the ASD closure when compared with baseline. There was no significant difference in the PFT parameters between controls and ASD patients 3 months after the transcatheter closure. These results mean that an element of airflow obstruction in the central and peripheral airway was observed at baseline, consistent with previous studies [4, 8, 9].

In this study, it was determined that respiratory functions were affected in ASD patients and that respiratory functions could be improved with closure.

Cardiac and pulmonary systems are two closely related systems. Ventilation should be compatible with cardiac output to provide the body's metabolic needs. In congenital anomalies of the cardiovascular system such as the ASD, this relationship almost decays [10]. In the presence of ASD, pulmonary blood flow increases in relation to the size of the defect and right ventricular compliance. The shunt causes excessive pulmonary blood flow and increases the return of pulmonary venous blood. Oxygenized blood is recruited from the lungs and congested in the pulmonary vascular bed. Increased hydrostatic forces in the pulmonary capillaries cause the fluid to go out of the veins of the capillaries. This pressure distorts capillary membrane integrity by causing capillary cracks that can be seen on an electron microscope [11]. As a result, fluid accumulates in the interstitium and alveoli and leads to pulmonary oedema. This also increases the amount of breathing work required to provide adequate ventilation. Narrow parenchymal airways due to peribronchial oedema cause wheezing and is called cardiac asthma [9, 12, 13]. Also, the shunt causes excessive pulmonary blood flow, resulting in pulmonary vascular changes and leading to progressive remodelling of the lung parenchyma [13] and even fibrotic changes [14]. As a result of this pathophysiology, airway obstruction [15], atelectasis [10], lower respiratory tract infection [16], pulmonary haemorrhage [16–18], pulmonary embolism [18], and PH [19, 20] can be seen.

Previous studies have reported that transcatheter closure of the ASD may restore right ventricle volume and decrease pulmonary blood flow [21]; therefore, we estimate that the correction of the defect arrested the left-to-right blood shunting, leading to volume reduction and improved FVC and FEV1. In most of the ASD patients in our study population, the pulmonary parameters improved rapidly at a significant level 3 months after the transcatheter closure of the ASD, indicating the increased percentage of ASD children with normal pulmonary function [22]. The incidence of ASD with PH in previous reports was 6–17%. The present study population did not include ASD with PH patients due to the small number of patients (five patients). This might have caused the results to be better than expected. Lee et al. [9] showed that there were significant increases in mean FVC and FEV1 after the transcatheter closure in ASD patients without PH, but increases were not observed in ASD patients with PH.

In addition, we classified each ASD patient before and after the procedure based on the spirometry result. Of the 30 children completing the spirometry tests, 5 (16.6%) had an obstructive defect, and 9 (30%) had a restrictive defect before the transcatheter closure. Three months after the transcatheter closure of the ASD, patients with normal PFT increased from 16 (53.3%) at baseline to 22 (73.3%), and 3 of 5 ASD patients with air flow obstruction and 3 of 9 with a restrictive defect at baseline were reclassified as normal. Many PFT abnormalities of ASD patients before and after correction in our study had restrictive defects, which is consistent with previous studies [4, 9].

Our study population did not include surgically treated ASD patients. FVC and FEV1 were found to be lower in a study of 46 children whose ASD were surgically closed, compared with ASD patients who underwent transcatheter closure [23]. The surgical procedure might damage the lungs because the patients fall into thoracotomy, cardiopulmonary bypass, and ventilation during the operation period, any one of which might cause considerable structural or functional cardiopulmonary changes [9].

We used spirometry in children to evaluate the changes in PFT after the transcatheter ASD closure. Spirometry is frequently used by clinicians for children with respiratory disease. Based on the significant changes in PFT in the study of Gonzales and et al. [13], it was claimed that PFT is an important test for non-invasive and periodic evaluation of CHD patients. Nevertheless, more comprehensive diagnostic methods may be needed besides PFT, like a 6-min walking test, or a carbon monoxide (CO) diffusion test for determining pulmonary functions.

Our study has some limitations. The follow-up PFT was performed only 3 months after the transcatheter closure of ASD. The study population did not include surgically - treated and PH patients due to the small number of patients.

## Conclusion

The present study shows that significant pulmonary function defect is observed in children with ADS before transcatheter closure of ASD, and pulmonary outcome can be improved after the shunt closure. Spirometry should be used to provide regular assessment of PFT in children with ASD before and after the transcatheter closure.

**Funding**This research has received no specific grant from any funding agency or from commercial or non-profit organizations.

**Compliance with Ethical Standards**

**Conflict of interest** None.

**Ethical Standards** The authors assert that all the procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975 as revised in 2008, and has been approved by the institutional committees of Inönü University/Turkey.

## References

1. Anderson RH, Edward J, Baker EJ et al (2010) Pediatric cardiology, 3rd edn. Churchill Livingstone, London. ISBN 978-0-7020-3064-2
2. Graham TP Jr (1991) Ventricular performance in congenital heart disease. Circulation 84:2259–2274
3. Cowen ME, Jeffrey RR, Drakeley MJ et al (1990) The results of surgery for atrial septal defect in patients aged fifty years and over. Eur Heart J 11:29–34
4. Yoshioka T, Kunieda T, Naito M et al (1985) Effects of pulmonary hemodynamics on lung function in adult patients with atrial septal defect. Jpn Circ J 49:960–966
5. Miller MR, Hankinson J, Brusasco V et al (2005) Standardisation of spirometry. Eur Respir J 26:319–338
6. Beydon N, Davis SD, Lombardi E et al (2007) An official American Thoracic Society/European Respiratory Society statement: pulmonary function testing in preschool children. Am J Respir Crit Care Med 175:1304–1345
7. Fischer G, Kramer HH, Stieh J et al (1999) Transcatheter closure of secundum atrial septal defects with the new self-centering Amplatzer Septal Occluder. Eur Heart J 20:541–549
8. Sulc J, Andrle V, Hruda J et al (1998) Pulmonary function in children with atrial septal defect before and after heart surgery. Heart 80:484–488
9. Lee YS, Jeng MJ, Tsao PC et al (2009) Pulmonary function changes in children after transcatheter closure of atrial septal defect. Pediatr Pulmonol 44:1025–1032
10. Healy F, Hanna B, Zinman R (2012) Pulmonary complications of congenital heart disease. Paediatr Respir Rev 13:10–15
11. Bucci G, Cook CD, Hamann JF (1961) Studies of respiratory physiology in children. Lung diffusing capacity, diffusing capacity of the pulmonary membrane and pulmonary capillary blood volume in congenital heart disease. J Clin Investig 8(Pt 1–2):1431–1441. https://doi.org/10.1172/JCI104374
12. Kocis KC, Meliones JN (2000) Cardiopulmonary interactions in children with congenital heart disease: physiology and clinical correlates. Prog Pediatr Cardiol 11:203–210
13. Alonso-Gonzalez R, Borgia F, Diller G-P et al (2013) Abnormal lung function in adults with congenital heart disease: prevalence, relation to cardiac anatomy, and association with survival. Circulation 127(8):882–890
14. Wallgren G, Geubelle F, Koch G (1960) Studies of the mechanics of breathing in children with congenital heart lesions. Acta Paediatrica 49:415–425
15. Wang EE, Law BJ, Stephens D (1995) Pediatric Investigators Collaborative Network on Infections in Canada (PICNIC) prospective study of risk factors and outcomes in patients hospitalized with respiratory syncytial viral lower respiratory tract infection. J Pediatr 126:212–219
16. Engelfriet PM, Duffels MG, Moller T et al (2007) Pulmonary arterial hypertension in adults born with a heart septal defect: the Euro Heart Survey on adult congenital heart disease. Heart 93:682–687
17. Rosenthal DN, Friedman AH, Kleinman CS et al (1995) Thromboembolic complications after Fontan operations. Circulation 92:287–293

18. Mahar T, Katzman P, Alfieris G (2009) A case of fatal septic pulmonary embolus arising from an infected Sano conduit. Pediatr Cardiol 30:181–183
19. Vogel M, Berger F, Kramer A et al (1999) Incidence of secondary pulmonary hypertension in adults with atrial septal or sinus venosus defects. Heart 82:30–33
20. Sachweh JS, Daebritz SH, Hermanns B et al (2006) Hypertensive pulmonary vascular disease in adults with secundum or sinus venosus atrial septal defect. Ann Thorac Surg 81:207–213
21. Schoen SP, Kittner T, Bohl S et al (2006) Transcatheter closure of atrial septal defects improves right ventricular volume, mass, function, pulmonary pressure, and functional class: a magnetic resonance imaging study. Congenit Heart Dis 92:821–826
22. Murphy JG, Gersh BJ, McGoon MD et al (1990) Long-term outcome after surgical repair of isolated atrial septal defect. Follow-up at 27 to 32 years. N Engl J Med 323:1645–1650
23. Zaqout M, De Baets F, Schelstraete P et al (2010) Pulmonary function in children after surgical and percutaneous closure of atrial septal defect. Pediatr Cardiol 20(31):1171–1175