Chinese Journal of Physiology 56(2): 110-116, 2013
DOI: 10.4077/CJP.2013.BAA086

Lower Exercise Capacity in Children with Asymptomatic Atrial Septal Defect Associated with Circulatory Impairment

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Abstract

The exercise capacity and limitation in children with asymptomatic atrial septal defect (ASD) have not been explored thoroughly. The aim of our study was to examine the influence of asymptomatic ASD on exercise capacity in children. Fifty children with asymptomatic ASD who had undergone medical interventions at least 4 years ago and fifty normal children were recruited in this study. The exercise capacity was assessed by the symptom-limited exercise test through the Bruce treadmill protocol. The pulmonary function was also evaluated by the spirometry. Circulatory and ventilatory impairments were respectively reflected by chronotropic incompetence (CI) and ventilatory limitation as measured by the exercise test and spirometry. Eleven (22%) of children with ASD failed to reach the age-predicted peak heart rate during the exercise test. Also, children with ASD had significantly lower oxygen consumption at anaerobic threshold and peak exercise ($P < 0.01$). The rate of circulatory impairment was significantly higher in children with ASD ($P < 0.01$). However, the pulmonary function and ventilatory limitation were comparable between these two groups. Within the ASD group, children with CI had significantly worse peak oxygen consumption than their peers without CI ($P < 0.01$). Our study examined a larger population sample and confirmed that children with asymptomatic ASD, who had previously undergone medical interventions, had significantly worse exercise capacity than normal children. This difference in exercise capacity was mainly related to circulatory impairment. Our findings support the concerns of exercise limitation in ASD children.

Key Words: chronotropic incompetence, congenital heart disease, oxygen consumption, pulmonary function

Introduction

Atrial septal defect (ASD) accounts for about 10 percent of congenital heart disease, and patients with ASD are usually asymptomatic in early life. Most patients with ASD, who are free of overt symptoms or only have mild symptoms, are unrecognized until later decades of life (4, 6, 20). Other long-term sequelae in patients with ASD include arrhythmia, cardiac emboli and stroke (15, 28). The options of surgical treatments for patients with ASD include device or surgery closure, depending on the defect type and size. However, some factors may contribute to the failure of surgery closing an ASD, such as a

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Received: November 22, 2011; Revised: April 16, 2012; Accepted: May 7, 2012.
 ISSN : 0304-4920. http://www.cps.org.tw

smaller defect size, advanced pulmonary hypertension and severe left ventricular dysfunction. Particularly, the last two factors are contraindicated to receive the closure (13, 28). One of the most common symptoms of patients with ASD is exercise intolerance in the form of exertional dyspnea or fatigue (26). Exercise intolerance could clinically be responsible for the exercise limitation in patients with ASD.

A few researchers have indicated that the subjective assessment of exercise performance does not validly reflect the clinical status of patients with ASD. Many patients with ASD have no complaints of limited exercise capacity, even in the status of significant volume overloading (19, 20). Clinically, a graded exercise test is useful for objective evaluation of exercise performance. Common purposes of the exercise test include the assessment of the effectiveness of medical or surgical interventions, the detection of occurrence of specific exercise-induced symptoms or signs, and the establishment of baseline data for follow-up of the rehabilitation programs (1, 17, 27). Data from exercise tests can also be used to differentiate possible factors contributing to exertional dyspnea (17). Recently, exercise tests are frequently used in clinical evaluation of congenital heart disease in children and adults, including pre- and post-operation efficacy evaluation (11, 16, 22). Previous studies have revealed that patients with congenital heart disease, such as ASD and tetralogy of Fallot, demonstrate significant decreases in the exercise capacity (3, 7). Patients with ASD may have normal or lower level of fitness depending on the severity of disease and comorbidity. After interventional closure of defects, exercise capacity of adults with ASD could be improved when compared with their pre-operative exercise performance (2, 9, 12, 23). However, studies on the exercise capacity and limitation in children with asymptomatic ASD have been limited. Thus, the aim of the present study was to examine and compare the exercise capacity between children with asymptomatic ASD and normal children.

Materials and Methods

Subjects

One hundred children participated in our study. Fifty children with asymptomatic ASD were recruited, and received the exercise test for evaluation of their exercise capacity at the Veterans General Hospital-Kaohsiung, Taiwan. In this study, the children with asymptomatic ASD had non-closure, surgery or device closure at least 4 years ago. Exclusion criteria were [a] older than 18 years old, [b] combined with other types of congenital heart disease or symptomatic heart disease, and [c] notable orthopedic problems and inability to participate in the exercise test. The children with ASD, aged 11.2 ± 3.5 years old, included 19 boys and 31 girls. Of these patients, 23 had received the device closure and 11 received the surgery closure. In the study, fifty normal children were recruited as the control group; the normal children, aged 10.7 ± 3.4 years old, included 25 boys and 25 girls. The Ethics Committee of Medicine at the Veterans General Hospital-Kaohsiung approved all procedures, and informed consent was obtained from each subject for participating in this study.

The Exercise Test

The symptom-limited treadmill exercise test was designed to measure the subjects' exercise capacity. The test system consisted of a treadmill, gas analyzer and electrocardiographic monitor (Metamax 3B, Cortex Biophysik GmbH Co., Leipzig, Germany). Two groups of children performed the symptom-limited exercise test according to the Bruce protocol suggested by American College of Sports Medicine (ACSM). When the children demonstrated subjective unbearable symptoms, the test was terminated (1, 17). The oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$) were measured by breath-by-breath ventilation during the test. In addition, metabolic equivalents (MET), minute ventilation (VE), blood pressure and heart rate were measured throughout the exercise test. The anaerobic threshold (AT) was determined by the VE/VO_2 and VE/VCO_2 methods which were suggested as indicators for assessing children (11, 16, 26). During the test, the condition of peak exercise heart rate lower than 80% of the age-predicted peak heart rate was considered as CI (14, 17).

Pulmonary Function Test

Pulmonary function test was performed by spirometry at rest in all subjects. The test included measurements of forced vital capacity (FVC), forced expiratory volume in one second (FEV_1) and maximal voluntary ventilation (MVV). The clinical specialists conducting the test had at least 2 years of experiences in conducting the measurement of pulmonary function for children. Data of the exercise test and pulmonary function test were combined (1-VEmax/MVV) to calculate the breathing reserve. Breathing reserve values lower than 30% were considered as ventilatory limitation (17).

Statistical Analysis

The variable distribution of our study was tested

Table 1. Demographic characteristics of the ASD and control groups

	ASD	Control	*P* Value
Male/Female	19/31	25/25	0.314
Age (yr)	11.2 ± 3.5	10.7 ± 3.4	0.467
Weight (kg)	38.5 ± 17.6	39.5 ± 15.5	0.763
Height (cm)	140.3 ± 18.1	142.2 ± 19.2	0.603
Body Mass Index	18.9 ± 4.5	21.1 ± 15.0	0.328
BMID	2.0 ± 0.8	2.1 ± 0.9	0.637
Body Fat (%)	19.3 ± 8.0	19.2 ± 8.7	0.983
Interventional Treatments			
Non-Closure	32% (16/50)		
Device-Closure	46% (23/50)		
Surgery-Closure	22% (11/50)		

Data are the means ± standard deviation. BMID: body mass index adjusted by age.

Table 2. Performance of exercise test of the ASD and control groups

Failure to reach PPHR	ASD	Control	*P* Value
Percentage	22% (11/50)**	0% (0/50)	0.001
Male: Female	2 : 9	0 : 0	

PPHR: age-predicted peak heart rate. $^{**}P < 0.01$ compared with the control group.

before further data analysis. Except for categorical variables, all of our estimated variables were approximately normally distributed. Data were expressed as means ± standard deviation (SD). An independent *t*-test was applied to compare the continuous variables, such as ages, exercise capacity, and pulmonary function between the ASD and normal groups. *Chi-Square* test was conducted to examine the categorical variables, such as gender. All statistical analyses were performed using Version 15.0 SPSS software (SPSS Inc., Chicago, IL, USA). Differences were considered significant at $P < 0.05$.

Results

The demographic characteristics of ASD and control groups in this study are shown in Table 1. There were no significant differences in gender, age, body weight, height, body mass index (BMI), age-adjusted BMI and body fat between the two groups. Among asymptomatic ASD participants, twenty-three (46%) of them received device closure and eleven (22%) received surgical closure in their early ages. The performance of exercise test between ASD and control groups is shown in Table 2. Eleven (22%) of the children with ASD failed to reach the age-predicted peak heart rate (PPHR). Among them, five children stopped the exercise test due to dyspnea, three stopped due to leg fatigue, and three others stopped due to other subjective unbearable symptoms. The failure rate in children with ASD was significantly higher than that in control subjects ($P < 0.01$).

The children with ASD had significantly lower diastolic blood pressure at rest, and lower MET and HR at anaerobic threshold and peak exercise than the control subjects ($P < 0.05$) (Table 3). Nine (18%) of children with ASD had CI, but this impairment did not exist in the control group. The rate of the circulatory impairment was significantly higher in the ASD group compared with the control group ($P < 0.01$). Moreover, within the ASD group, subjects with CI had significantly worse peak oxygen consumption than their peers without CI ($P < 0.01$) (Fig. 1).

The spirometric data demonstrated that these two groups had similar pulmonary function, although the ASD group had slightly higher FEV1/FVC than the control group (Table 3). Objectively, the occurrence of ventilatory limitation in the ASD and control groups was 58% and 52%, respectively. None of them were defined as the restrictive or obstructive lung disease based on the clinical criteria.

Based on the exercise test data, the ASD group had significantly lower AT MET and peak MET values than the control subjects. The data of children with ASD were further divided into 3 subgroups depending on the different medical and surgical treatments, *i.e.* non-operated (non-OP), operated (OP) and transcatheter closure (Cath) subgroups, and were compared with the control group (Table 4). The results showed

Table 3. Comparison of exercise test and spirometric data between the ASD and control groups

	ASD	Control	*P* Value
Exercise Test			
Rest SBP (mmHg)	103.8 ± 14.1	105.4 ± 17.0	0.634
Rest DBP (mmHg)	59.3 ± 8.1*	63.2 ± 7.3	0.015
Rest HR (beat/min)	85.8 ± 12.7	89.7 ± 18.5	0.220
AT $\dot{V}O_2$ (ml/kg/min)	21.2 ± 5.2**	26.9 ± 6.3	< 0.001
AT MET	6.1 ± 1.5**	7.7 ± 1.8	< 0.001
AT HR (beat/min)	135.2 ± 20.8**	145.8 ± 13.4	0.004
Peak $\dot{V}O_2$ (ml/kg/min)	31.8 ± 6.8**	37.5 ± 7.9	< 0.001
Peak MET	9.1 ± 1.9**	10.7 ± 2.3	< 0.001
Peak HR (beat/min)	177.7 ± 14.1*	182.8 ± 4.8	0.018
PPHR (%)	85.2 ± 7.0*	87.4 ± 2.6	0.038
Peak SBP (mmHg)	164.9 ± 26.4	159.5 ± 28.5	0.336
Peak DBP (mmHg)	90.4 ± 31.9	87.9 ± 17.3	0.640
CI	9/50**	0/50	0.003
Spirometry			
FEV_1 (l)	2.4 ± 1.6	2.2 ± 1.0	0.864
FVC (l)	2.5 ± 1.2	2.5 ± 1.3	0.314
FEV_1/FVC (%)	91.3 ± 10.7	88.6 ± 10.0	0.202
MVV (l/min)	103.8 ± 38.2	143.8 ± 44.5	0.132
VL	29/50	26/50	0.666

Data are the means ± standard deviation. SBP: systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate, AT: anaerobic threshold, $\dot{V}O_2$: oxygen consumption, MET: metabolic equivalents, PPHR: age-predicted peak heart rate, CI: chronotropic incompetence, FEV_1: forced expiratory volume at 1 min, FVC: forced vital capacity, MVV: maximal voluntary ventilation, VL: ventilatory limitation. *$P < 0.05$, **$P < 0.01$ compared with the control group.

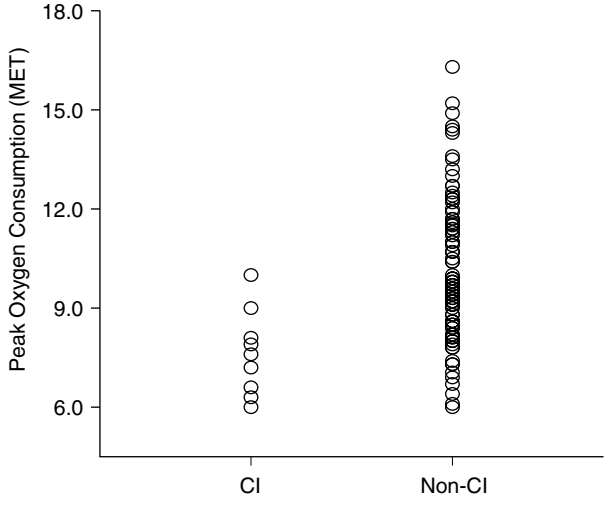

Fig. 1. Peak oxygen consumption of subjects with chronotropic incompetence (CI) and non-CI. Peak oxygen consumption was significantly lower in subjects with CI than those with non-CI ($P < 0.01$).

that the data of AT MET and peak MET in each subgroup were significantly lower than in the control group ($P < 0.05$). Data of AT HR were significantly lower in the OP and Cath subgroups ($P < 0.05$), and the peak heart rate was significantly lower in the OP subgroup compared with the control group ($P < 0.05$).

Discussion

The current study may be the first work to examine a larger sample population to confirm that children with asymptomatic ASD had significantly a worse exercise capacity than control subjects. Our results clearly demonstrated that children with asymptomatic ASD had a higher failure rate than the control group during the exercise test. They had significantly lower oxygen consumption at anaerobic threshold and peak exercise and higher rate of circulatory impairment as indicated by CI, but this impairment did not exist in the control group. However, these two groups had comparable pulmonary function. Within the ASD group, subjects with CI had significantly worse peak oxygen consumption than their peers without CI.

Using the exercise test, we found that children with asymptomatic ASD had obviously worse exercise capacity, as indicated by a higher failure rate to reach the age-predicated peak heart rate. On the contrary, all subjects of the control group reached the age-predicted peak heart rate. This finding was consistent

Table 4. Comparison of exercise test data of each ASD subgroup with the control group

Exercise Test	*P* Value		
Subgroups	Non-OP (n = 16)	OP (n = 11)	Cath (n = 23)
AT MET	< 0.01**	0.028*	< 0.01**
AT HR (beat/min)	0.296	0.011*	0.042*
Peak MET	< 0.01**	< 0.01**	0.011*
Peak HR (beat/min)	0.787	0.013*	0.107

Non-OP: non-operated subgroup, OP: operated closure subgroup, Cath: transcatheter closure subgroup, AT: anaerobic threshold, MET: metabolic equivalents, HR: heart rate. $*P < 0.05$, $**P < 0.01$ compared with the control group.

with some previous studies (2, 7). Fredriksen *et al*. stated that adults with various congenital heart diseases (including ASD) had significantly diminished exercise capacity and achieved lower heart rate than their predicted value (7). In addition, Brochu *et al*. indicated that adults with ASD who considered themselves asymptomatic had 11% less maximal oxygen consumption than their predicted value. They also suggested that the subjective evaluation of clinical functional class would lead to underestimation of the cardiovascular burden of the left-to-right shunt (2). The present study was designed to objectively evaluate exercise capacity in children with asymptomatic ASD by the exercise test. The results would be helpful for early detection and management of exercise intolerance or limitation for children with ASD clinically. A previous study has encouraged the application of regular exercise intervention for all ages in patients with congenital heart disease (25). After the intervention, peak $\dot{V}O_2$ and work rate would be improved significantly. However, exercise intervention for those patients with ventricular dysfunction or recent arrhythmia should be performed with caution (25).

Our finding revealed that children with ASD had a higher failure rate than the control group during the exercise test, and they had significantly lower oxygen consumption at anaerobic threshold and peak exercise. Some previous studies have also indicated that adults with non-operated ASD had a lower exercise capacity. After the ASD was repaired, the exercise capacity and oxygen uptake at anaerobic threshold and peak exercise were significantly improved in adults (2, 8, 12, 24). Similar results have been reported in children with ASD receiving transcatheter closure (10). Among those previous studies, only a few works specifically compared children with ASD with the healthy population. Pfammatter *et al*. (16 children with ASD) and Rosenthal *et al*. (22 children with ASD) indicated that after surgery, maximal exercise performance was comparable between children with ASD and control groups (19, 21). We speculated that these different findings of the exercise capacity for children with ASD may be due to different modes of exercise test or varied severity of pathophysiologic conditions. In this study, we chose the treadmill rather than the bicycle as the tool of exercise test. Clinically, the treadmill has been a preferred tool for ill children (11, 22). When the exercise test was performed by the treadmill, peak oxygen consumption would be higher than bicycle ergometry due to recruitment of more muscle groups. Patient may tend to stop the exercise test earlier by using bicycle ergometry because of the exercise intolerance of the increasing resistances (22). Based on our findings, we suggest that the treadmill exercise test could be more sensitive in assessing exercise capacity and functional limitation occurred in children with ASD.

Exercise intolerance has been known as a common symptom in children with congenital heart disease, which may be caused by circulatory or ventilatory impairments, or deconditioning (17, 20, 28). We used the clinical flowchart of the exertional dyspea to differentiate possible factors determining poor exercise performance (17). As a result, the possible cause of poor exercise performance in our study might be the circulatory impairment, rather than the ventilatory impairment and deconditioning. Our data revealed that children with ASD had a higher rate of CI which represented circulatory impairment, but the pulmonary function was comparable between the ASD and control groups. In consistent with our finding, a previous study has shown the tendency of CI in children with ASD before and after the defect closure (18). Also, Epstein *et al*. pointed out that children with asymptomatic operation-closed ASD may have residual reduction of their cardiac output responses to intensive upright exercise (5). Moreover, within the ASD group, we found that subjects with CI significantly had worse peak oxygen consumption than their peers without CI. This finding implicated that the circulatory impairment was strongly associated with lower exercise performance in children with ASD. However, further studies should be conducted to differentiate the etiology of the diminished ex-

ercise performance in children with ASD.

Our spirometric data showed that the pulmonary function at rest in children with ASD were similar to those of the control subjects, consistent with previous studies (12, 19). Many researchers have reported that resting ventilatory function is normal or bordering normal in children with uncomplicated ASD (12, 19). Also, FVC and FEV_1 in children with ASD were found similar with normal population. Before and after the ASD operation, FVC and FEV_1 remained unchanged. Moreover, Fredriksen *et al*. found that FVC was lower in various congenital heart diseases except for those with ASD (7). These findings suggested that the ventilatory impairment might not be responsible for the limited exercise capacity in children with ASD.

In the present study, we divided the children with ASD into 3 subgroups depending on different interventional treatments (*i.e*. non-OP, OP and Cath subgroups), and compared with data of the control group. The results indicated that, in each ASD subgroup, oxygen consumption at anaerobic threshold and peak exercise was significantly lower than those in the control group. However, no significant difference of the peak heart rate existed when comparing the control group with either the Cath or non-OP subgroup. Some investigators suggested that the peak heart rate seemed not sensitive enough in evaluating peak exercise performance in children (11, 22). They pointed out that the peak heart rate should not be used as a single exercise parameter in children because of large inter-individual differences in maximal heart rate. Moreover, peak heart rate would not be recommended to assess the exercise capacity in chronotropic impaired children. Consistently, our study suggested that, in addition to the peak heart rate, some parameters of the exercise test (*e.g*. peak oxygen consumption) should be used to sensitively evaluate peak exercise performance in children with ASD.

In conclusion, our study examined a larger population sample to confirm that children with asymptomatic ASD, who had undergone medical interventions at least 4 years ago, had significantly lower exercise capacity than normal children. This was mainly related to circulatory impairment. Our findings support the clinical evaluation and treatment of exercise limitation in children with asymptomatic ASD.

Acknowledgments

This study was supported by grants from the Veterans General Hospital – Kaohsiung (No. VGHKS96-CT1-29) and the Institute of Statistics at National University of Kaohsiung, Taiwan, ROC. We are grateful to Dr. Kam-Fai Wong for his comments on this manuscript.

References

1. American College of Sports Medicine. ACSM's Guidelines for exercise testing and prescription. 7th ed. Philadelphia: Lippincott Williams & Wilkins, 2006.
2. Brochu, M.C., Baril, J.F., Dore, A., Juneau, M., De Guise, P. and Mercier, L.A. Improvement in exercise capacity in asymptomatic and mildly symptomatic adults after atrial septal defect percutaneous closure. *Circulation* 106: 1821-1826, 2002.
3. Casey, F.A., Craig, B.G. and Mulholland, H.C. Quality of life in surgically palliated complex congenital heart disease. *Arch. Dis. Child*. 70: 382-386, 1994.
4. Dave, K.S., Pakrashi, B.C., Wooler, G.H. and Ionescu, M.I. Atrial septal defect in adult. *Am. J. Cardiol.* 31: 7-13, 1973.
5. Epstein, S.E., Beiser, G.D., Goldstein, R.E., Rosing, D.R., Redwood, D.R. and Morrow, A.G. Hemodynamic abnormalities in response to mild and intense upright exercise following operative correction of an atrial septal defect or tetralogy of fallot. *Circulation* 47: 1065-1075, 1973.
6. Feldt, R.H., Avasthey, P., Yoshimasu, F., Kurland, L.T. and Titus, J.L. Incidence of congenital heart disease in children born to residents of Olmsted County, Minnesota, 1950-1969. *Mayo Clin. Proc*. 46: 794-799, 1971.
7. Fredriksen, P.M., Veldtman, G., Hechter, S., Therrien, J., Chen, A., Warsi, M.A., Freeman, M., Liu, P., Siu, S., Thaulow, E. and Webb, G. Aerobic capacity in adults with various congenital heart diseases. *Am. J. Cardiol*. 87: 310-314, 2001.
8. Gatzoulis, M.A., Redington, A.N., Somerville, J. and Shore, D.F. Should atrial septal defects in adults be closed? *Ann. Thorac. Surg*. 61: 657-659, 1996.
9. Giardini, A., Donti, A., Formigari, R., Specchia, S., Prandstraller, D., Bronzetti, G., Bonvicini, M. and Picchio, F.M. Determinants of cardiopulmonary functional improvement after transcatheter atrial septal defect closure in asymptomatic adults. *J. Am. Coll. Cardiol*. 43: 1886-1891, 2004.
10. Giardini, A., Donti, A., Specchia, S., Formigari, R., Oppido, G. and Picchio, F.M. Long-term impact of transcatheter atrial septal defect closure in adults on cardiac function and exercise capacity. *Int. J. Cardiol*. 124: 179-182, 2008.
11. Hebestreit, H. Exercise testing in children — what works, what doesn't, and where to go? *Paediatr. Respir. Rev.* 5: S11-S14, 2004.
12. Helber, U., Baumann, R., Seboldt, H., Reinhard, U. and Hoffmeister, H.M. Atrial septal defect in adults: cardiopulmonary exercise capacity before and 4 months and 10 years after defect closure. *J. Am. Coll. Cardiol*. 29: 1345-1350, 1997.
13. Horvath, K.A., Burke, R.P., Collins, J.J. Jr. and Cohn, L.H. Surgical treatment of adult atrial septal defects: early and long-term results. *J. Am. Coll. Cardiol*. 20: 1156-1159, 1992.
14. Katritsis, D. and Camm, A.J. Chronotropic incompetence: a proposal for definition and diagnosis. *Brit. Heart J*. 70: 400-402, 1993.
15. Kedia, G., Tobis, J. and Lee, M.S. Patent foramen ovale: clinical manifestations and treatment. *Rev. Cardiovasc. Med.* 9: 168-173, 2008.
16. Matthys, D. Pre- and postoperative exercise testing of the child with atrial septal defect. *Pediatr. Cardiol*. 20: 22-25, 1999.
17. Milani, R.V., Lavie, C.J., Mehra, M.R. and Ventura, H.O. Understanding the basics of cardiopulmonary exercise testing. *Mayo Clin. Proc*. 81: 1603-1611, 2006.
18. Norozi, K., Gravenhorst, V., Hobbiebrunken, E. and Wessel, A. Normality of cardiopulmonary capacity in children operated on to correct congenital heart defects. *Arch. Pediatr. Adolesc. Med*. 159: 1063-1068, 2005.
19. Pfammatter, J.P., Zanolari, M. and Schibler, A. Cardiopulmonary exercise parameters in children with atrial septal defect and in-

creased pulmonary blood flow: short-term effects of defect closure. *Acta Paediatr*. 91: 65-70, 2002.
20. Reybrouck, T. and Mertens, L. Physical performance and physical activity in grown-up congenital heart disease. *Eur. J. Cardiovasc. Prev. Rehabil*. 12: 498-502, 2005.
21. Rosenthal, M., Redington, A. and Bush, A. Cardiopulmonary physiology after surgical closure of asymptomatic secundum atrial septal defects in childhood. Exercise performance is unaffected by age at repair. *Eur. Heart J*. 18: 1816-1822, 1997.
22. Stephens, P. Jr. and Paridon, S.M. Exercise testing in pediatrics. *Pediatr. Clin. North Am*. 51: 1569-1587, 2004.
23. Suchon, E., Tracz, W., Podolec, P. and Sadowski, J. Atrial septal defect in adults: echocardiography and cardiopulmonary exercise capacity associated with hemodynamics before and after surgical closure. *Interact. Cardiovasc. Thorac. Surg*. 4: 488-492, 2005.
24. Suchon, E., Tracz, W., Podolec, P. and Sadowski, J. Atrial septal defect in adults: the influence of age and haemodynamic parameters on the results of surgical repair. *Kardiol. Pol*. 64: 470-476, 2006.
25. Ten Harkel, A.D.J. and Takken, T. Exercise testing and prescription in patients with congenital heart disease. *Int. J. Pediatr*. doi:10.1155/2010/791980, 2010.
26. Trojnarska, O., Szyszka, A., Gwizdala, A., Oko-Sarnowska, Z., Katarzynski, S., Siniawski, A., Chmara, E. and Cieslinski, A. Evaluation of exercise capacity with cardiopulmonary exercise testing and type B natriuretic peptide concentrations in adult patients with patent atrial septal defect. *Cardiology* 106: 154-160, 2006.
27. Washington, R.L. Cardiorespiratory testing: anaerobic threshold/respiratory threshold. *Pediatr. Cardiol*. 20: 12-15, 1999.
28. Webb, G. and Gatzoulis, M.A. Atrial septal defects in the adult: recent progress and overview. *Circulation* 114: 1645-1653, 2006.