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Does obesity affect the short-term outcomes after cardiothoracic surgery in adolescents with congenital heart disease?

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Original Article

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Abstract

Background: Obesity is a modifiable, independent risk factor for mortality and morbidity after cardiovascular surgery in adults. Our objective was to evaluate the impact of obesity on short-term outcomes in adolescents undergoing surgery for congenital heart disease (CHD). *Methods:* This retrospective chart review included patients 10–18 years of age who underwent CHD surgery. Our exclusion criteria were patients with a known genetic syndrome, heart transplantation, and patients with incomplete medical records. The clinical data collected included baseline demographics and multiple perioperative variables. Charting the body mass index in the Centers for Disease Control and Prevention growth curves, the entire cohort was divided into three categories: obese (>95th percentile), overweight (85th–95th percentile), and normal weight (<85th percentile). The composite outcome included survival, arrhythmias, surgical wound infection, acute neurologic injury, and acute kidney injury. *Results:* The study cohort (n = 149) had a mean standard deviation (SD), body mass index (BMI) of 22.6 ± 6.5 g/m^2, and 65% were male. There were 27 obese (18.1%), 24 overweight (16.1%), and 98 normal weight (65.8%) patients. Twenty-seven (18%) patients had composite adverse outcomes. Overweight and obese patients had significantly higher adverse outcomes compared with normal weight patients (odds ratio (OR): 2.9; confidence interval (CI): 1–8.5, p = 0.04 and OR: 3; CI: 1–8.5, p = 0.03, respectively). In multivariate analysis, obesity was an independent predictor of adverse outcome in our cohort (p = 0.04). *Conclusions:* Obesity is associated with short-term adverse outcome and increased health resource utilisation in adolescents following surgery for CHD. Further studies should evaluate if intervention in the preoperative period can improve outcomes in this population.

In the United States, the prevalence of obesity has been increasing at an alarming rate, and recent data show the prevalence of obesity in children is as high as18.5%. Rates of obesity were higher in adolescents and school-aged children versus preschool-aged children. In addition, Hispanic and non-Hispanic black children have a significantly higher prevalence of obesity when compared to non-Hispanic white and non-Hispanic Asian youth.[1] Concerning trends are emerging in the paediatric population where the rate of rise in worldwide childhood obesity is exceeding that among adults.[2] Childhood obesity is associated with multiple adverse health consequences including atherosclerosis, hypertension, obstructive sleep apnea, asthma, type 2 diabetes, fatty liver disease, and the metabolic syndrome.[3] Ray et al. reported low rates of physical activity in children born with congenital heart disease (CHD) compared to healthy children (10–14 years old), and an alarming 26% were obese, higher than the general adolescent population.[4] However, Tamayo et al, in a longitudinal cohort of 725 patients with CHD, showed a similar prevalence of obesity to the general population.[5] A few studies have reported the impact of obesity on length of stay, morbidity, and mortality in hospitalised critically ill children and adolescents, and the results have been conflicting.[6-8] In adults with CHD, obesity is associated with increased morbidity after pulmonary valve replacement, including longer hospitalisation, and higher risk for post-operative arrhythmias.[9] Furthermore, the society of thoracic surgeons database was queried between 2010 and 2015, and for all ages (10–35 years), being obese and underweight by body mass index were associated with increased risk of composite adverse outcome independently.[10] However, data on the effect of obesity on outcomes in adolescents undergoing surgery for CHD are lacking. This study was performed with an objective to evaluate the short-term impact of obesity in the population of adolescents undergoing surgery for various CHD.

Materials and methods

This was a single center, retrospective study involving patients with CHD between 10 and 18 years of age who underwent cardiac surgery using cardiopulmonary bypass at Children's Hospital of Michigan from January 2012 to December 2017. Patients with a known genetic

Table 1. Comparison of the baseline characteristics among the three groups

Baseline characteristics median (IQR) or n (%)	Total (n = 149)	Weight for age		
		Normal (n = 98)	Overweight (n = 24)	Obese (n = 27)
Age, years	14.9 (12.7–16.9)	15 (12.7–16.9)	14.8 (13.5–17.8)	14.5 (12.7–16.3)
Weight (kg)	58 (44–69.5)	**49.5 (39.7–60.3)***	**66.5 (58.3–75)***	**78 (71–96)***
Gender (male), n (%)	97 (65.1)	65 (66.3)	17 (70.8)	15 (55.6)
Caucasian race, n (%)	95 (63.8)	66 (67.3)	14 (58.3)	15 (55.6)
STAT score n (%)				
Low score (1–3)	135 (90.6)	89 (90.8)	20 (83.3)	26 (96.3)
High score (4–5)	14 (9.4)	9 (9.2)	4 (16.7)	1 (3.7)

Data are presented as n (%) for categorical variables and median (25th–75th percentiles) for continuous variables. IQR: inter quartile range, STAT: Society of Thoracic Surgery and European Association for Cardiothoracic risk stratification system. Numbers in bold represent statistically significant results; p value <0.05
*For comparisons in between all three groups

or metabolic syndrome, patients undergoing orthotropic heart transplantation, and those with incomplete medical records were excluded. Approval for the study and waiver of parental consent and patient assent were obtained from the Institutional Review Board at Wayne State University. For patients requiring multiple surgeries during the study period, only the first surgery was considered for analysis. Demographic data including age, weight, height, gender, race, primary cardiac diagnosis, and details of surgery performed were collected. Body mass index (BMI) was used to classify overweight, underweight, obesity, and severe obesity in our cohort. Overweight was defined as a BMI between the 85th and 94th percentile for age and sex, and obesity was defined as a BMI ≥ 95th percentile for age and sex as plotted on Centers for Disease Control and Prevention growth curves.[11] Underweight was defined as a BMI less than 5th percentile for age and sex. In addition, severe obesity was defined as having a BMI ≥ 120% of the 95th percentile or an absolute BMI ≥ 35 kg/m^2, whichever was lower based on age and sex.[12]

Perioperative variables such as aortic cross-clamp time, cardiopulmonary bypass time, duration of hospitalisation, time to first negative fluid balance (defined as time from ICU admission to the end of the first 8-hour shift in which total output exceeded input), length of initial intubation (from the time of ICU admission to first time extubation), and presence of acute kidney injury (defined by the pRIFLE criteria) were collected.[13] The primary outcome was composite adverse outcome, defined as any of the following before discharge: death, need for cardiopulmonary resuscitation, mechanical circulatory support, arrhythmias (defined as the presence of haemodynamically significant supraventricular tachycardia, junctional ectopic tachycardia, or ventricular tachycardia/fibrillation that required medical intervention), culture positive surgical wound infection requiring chest exploration or antibiotics, acute neurologic injury (defined as the presence of stroke demonstrated on imaging or clinical seizures that required medical intervention), and acute kidney injury. The complexity of their cardiac diagnoses and operations was categorised using the Society of Thoracic Surgery and European Association for Cardiothoracic risk stratification system with category 1 being the lowest mortality risk and 5 being the highest mortality risk.[14]

Statistical analysis

Data were analysed using SPSS software for PC (IBM SPSS Statistics, Version 22.0. Armonk, NY: IBM Corp). Results were expressed as mean ± standard deviation (SD) or median (interquartile range) for continuous variables and numbers (percentage) for nominal/categorical variables. Comparison of variables among groups was performed by chi square test, student *t*-test, and one-way analysis of variance (ANOVA) as appropriate. Logistic regression was used for multivariate analysis since our dependent variable, composite adverse outcome, was dichotomous. Significance was taken as a p value of <0.05.

Results

The study cohort (n = 149) had a mean SD age of 14.9 (SD) and 65% were males. The primary cardiac diagnosis was Tetralogy of Fallot (n = 34; 23%), followed by atrial septal defects (n = 16; 11%). The cohort had a mean (SD) BMI of 22.6 ± 6.5 and included 24 overweight (16.1%, mean (SD) BMI = 24.6 ± 2.4), 27 obese (18.1%, mean (SD) BMI = 32.8 ± 7.7), and 98 normal weight (65.8%, mean (SD) BMI = 19.3 ± 2.7) patients. We had three underweight patients during the study period and were excluded from the statistical analysis. The three groups were similar in demographics in regard to age, gender, race, complexity of CHD, and operation complexity. Utilising the ANOVA statistic, there was no difference among the groups in time to first negative fluid balance, time of mechanical ventilation, post-operative arrhythmia, and acute renal injury. However, there were significant differences among the groups in regard to cardiopulmonary bypass time, aortic cross-clamp time, length of stay in cardiac intensive care unit, and rate of post-operative wound infection (Tables 1 and 2).

The intraoperative variables, obese patients had significantly longer cardiopulmonary bypass time (mean (SD) = 166 ± 116 min) compared to the normal weight group (mean (SD) = 111 ± 60 min); p = 0.004. Similarly, the obese group had longer aortic cross-clamp time (mean (SD) = 87 ± 97 min) compared to the normal weight group (mean (SD) = 46 ± 57 min; p = 0.022). Post-operative variables, the obese group had statistically significant longer duration of mechanical ventilation (mean (SD) = 20 ± 16 hours versus mean (SD) = 11 ± 12 hours; p = 0.017) and prolonged length of stay in cardiac intensive care unit (mean (SD) = 112 ± 85 hours versus mean (SD) = 70 ± 67 hours; p = 0.034) compared to the normal weight group. There were no deaths recorded in our cohort, although two patients who died during the study period were excluded from the study due to incomplete medical records, specifically several physician and nurse perioperative notes were not scanned into the electronic medical records in those two patients.

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Table 2. Comparison of perioperative variables among the three groups

Clinical characteristics median (IQR) or n (%)	Total (n = 149)	Weight for age		
		Normal (n = 98)	Overweight (n = 24)	Obese (n = 27)
Cardiopulmonary bypass time, min	102 (71–152.5)	99.5 (69.3–135)	111.5 (73.7–183.7)	**120 (81–244)***
Aortic cross clamp time, min	40 (0–87)	32 (0–67.5)	52.5 (23–120)	**62 (0–143)***
Length of stay in ICU, hours	48 (48–96)	48 (24–72)	48 (24–72)	**96 (48–144)***
Length of stay in hospital, days	5 (4–6)	4 (4–5)	6 (4–8)	7 (5–8)
Time to extubation, hours	8 (5–16)	7 (5–11)	7.5 (4–15.7)	14 (8–35)
Time to first negative balance, hours	19 (14–25)	19.5 (14–24)	18 (11.5–26.7)	18 (13–27)
Arrhythmia, n (%)	25 (16.8)	12 (12.2)	7 (29.2)	6 (22.2)
Post operative infection, n (%)	5 (3.4)	2 (2)	0 (0)	**3 (11.1)***
Acute kidney injury n (%)	4 (2.7)	2 (2)	0 (0)	2 (7.4)

Data are presented as n (%) for categorical variables and median (25th–75th percentiles) for continuous variables. IQR: inter quartile range. Numbers in bold represent statistically significant results; p value < 0.05
*Obese compared to normal weight group

Table 3. Relationship between BMI and composite adverse outcome

Body mass index, n (%)	Composite adverse outcomes			
	Yes	No	Total	P value*
Obese	8 (29.6)	19 (15.6)	27 (18.1)	0.03
Overweight	7 (26)	17 (13.9)	24 (16.1)	
Normal weight	12 (44.4)	86 (70.5)	98 (65.8)	
Total	27	122	149	

*The P value is for the chi-square test for categorical variables. Data are presented as n (%) for categorical variables

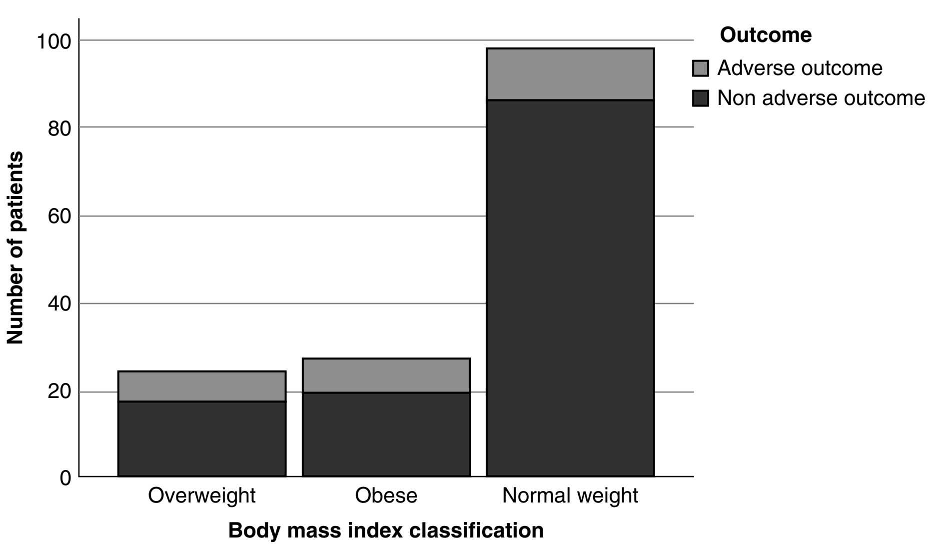

Figure 1. Composite adverse outcome distribution by BMI.

There were 27 (18.1%) patients who had composite adverse outcome. Table 3 presents the overall relationship between the composite adverse outcome and BMI in our cohort. Overweight and obese patients were at higher risk to have composite adverse outcomes compared with normal weight patients (odds ratio (OR): 2.9; confidence interval (CI): 1–8.5, p = 0.046 and OR: 3; CI: 1–8.5, p = 0.03; respectively). However, there was no significant difference between the overweight and obese groups in regard to the composite adverse outcome (p = 0.79). Figure 1 illustrates the relationship between the adverse outcome, overweight, and obese variables.

Multivariate analysis by logistic regression including the variables cardiopulmonary bypass time, aortic cross clamp time, time to extubation, arrhythmias, and obesity revealed that obesity remained an independent predictor of adverse outcome in our population (p = 0.04).

A secondary analysis was performed with only two groups: 27 obese (18.1%, mean (SD) BMI = 32.8 ± 7.7) and 122 non-obese

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Table 4. Obese patients compared to the rest of the cohort

		Obese (≥95% of BMI percentile for age and sex)		
Clinical characteristics median (IQR) or n (%)	Total (n = 149)	Yes (n = 27)	No (n = 122)	P value*
Cardiopulmonary bypass time, min	102 (71–152)	120 (81–244)	100 (70–138)	0.041
Aortic cross clamp time, min	40 (0–87)	62 (0–143)	40 (0–70)	0.075
Length of stay in hospital, days	5 (4–6)	7 (5–8)	5 (4–5)	<0.001
Time to extubation, hours	8 (5–16)	14 (8–35)	7 (5–14)	0.001
Arrhythmia	25 (16.8)	6(22.2)	19 (15.6)	0.465
Post-operative infection	5 (3.4)	3 (11.1)	2 (1.6)	0.016
Acute kidney injury n (%)	4 (2.7)	2 (7.4)	2 (1.6)	0.150

*The P value is for the chi-square test for categorical variables and T test for continuous variables for between-group comparisons. Data are presented as n (%) for categorical variables and median (25th–75th percentiles) for continuous variables. IQR: inter quartile range, BMI: body mass index

(81.9%, mean (SD) BMI = 20.3 ± 3.3) patients, which included our previous overweight and normal weight groups. Obese patients had longer bypass time, longer duration of mechanical ventilation, and longer hospital length of stay, compared to their non-obese counterparts, as shown in Table 4. In addition, obesity significantly increased the risk of post-operative wound infection (OR 7.14; 95% C.I.: 1.13–44.98, p = 0.037). Further subgroup analysis was performed for the patients who were severely obese (n = 11) within the obese group. Similarly, severely obese patients had higher risk for surgical wound infection (p = 0.005), longer cardiac intensive care stay (p < 0.001), longer hospital stay (p = 0.006), and longer need for mechanical ventilation (p = 0.007) compared to the rest of the cohort. There was no significant difference between the obese and severe obese groups in regard to composite adverse outcome.

Discussion

Previous studies have shown a prevalence of obesity in adolescent patients with CHD ranging at 17–26%.[4,5,15] In our cohort, 18.1% patients were obese, although there is selection bias as not all adolescents with CHD and obesity require surgical intervention. A few studies have investigated the short-term deleterious effect of obesity following cardiovascular surgery in the population with CHD. In the adult population, a cohort that included 71 post-operative patients after pulmonary valve replacement reported that obesity was independently associated with hospital length of stay >5 days (odds ratio (OR) = 5.2; 95% CI: 1.5–18.2, P = 0.01) and with increased post-operative arrhythmias (OR = 4.2; 95% CI: 1.7–40, P < 0 .01).[9] An analysis from the Society of Thoracic Surgeons Congenital Heart Surgery Database (STS), which included patients aged 10–35 years, revealed that obese (OR: 1.28 p = 0.008) and underweight subjects (OR: 1.39 p = 0.002) were independently associated with increased risk of adverse composite outcome.[10]

Obesity and short-term outcomes in General Paediatric Critical Care

The relationship between obesity and short-term outcome in the critically ill pediatric population has been investigated in recent years with conflicting results. Goh et al reviewed a cohort of 1030 patients aged 2- to 18-year-old admitted to a general paediatric intensive care unit. The risk-adjusted mortality rates in obese (OR, 0.68; 95% CI, 0.31–1.48) and severely obese patients (OR, 1.02; 95% CI, 0.45–2.34) were not significantly different compared to the normal weight group, and surprisingly obesity had a small protective effect. Interestingly, they defined obesity and severe obesity using only weight Z scores (1.66–2.33 and >2.33; respectively) for age and without taking into consideration the height of the patients.[6] Brown et al. reported the effect of obesity in 316 paediatric trauma patients (6–19 years old). They reported no difference in mortality among obese and non-obese patients, but obese children had more complications (41% versus 22%, p = 0.04) and required longer intensive care unit stay (8 ± 9 versus 6 ± 6 days, p = 0.05).[7] In a review of the virtual PICU systems database that included 127,607 patients, Ross et al. reported that risk-adjusted PICU mortality significantly increased as BMI increased into the overweight and obese ranges. Being overweight was independently associated with increased PICU mortality after controlling for severity of illness with the Pediatric Index of Mortality 2 score and pre-existing comorbidities.[8] We included height into the determination of obesity in our cohort by calculating BMI, and although, we did not have mortality in our study cohort, the short-term outcomes of obese and overweight patients were adversely affected.

Obesity and short-term outcomes in Paediatric Cardiac Critical Care

Shamszad et al. reported the association of obesity and post-operative outcomes after cardiothoracic surgery in the adolescent population. Utilising the Pediatric Health Information System database, they performed a case–control study including 629 obese or diabetic patients and 629 controls. The median age was 17 years (interquartile range (IQR) 12–32). Cases had longer paediatric intensive care unit length of stay than controls (3 versus 2 days, P = 0.001) The mortality was low and similar between cases and controls (2% versus 1.9%, P = 0 .692), and surgical complications occurred similarly between cases and controls (13.5% versus 12.4%, P = 0 .535).[16] In the analysis by O'Byrne et al of the STS Database (2010–2015), they included 18,337 patients, 10–35 years of age and found that obese (OR: 1.28 p = 0.008), severely underweight (OR: 1.29 p < 0.0001), and underweight subjects (OR: 1.39 p = 0.002) subjects were associated with increased risk of adverse composite outcome.[10] Although we had similar outcomes, our cohort differs from these two previous studies in that we did not include adult patients or patients with diabetes since it could lead to confounders in the determination and measurement of the short-term effect of obesity in the adolescent population undergoing cardiothoracic surgery. In addition, given the small number of underweight patients during the study period (n = 3), no statistical analysis was performed in this small group, and they were excluded from the study cohort.

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How obesity increases perioperative morbidity?

Obesity-related complications may have a significant impact in the perioperative period in adolescents. Obese adolescents have a higher prevalence of obstructive sleep apnea, which can increase pulmonary vascular resistance due to persistent hypoxia.[3] This would lead to difficulty in weaning the ventilator support after surgery, leading to prolong intensive care time and increased morbidity after cardiothoracic surgery. In addition, the chronic inflammatory state associated with obesity in children is another factor affecting the post-operative outcomes in this population.[17] Our data show that the obese patients had increased risk of surgical wound infection after cardiothoracic surgery; similarly, Train et al. query the National Surgical Quality Improvement Program database from 2012 to 2014, including patients aged 2–17 years who underwent a surgical procedure. They reported that obesity was associated with a greater risk of wound complications (OR 1.24, 95% CI 1.13–1.36).[18] Obese patients have relative hypoxia in the subcutaneous tissue that impairs wound healing.[19,20] Additionally, antibiotics have different pharmacokinetics and clearance in obese patients that may require dosing adjustment for the desired prophylactic or therapeutic effect.[21,22]

Obesity as an opportunity for improvement

Obesity is a known modifiable risk factor for various morbidities in adults. A recent study from a group in Philadelphia had reported the positive effect of exercise on BMI in the adolescent population with CHD and found that increasing exercise duration was associated with lower BMI ($P = 0.01$).[23] The possibility of intervention into a modifiable risk factor before non-emergent cardiothoracic surgery represents a great opportunity to improve outcomes in this population. Further studies should evaluate if intervention in the preoperative period with a structured program aimed to decrease BMI can improve short-term post-operative outcomes in this population.

Our study has limitations including its retrospective nature and the limitation in data collection by the extent of documentation in the electronic medical record. However, this study is one of few to evaluate the relationship of obesity to short-term post-operative outcomes exclusively in the adolescent population growing with CHD. In addition, even though we controlled for complexity of repair and other variables, there is the possibility that other factors may be affecting the outcomes in this population; therefore, a direct cause and effect relationship is difficult to establish.

Conclusions

Obesity is associated with short-term adverse outcome and increases health resource utilisation in adolescents following CHD surgery. Our findings strengthen the importance of routinely encouraging a multidisciplinary approach to a healthy lifestyle in adolescent patients with CHD in order to prevent obesity. Further studies should evaluate if intervention in the preoperative period with a structured program aimed to decrease BMI can improve short-term post-operative outcomes in this population.

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Conflicts of Interest. None.

References

1. Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of obesity among adults and youth: United States, 2015–2016. NCHS Data Brief 2017 Oct: 1–8.
2. Collaborators GBDO, Afshin A, Forouzanfar MH, et al. Health effects of overweight and obesity in 195 countries over 25 years. N Engl J Med 2017; 377: 13–27.
3. Daniels SR. Complications of obesity in children and adolescents. Int J Obes (Lond) 2009; 33: S60–S65.
4. Ray TD, Green A, Henry K. Physical activity and obesity in children with congenital cardiac disease. Cardiol Young 2011; 21: 603–607.
5. Tamayo C, Manlhiot C, Patterson K, Lalani S, McCrindle BW. Longitudinal evaluation of the prevalence of overweight/obesity in children with congenital heart disease. Can J Cardiol 2015; 31: 117–123.
6. Goh VL, Wakeham MK, Brazauskas R, Mikhailov TA, Goday PS. Obesity is not associated with increased mortality and morbidity in critically ill children. J Parenter Enteral Nutr 2013; 37: 102–108.
7. Brown CV, Neville AL, Salim A, Rhee P, Cologne K, Demetriades D. The impact of obesity on severely injured children and adolescents. J Pediatr Surg 2006; 41: 88–91; discussion 88–91.
8. Ross PA, Newth CJ, Leung D, Wetzel RC, Khemani RG. Obesity and mortality risk in critically ill children. Pediatrics 2016; 137: e20152035.
9. Buelow MW, Earing MG, Hill GD, et al. The impact of obesity on postoperative outcomes in adults with congenital heart disease undergoing pulmonary valve replacement. Congenit Heart Dis 2015; 10: E197–E202.
10. O'Byrne ML, Kim S, Hornik CP, et al. Effect of obesity and underweight status on perioperative outcomes of congenital heart operations in children, adolescents, and young adults: an analysis of data from the society of thoracic surgeons database. Circulation 2017; 136: 704–718.
11. Barlow SE, Expert C. Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. Pediatrics 2007; 120: S164–S192.
12. Kelly AS, Barlow SE, Rao G, et al. Severe obesity in children and adolescents: identification, associated health risks, and treatment approaches: a scientific statement from the American Heart Association. Circulation 2013; 128: 1689–1712.
13. Lex DJ, Toth R, Cserep Z, et al. A comparison of the systems for the identification of postoperative acute kidney injury in pediatric cardiac patients. Ann Thorac Surg 2014; 97: 202–210.
14. O'Brien SM, Clarke DR, Jacobs JP, et al. An empirically based tool for analyzing mortality associated with congenital heart surgery. J Thorac Cardiovasc Surg 2009; 138: 1139–1153.
15. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity and trends in body mass index among US children and adolescents, 1999–2010. JAMA 2012; 307: 483–490.
16. Shamszad P, Rossano JW, Marino BS, Lowry AW, Knudson JD. Obesity and diabetes mellitus adversely affect outcomes after cardiac surgery in children's hospitals. Congenit Heart Dis 2016; 11: 409–414.
17. Singer K, Eng DS, Lumeng CN, Gebremariam A, J M Lee. The relationship between body fat mass percentiles and inflammation in children. Obesity 2014; 22: 1332–1336.
18. Train AT, Cairo SB, Meyers HA, Harmon CM, Rothstein DH. The impact of obesity on 30-day complications in pediatric surgery. Pediatr Surg Int 2017; 33: 1167–1175.
19. Kabon B, Nagele A, Reddy D, et al. Obesity decreases perioperative tissue oxygenation. Anesthesiology 2004; 100: 274–280.
20. Sen CK. Wound healing essentials: let there be oxygen. Wound Repair Regen 2009; 17: 1–18.
21. Falagas ME, Karageorgopoulos DE. Adjustment of dosing of antimicrobial agents for bodyweight in adults. Lancet 2010; 375: 248–251.
22. Martin JH, Saleem M, Looke D. Therapeutic drug monitoring to adjust dosing in morbid obesity - a new use for an old methodology. Br J Clin Pharmacol 2012; 73: 685–690.
23. O'Byrne ML, McBride MG, Paridon S, Goldmuntz E. Association of habitual activity and body mass index in survivors of congenital heart surgery: a study of children and adolescents with tetralogy of fallot, transposition of the great arteries, and fontan palliation. World J Pediatr Congenit Heart Surg 2018; 9: 177–184.