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Original Article

Exercise restriction is not associated with increasing body mass index over time in patients with anomalous aortic origin of the coronary arteries

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Abstract Anomalous aortic origin of the coronary arteries is associated with exercise-induced ischaemia, leading some physicians to restrict exercise in patients with this condition. We sought to determine whether exercise restriction was associated with increasing body mass index over time. From 1998 to 2015, 440 patients ⩽30 years old were enrolled into an inception cohort. Exercise-restriction status was documented in 143 patients. Using linear mixed model repeated-measures regression, factors associated with increasing body mass index z-score over time, including exercise restriction and surgical intervention as time-varying covariates, were investigated. The 143 patients attended 558 clinic visits for which exercise-restriction status was recorded. The mean number of clinic visits per patient was 4, and the median duration of follow-up was 1.7 years (interquartile range (IQR) 0.5–4.4). The median age at first clinic visit was 10.3 years (IQR 7.1–13.9), and 71% (101/143) were males. All patients were alive at their most recent follow-up. At the first clinic visit, 54% (78/143) were exercise restricted, and restriction status changed in 34% (48/143) during follow-up. The median baseline body mass index z-score was 0.2 (IQR 0.3–0.9). In repeated-measures analysis, neither time-related exercise restriction nor its interaction with time was associated with increasing body mass index z-score. Surgical intervention and its interaction with time were associated with decreasing body mass index z-score. Although exercise restriction was not associated with increasing body mass index over time, surgical intervention was associated with decreasing body mass index z-score over time in patients with anomalous aortic origin of the coronary arteries.

Keywords: Anomalous coronary arteries; exercise restriction; body mass index; repeated-measures analysis

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THE RISK OF SUDDEN CARDIAC DEATH FROM coronary artery anomalies has been well described previously.[1,2] Coronary arteries that arise from the aorta outside of its ipsilateral sinus of Valsalva, anomalous aortic-origin coronary arteries, with an interarterial course impart a greater risk.[3]

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In an autopsy series of patients who died suddenly, 0.2–6.3% were diagnosed with anomalous aortic-origin coronary arteries.[4]

Little high-quality evidence exists to guide the management of these patients. Restriction of exercise level and surgery comprise the primary management strategies.[5,6] In general, concern exists regarding the merit of exercise restriction in children. It may result in decreased physical activity, leading to caloric imbalance and increased adiposity. Children with congenital heart disease have at least an equal risk of obesity as the general paediatric population.[7,8] Obesity may be even more common in adults with congenital heart disease and may promote the early development of acquired cardiovascular disease as well.[9,10]

In this investigation, we used the Congenital Heart Surgeons' Society Data Center's registry of patients diagnosed with anomalous aortic-origin coronary arteries to gain insight into the relationship between changes in body mass index over time in patients who were exercise restricted versus those who were not. We hypothesised that exercise restriction in patients with anomalous aortic-origin coronary arteries was associated with increasing body mass index over time.

Materials and methods

The details of the Congenital Heart Surgeons' Society's anomalous aortic-origin coronary arteries registry have been previously described.[11] In brief, an ongoing inception cohort of 440 patients diagnosed with anomalous aortic-origin coronary arteries from January 1998 to September 2015 was enrolled by 38 institutions. Patients were less than 30 years of age at the time of enrolment. Patients with any of type of haemodynamically significant structural cardiac disease were excluded. Only patients with both documented height and weight measurements and exercise-restriction status were included in this analysis, which comprised the study population (n = 143). If exercise-restriction status had never been documented, the patient was excluded.

Data acquisition and follow-up

Institutional Review Board approval for enrolment was obtained from each of the 38 participating institutions. Patient participation in the study was voluntary, and patient medical information was kept confidential. Parental consent was obtained for patients under 18 years of age before enrolment. For patients over 18 years of age, consent was obtained directly. Diagnostic, surgical, echocardiographic, and clinical characteristics were abstracted from de-identified institutional patient medical records, as previously described.[12] Annual follow-up of patient medical history was performed by the Congenital Heart Surgeons' Society Data Center staff.

Statistical analyses

Baseline demographic, clinical, operative, echocardiographic, and anatomical characteristics were summarised. Z-scores for weight, height, and body mass index were calculated for all patients using the 2000 standards from the Centers for Disease Control and Prevention in order to account for the age-dependency of body mass index.[13] The macros used to generate the z-scores were downloaded from http://www.cdc.gov/nccdphp/dnpao/growthcharts/resources/sas.htm. Categorical variables are reported as percentages and frequencies and were compared using the χ^2 test or Fisher's exact test, as appropriate. Continuous variables are summarised as means and standard deviations or medians with interquartile ranges (IQR). The normality of their distributions was evaluated using the Shapiro–Wilk test and were compared using Student's t-test or the Mann–Whitney U-test, as appropriate. A p-value of 0.05 was considered significant. For time-related exercise restriction, informative imputation based on the previous clinic visit's status was utilised if exercise-restriction status of subsequent visits was missing.

Univariable and multivariable associations between body mass index z-score and exercise-restriction status over time were assessed using linear mixed model regression (PROC MIXED) with repeated measures of body mass index z-scores. Covariates entered into the multivariable model included baseline exercise-restriction status, sex, baseline symptomatic state, age at diagnosis, age at operation, coronary arterial anatomical characteristics, and exercise restriction and surgical intervention over time, as time-varying covariates, where their values were allowed to change at each clinic visit. The covariates with significant associations with body mass index z-score over time in the univariable analysis were entered into a multivariable linear mixed model repeated-measures analysis. Stepwise selection was performed manually, as PROC MIXED does not include automatical variable selection. A threshold for significance of $p = 0.05$ was used for univariable associations; $p = 0.10$ was used for covariate entry into the model; and $p = 0.05$ was used for covariate retention. For all significant covariates, interaction terms with time were created and tested for statistical significance. All analyses were performed using SAS 9.2 (SAS Institute Inc., Cary, North Carolina, United States of America).

Results

Baseline characteristics

In total, 143 patients who attended 558 clinic visits were included in this analysis. Patients attended a

Table 1. Baseline and demographic characteristics.

	Study population
Sex, male	71% (101/143)
Symptomatic	54% (77/143)
Alive at last follow-up	100% (143/143)
Underwent an operation	64% (92/143)
Operation before study period	5.4% (5/92)
Operation during study period	95% (87/92)
Exercise restricted	55% (78/143)
Change in exercise restriction during the study period	34% (48/143)
Age at diagnosis (years)	10.3 (7.1–13.9)
Baseline BMI z-score	0.2 (−0.3 to 0.9)
Baseline BMI	17.7 (15.8–20.9)
Follow-up interval (years)	1.7 (0.5–4.4)
Total number of clinic visits	3 (2–5)

BMI = body mass index

median of three clinic visits, with an interquartile range of two to five visits and an absolute range of 1–13 clinic visits. Baseline patient demographic characteristics are shown in Table 1. Males accounted for 71% of patients. At the first clinic visit, 54% were symptomatic, and exercise restriction was recommended for 55% or 78/143 patients. Symptoms were present in 63%, or 49/78, of restricted patients. Surgery for anomalous aortic-origin coronary arteries was performed in five patients before the study period and in 87 during the study period. At their first clinic visit, 55% were exercise restricted, and 34% (48) of patients' exercise-restriction status changed during follow-up. Of the 48 patients whose exercise-restriction status changed, 39 underwent surgery. Exercise restriction was lifted in all 39 of these patients. Patients were diagnosed at a median age of 10.3 years, with an IQR of 7.1–13.9 years, and were followed-up for a median of 1.7 years (IQR 0.5–4.4). All patients were alive at the end of the study period. The median baseline body mass index z-score was +0.2 (IQR −0.3 to +0.9).

Anatomical characteristics of surgically managed patients

Detailed anatomical data were available for patients who underwent repair (n = 92, Table 2). A single operation was performed for 86 patients, two operations for five patients, and three operations for a single patient. Anomalous right coronary arteries were present in 73% of patients, whereas 27% had an anomalous left coronary arteries. An interarterial or an intramural course was present in 91 and 95%, respectively, whereas none of them had an intraconal course. Acute angulation of the take-off from the anomalous sinus was observed in 91%. A slit-like or stenotic orifice was seen in 57 and 42%, respectively.

Table 2. Anatomical characteristics of surgical patients.

	Underwent surgery (n = 92)*
Anomalous coronary laterality	
Right	73% (67/92)
Left	27% (25/92)
Origin of the anomalous coronary	
Right sinus	25% (23/92)
Left sinus	67% (62/92)
Non-coronary sinus	1% (1/92)
Supra-sinus**	7% (6/92)
Interarterial	91% (84/92)
Intramural	95% (87/92)
Intraconal	0% (0/91)
Ostia	
Two ostia on left sinus	70% (63/90)
Two ostia on right sinus	24% (22/90)
One ostia on left sinus	3% (3/90)
One ostia on right sinus	2% (2/88)
Acute, angulated angle of take-off from the anomalous sinus	91% (79/86)
Orifice	
Slit-like	57% (47/83)
Round	12% (10/84)
Stenotic	42% (35/84)

*Complete descriptions of all anatomic features were not available for all patients from their operative notes
**Refers to coronary arteries found explicitly superior to the sinus ridge. For specific definitions and descriptions of the anatomic features[12,14]

Univariable associations with body mass index z-score over time

Univariable associations of baseline characteristics, anatomical characteristics, time-varying exercise restriction, and surgical intervention with body mass index z-score over time were tested using repeated-measures analysis. Male sex, exercise restriction at baseline, Grade 4 dual orifices of the left coronary sinus, in which a single orifice within the coronary sinus with a common coronary arterial trunk that bifurcates into two separate coronary arteries outside of the aorta, time-related exercise-restriction status, and time-related surgical intervention were all associated with increasing body mass index z-score over time (Table 3). All, except for male sex, had significant interactions with time.

In Figure 1, all patients' body mass index z-scores are plotted over time. Regression lines, derived from the parameter estimates from repeated-measures analysis, were solved for exercise-restriction status (parameter estimate = 0.41, $p = 0.05$) and its interaction term with time (parameter estimate = −0.03, $p = 0.55$) and were plotted. As displayed, body mass index z-scores over time did not differ by time-related exercise-restriction status.

Table 3. Univariable associations with body mass index z-score over time.

	Estimate	p	Interaction with time	p (Time)
Time	0.03	0.19		
Exercise restriction at baseline	0.41	0.03	0.50	0.01
Interaction term, time with exercise restriction at baseline			−0.05	0.10
Sex, male	0.60	0.003	0.52	0.02
Interaction term, time with male sex			0.04	0.26
Dual orifices, left coronary sinus, Grade 4	1.07	0.09	0.42	0.56
Interaction term, time with Grade 4			0.35	0.03
Time-related exercise restriction	0.35	0.06	0.41	0.05
Interaction term, time with time-related exercise restriction			−0.03	0.55
Surgical intervention	0.10	0.38	0.30	0.03
Interaction term, time with surgical intervention			−0.11	0.01

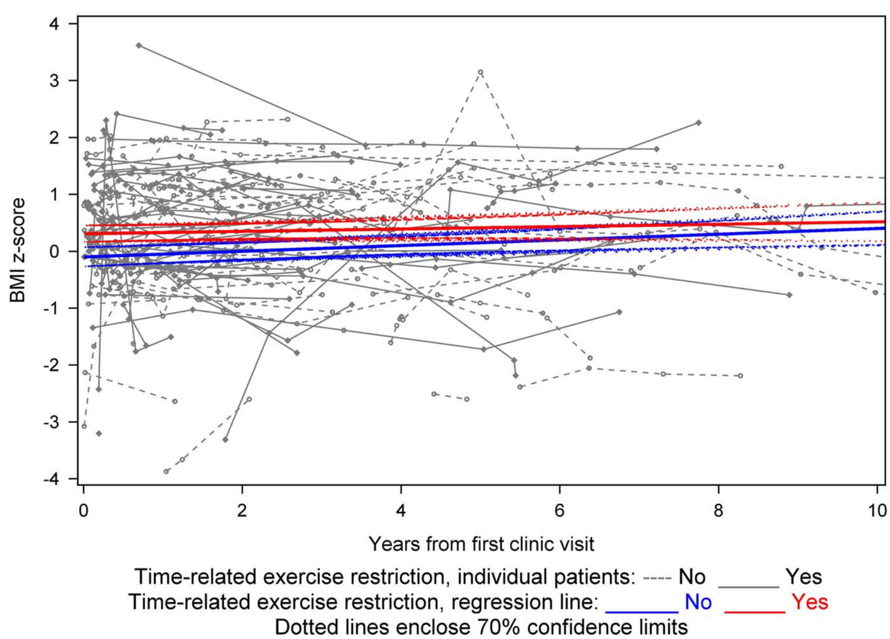

Figure 1.
Body mass index z-scores over time stratified by time-related exercise-restriction status. Individual patient body mass index z-scores are plotted over time since the patient's first clinic visit. Body mass index z-scores for patients who were exercise restricted during the study period are connected by solid grey lines. Body mass index z-scores for patients who were not exercise restricted are connected by dashed grey lines. Regression lines, which incorporate time-related exercise restriction (parameter estimate = 0.41, p = 0.05) and its interaction term with time (parameter estimate = −0.03, p = 0.55), are plotted. The solid blue line represents the regression line in which time-related exercise restriction was not present, with the dotted blue lines enclosing the 70% confidence limits. The solid red line represents the regression line in which time-related exercise restriction was present, with the dotted red lines enclosing the 70% confidence limits.

Multivariable associations with body mass index z-score over time

All covariates with significant associations with body mass index z-score over time in the univariable analysis were evaluated in the multivariable repeated-measures analysis as candidate-associated factors. As shown in Table 4, the final multivariable model included male sex, surgical intervention as a time-varying covariate, and its interaction term with time. Neither time-related exercise-restriction

Table 4. Multivariable associations with body mass index z-score over time.

	Parameter estimate	p-value
Time	−0.04	0.02
Male sex	0.59	0.004
Surgical intervention	0.28	0.04
Interaction term, time with surgical intervention	−0.11	0.01

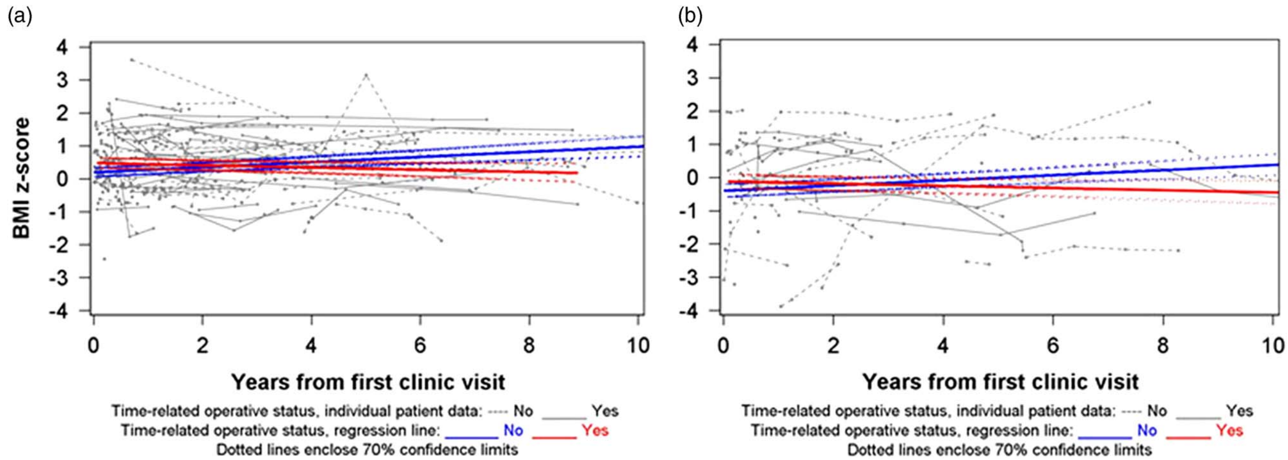

Figure 2.
*(**a** and **b**) Body mass index z-scores over time stratified by time-related surgical intervention in male patients (**a**) and female patients (**b**). Individual patient body mass index z-scores are plotted over time since the patient's first clinic visit. Body mass index z-scores for patients who were underwent surgical intervention during the study period are connected by solid grey lines. Body mass index z-scores for those who did not undergo surgical intervention are connected by dashed grey lines. Regression lines, which incorporate male sex (parameter estimate = 0.59, p = 0.004), time-related surgical intervention (parameter estimate = 0.28, p = 0.04), and its interaction term with time (parameter estimate = – 0.11, p = 0.01), are plotted. The solid blue line represents the regression line in which time-related surgical intervention did not occur, with the dotted blue lines enclosing the 70% confidence limits. The solid red line represents the regression line in which time-related surgical intervention did occur, with the dotted red lines enclosing the 70% confidence limits.*

status nor its interaction with time was significantly associated with body mass index z-score over time in the multivariable analysis ($p = 0.84$ and 0.49, respectively). In Figures 2a and b, regression lines solved for the effect of surgical intervention and its interaction term with time are shown, for male (Fig 2a) and female patients (Fig 2b). The slope of body mass index z-score of those who underwent an operation during the study period indicated a decreasing body mass index z-score over time, compared with an increasing body mass index z-score over time in those who did not undergo an operation.

Discussion

The risk of obesity in children with congenital heart disease is almost equal to those of healthy children.[7,8] Multiple studies have shown that children with congenital heart disease are not as physically active as children without heart disease.[15–17] Concern exists regarding the effects of exercise restriction on body composition. Using a subset of a multi-institutional cohort of patients with anomalous aortic-origin coronary arteries and repeated-measures analysis, we found that time-related exercise restriction was not associated with increasing body mass index z-score over time; however, surgical intervention was associated with decreasing body mass index z-score over time.

Exercise restriction over time

Several investigations have provided initial insight into the effects of exercise restriction on children with congenital heart disease. In 2010, Brown et al demonstrated little benefit of exercise restricting patients with critical aortic stenosis after balloon valvuloplasty. In 528 patients followed-up for a median time of 12 years, only a single sudden death occurred – the patient died while asleep. Although this study did not directly assess the effect of exercise restriction on body composition, the investigators concluded that the benefits of exercise restriction in young patients with critical aortic stenosis in terms of preventing sudden death may be overstated.[18] The accompanying editorial highlighted the potential risks of exercise restriction – depriving children of the many known benefits of physical activity.[19] In our study population of 143 patients with known exercise-restriction status, no sudden death occurred in either the restricted group or the non-restricted group.

The effect of exercise restriction on body composition was directly investigated in a single-centre study of 110 patients with various forms of congenital heart disease. With a mean follow-up period of 8.4 years, exercise restriction was associated with an increase in absolute body mass index and body mass index percentile;[20] however, their analysis did not analyse repeated measures of body mass index over time or incorporate exercise restriction as a time-varying covariate. Although our study's follow-up period was shorter, our results, generated using more sophisticated techniques, indicate that exercise restriction does not appear to detrimentally impact body mass index over time.

Surgical intervention over time

The association of surgical intervention with decreasing body mass index z-score over time represents a novel finding in patients with anomalous aortic-origin coronary arteries. In a cohort of patients with various forms of congenital heart disease, Shustak et al found no effect of surgical intervention on the risk of obesity; however, male patients who had undergone surgery were twice as likely to be overweight or obese.[8] It must also be emphasised that the confidence limits of the regression lines in Figure 2 do not diverge until ~8 or more years after the first clinic visit. It would appear that an operation would have little short-term effect on body mass index z-score during childhood. The beneficial effect may be seen in late adolescence or early adulthood in many children, given that the median age at diagnosis was 10 years. This finding is puzzling when taking into account the evidence that physical activity levels decrease as children approach adulthood.[21,22]

Study limitations

We acknowledge several significant limitations of this study. First, this is a retrospective study with the inherent limitations of analysing a non-random sample of patients.

Only one-third (143/440) of this cohort of patients with anomalous aortic-origin coronary arteries had documentation of their exercise-restriction status. It would seem that the discussion and documentation of the exercise-restriction status would be part of best practices for this patient population, as recommended by the Bethesda Guidelines.[23] Although these guidelines do not technically apply to pre-adolescent children, they have been used to guide decision making for these patients.[18,20] It is unclear whether this is due to lack of discussion, documentation, or both. The fact that a minority of patients had a change in their exercise-restriction status likely decreases our ability to detect whether time-related exercise-restriction status does lead to changes in body mass index over time. Furthermore, there was no way to truly ascertain patients' level of physical activity before the imposition of exercise restriction, as these data were not collected. Finally, the relatively modest length of follow-up may represent another limitation. This highlights the importance that the lack of overlapping confidence limits seen in Figure 2 represents projections based on the parametric linear mixed model regressions.

The fact that exercise restriction was discussed with patients and their parents may result in changes in patients' exercise level. Parents may have heightened awareness of their child's activity level, which may lead to the imposition of intended or unintended limitations. Although previous reports have shown that physicians may not adequately emphasise the importance of physical activity in children with congenital heart disease to parents, many parents are also unable to correctly describe their child's exercise restrictions, leading to unnecessary and potentially harmful exercise limitation.[24–26]

These discrepancies have also been described in patients with Fontan circulation who require anticoagulation, and are thus exercise restricted. Longmuir and McCrindle[27] reported that, although parents reported a higher rate of exercise restriction than cardiologists, more than 40% of parents were unaware of restrictions on their child's participation in competitive athletics, indicating the many gaps in effectively enforcing exercise restriction. There was also no way to know with certainty patients' adherence to physician guidance regarding exercise restriction following counselling. Finally, the possibility exists that parents could receive information on exercise restriction from multiple physicians, some of whom may contradict one another.

Conclusions

In a multi-institutional study of patients with anomalous aortic-origin coronary arteries, exercise restriction was not associated with increasing body mass index z-score over time. Although surgical intervention was associated with decreasing body mass index z-score over time, its effect was not significant for nearly a decade after the patient's first presentation with an anomalous aortic-origin coronary artery. Future investigations should focus on defining patients who will benefit most from surgical intervention. Given that they may be at high risk for sudden cardiac death during physical activity, we recommend that physicians discuss and document exercise status with patients and their parents at every clinic visit. Finally, efforts to improve patient and parental comprehension of the level of exercise restriction are critical.

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Conflicts of Interest

None.

References

1. Frescura C, Basso C, Thiene G, et al. Anomalous origin of coronary arteries and risk of sudden death: a study based on an autopsy population of congenital heart disease. Hum Pathol 1998; 29: 689–695.
2. Basso C, Maron BJ, Corrado D, Thiene G. Clinical profile of congenital coronary artery anomalies with origin from the wrong aortic sinus leading to sudden death in young competitive athletes. J Am Coll Cardiol 2000; 35: 1493–1501.
3. Maron BJ, Thompson PD, Ackerman MJ, et al. Recommendations and considerations related to preparticipation screening for cardiovascular abnormalities in competitive athletes: 2007 update: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation. Circulation 2007; 115: 1643–1455.
4. Brothers J, Carter C, McBride M, Spray T, Paridon S. Anomalous left coronary artery origin from the opposite sinus of Valsalva: evidence of intermittent ischemia. J Thorac Cardiovasc Surg 2010; 140: e27–e29.
5. Brothers J, Gaynor JW, Paridon S, Lorber R, Jacobs M. Anomalous aortic origin of a coronary artery with an interarterial course: understanding current management strategies in children and young adults. Pediatr Cardiol 2009; 30: 911–921.
6. Van Hare GF, Ackerman MJ, Evangelista J-aK, et al. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: task force 4: congenital heart disease: a scientific statement from the American Heart Association and American College of Cardiology. J Am Coll Cardiol 2015; 66: 2372–2384.
7. Pinto NM, Marino BS, Wernovsky G, et al. Obesity is a common comorbidity in children with congenital and acquired heart disease. Pediatrics 2007; 120: e1157–e1164.
8. Shustak RJ, McGuire SB, October TW, Phoon CK, Chun AJ. Prevalence of obesity among patients with congenital and acquired heart disease. Pediatr Cardiol 2012; 33: 8–14.
9. Lamotte C, Iliescu C, Libersa C, Gottrand F. Increased intima-media thickness of the carotid artery in childhood: a systematic review of observational studies. Eur J Pediatr 2011; 170: 719–729.
10. Woo KS, Chook P, Yu CW, et al. Overweight in children is associated with arterial endothelial dysfunction and intima-media thickening. Int Obes Relat Metab Disord 2004; 28: 852–857.
11. Brothers JA, Gaynor JW, Jacobs JP, et al. The registry of anomalous aortic origin of the coronary artery of the Congenital Heart Surgeons' Society. Cardiol Young 2010; 20 (Suppl 3): 50–58.
12. Poynter JA, Williams WG, McIntyre S, Brothers JA, Jacobs ML, Congenital Heart Surgeons Society AWG. Anomalous aortic origin of a coronary artery: a report from the Congenital Heart Surgeons Society Registry. World J Pediatr Congenit Heart Surg 2014; 5: 22–30.
13. Kuczmarski RJ, Ogden CL, Guo SS, et al. 2000 CDC growth charts for the United States: methods and development. Vital Health Stat 11 2002; 246: 1–190.
14. Poynter JA, Bondarenko I, Austin EH, et al. Repair of anomalous aortic origin of a coronary artery in 113 patients: a Congenital Heart Surgeons' Society report. World J Pediatr Congenit Heart Surg 2014; 5: 507–514.
15. Arvidsson D, Slinde F, Hulthen L, Sunnegardh J. Physical activity, sports participation and aerobic fitness in children who have undergone surgery for congenital heart defects. Acta Paediatr 2009; 98: 1475–1482.
16. Massin MM, Hovels-Gurich HH, Gerard P, Seghaye MC. Physical activity patterns of children after neonatal arterial switch operation. Ann Thorac Surg 2006; 81: 665–670.
17. McCrindle BW, Williams RV, Mital S, et al. Physical activity levels in children and adolescents are reduced after the Fontan procedure, independent of exercise capacity, and are associated with lower perceived general health. Arch Dis Child 2007; 92: 509–514.
18. Brown DW, Dipilato AE, Chong EC, et al. Sudden unexpected death after balloon valvuloplasty for congenital aortic stenosis. J Am Coll Cardiol 2010; 56: 1939–1946.
19. Rome JJ. Exercise restriction to prevent sudden death in congenital aortic stenosis: whom are we treating? J Am Coll Cardiol 2010; 56: 1947–1948.
20. Stefan MA, Hopman WM, Smythe JF. Effect of activity restriction owing to heart disease on obesity. Arch Pediatr Adolesc Med 2005; 159: 477–481.
21. Centers for Disease Control and Prevention, Brener ND, Kahn L, Shanklin S, et al. Methodology of the Youth Risk Behavior Surveillance System–2013; United States Centers for Disease Control and Prevention. MMWR 2013; 62: 1–20.
22. Centers for Disease Control and Prevention. The association between school based physical activity, including physical education, and academic performance. Atlanta, GA: U.S. Department of Health and Human Services; 2010.
23. Dean PN, Gillespie CW, Greene EA, et al. Sports participation and quality of life in adolescents and young adults with congenital heart disease. Congenit Heart Dis 2015; 10: 169–179.
24. Cheuk DK, Wong SM, Choi YP, Chau AK, Cheung YF. Parents' understanding of their child's congenital heart disease. Heart 2004; 90: 435–439.
25. Lentzner BJ, Connolly DM, Phoon CK. Do paediatric cardiologists discuss cardiovascular risk factors with patients and their families? Cardiol Young 2003; 13: 551–558.
26. Swan L, Hillis WS. Exercise prescription in adults with congenital heart disease: a long way to go. Heart 2000; 83: 685–687.
27. Longmuir PE, McCrindle BW. Physical activity restrictions for children after the Fontan operation: disagreement between parent, cardiologist, and medical record reports. Am Heart J 2009; 157: 853–859.