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Review

What influences outcomes in pediatric and congenital cardiovascular disease?: A healthy lifestyle; obesity and overweight

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ABSTRACT

The prevalence of childhood overweight and obesity has risen dramatically over the past forty years. Despite significant public health efforts, over one third of children in the United States are presently overweight or obese (Hales et al., 2017). Obesity also impacts children with congenital and acquired heart disease (HD). In otherwise healthy children, obesity is a well-known risk factor for the development of metabolic syndrome, type II diabetes, and future cardiovascular disease (Dietz, 1998). Much less is known about the cardiovascular implications of obesity in children with HD. Given that structural abnormalities related to HD and past cardiac surgery cannot be altered, obesity may be one of the few modifiable risk factors for preventing future cardiovascular disease in this patient population.

1. Introduction

Over the past four decades, there have been significant medical and technological advances in the fields of pediatric cardiology and cardiothoracic surgery. These advances have resulted in a marked decline in mortality rates for children with HD [3,4]. Currently, there are over 1.5 million adults with congenital heart disease (CHD) and this population is expected to grow [5–7]. Over the same forty-year time period, there has been a significant rise in the rates of pediatric overweight and obesity. The 2013–2014 National Health and Nutrition Examination Survey (NHANES) reported that the prevalence of overweight and obese children aged 2–19 years was 34% [8]. Particularly concerning was the sharp upward trend in obesity rates for children aged 2–5 years. NHANES found that 13.9% of this young population was obese in 2015–2016 compared to 8.4% in 2011–2012 [1,9,10]. Data suggests that children with HD have similar rates of overweight and obesity compared to the general population [11,12]. Thus, obesity in the setting of HD may cause significant morbidity and even early mortality for these patients who are already vulnerable because of their underlying structural or acquired cardiac abnormalities. A healthy lifestyle directed toward normal weight could be as important as many of the medications we use to treat our patients as pediatric cardiologists.

2. Complications of childhood obesity

Childhood obesity is associated with significant physical and psychosocial comorbidities once thought to be confined to the adult population. Overweight and obese children are at an increased risk of developing type II diabetes, hyperlipidemia, systemic hypertension, obstructive sleep apnea, depression, and anxiety [2]. Multiple studies have shown that in the general pediatric population, childhood obesity can be accompanied by cardiovascular changes even prior to adulthood. Severe obesity in children has been associated with increased arterial wall stiffness and endothelial dysfunction [13]. In adolescents, obesity has been associated with an increase in carotid media intima thickness (CIMT), a marker of coronary artery disease and a risk factor for myocardial infarction and stroke in adulthood [14,15]. In an autopsy series of young adults aged 15–34 years, Berenson et al. found an association between higher BMI and the presence and severity of atherosclerotic lesions in the coronary arteries of asymptomatic young males [16].

In addition to vascular changes, childhood obesity has been associated with increased epicardial fat, ventricular dimensions, and left ventricular mass on echocardiography [17]. A Danish prospective cohort study of almost 1000 children found a significant increase in left ventricular mass among obese children as young as 2 years of age [18]. This association was also described in the Strong Heart Study which found that left ventricular hypertrophy was more prevalent in obese

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(33.5%) and overweight (12.4%) adolescents, compared to those of normal weight (3.5%) [19]. In the adult population, higher left ventricular mass has been associated with cardiovascular events and premature death [20].

Childhood obesity may have implications in adulthood. We now know that obese children, even those as young as preschool age, are likely to become obese adults [21]. There are other long-term concerns as well. In Native Americans, a population particularly vulnerable to obesity, higher BMI in early to late childhood was associated with premature death from endogenous causes such as heart disease and cancer [22]. A longitudinal retrospective review of over 275,000 Danish adults followed since childhood found that higher childhood BMI was associated with myocardial infarction in adulthood [23]. Moreover, the Harvard Growth Study, a 55-year longitudinal study of over 500 individuals found that adults who were overweight in adolescence had an increased risk of morbidity and mortality from coronary artery disease regardless of their adult weight [24].

3. Obesity in children with congenital heart disease

While much has been written on the effects, prevention, and management of obesity in the general pediatric population, much less in known about the effects of obesity on children with HD. In 2009, the National Heart, Lung, and Blood Institute convened a Working Group on obesity and other cardiovascular risk factors in congenital heart disease to address these knowledge gaps. They identified a few potential and unique risk factors for obesity in the HD population including supplemental tube feeds, high calorie infant formulas, and physical activity limitations/restrictions [25].

4. Prevalence of obesity in children with HD

There has been some variation in the reported prevalence of overweight and obesity in the HD population and how it compares to that of the general pediatric population. The first study on obesity in CHD was a cross-sectional analysis of 2921 pediatric cardiology outpatients aged 6–19 years at the Children's Hospital of Philadelphia and Children's Hospital of Boston [11]. They found the prevalence of overweight and obesity in patients with any type of HD to be 26.2%, a substantial percentage but one that was lower than the rate in healthy controls [11]. The difference was related to the Fontan population in whom the prevalence of overweight and obesity was 16%. They also found that only 15% of the pediatric cardiologists remarked about the obesity or overweight in their letters to referring physicians. Alternatively, a more recent study from the Cleveland Clinic found that the prevalence of overweight and obesity was 31.5% and 16.4% respectively. The study did not have a control group but these rates were comparable to those found by the NHANES 2013–2014 study in the general pediatric population. In addition to reporting rates of obesity, the investigators were able to identify a transition period at age 6–10 years when patients who were of normal weight were most likely to become overweight or obese. They also found that after adjusting for age, there was an increased risk for overweight and obesity in patients born in the most recent era (2001–2015 compared to 1996–2001) suggesting that the prevalence of overweight and obesity is on the rise in the CHD population [26]. Others have reported similar rates of obesity in the CHD population [12,27–29].

Obesity has impacted even the most vulnerable patient population of pediatric cardiology, those with single ventricle heart disease requiring Fontan palliation. As previously mentioned, Pinto et al. reported that this group were less likely to be obese than patient's with biventricular CHD [11]. However, a 2015 study by Wellnitz et al. found that there was an increasing prevalence of overweight and obesity during the 5 years following Fontan palliation. While 10.7% of patients were overweight or obese before Fontan palliation, 20.3% met criteria one year following surgery, and 30% met criteria 5 years after surgery [30]. This is particularly concerning as obesity may place a significant burden on the single ventricle. Ventricular hypertrophy in this setting is particularly damaging because higher diastolic pressures result in higher Fontan baffle pressures. It should not be surprising then that Martinez et al. reported an association between obesity and symptomatic heart failure in Fontan patients [31].

5. Risk factors for obesity in children with HD

Children with CHD have many traditional as well as some unique risk factors for obesity. A cross-sectional study of adolescents and young adults (ages 15–39 years) with CHD found high rates of saturated fat consumption comparable to the amounts found in adults with elevated LDL cholesterol levels [32]. Likewise, children with CHD in Germany were found to have poor eating habits; 68% did not eat fruit daily, 60% did not eat vegetables daily. 41% drank sugar sweetened beverages, and 89% ate foods high in fat at least three times a week [33]. Interestingly, only 18.2% of the study population was overweight or obese, a prevalence far less than in studies performed in the United States [33]. Given these findings one could hypothesize that the rates of poor dietary habits are even worse in the United States.

In addition to traditional dietary risk factors, there are unique factors in the pediatric HD population that may contribute to the development of obesity. Patients with complex two ventricle or single ventricle heart disease are frequently underweight in infancy [34]. As a result, pediatric cardiologists and nutritionists often focus on maximizing calories in early childhood. Many infants and even toddlers rely on high caloric formulas and/or tube feeds for adequate nutrition [35,36]. The long-term consequences of these early feeding practices on growth, satiety cues, and oromotor skills remains poorly understood. With the high rate of non-oral feeding in this population, it should not be surprising that children with HD may develop abnormal long-term eating habits.

Exercise restriction is another unique risk factor in children with HD. Restriction from competitive sports and isometric exercises is generally recommended for certain forms of HD such as hypertrophic cardiomyopathy, long QT syndrome, moderate to severe aortic stenosis, and anomalous coronary arteries, though even for these diseases, recommendations are changing [37–41]. These restrictions do not apply to the majority of children and adolescents with HD. Yet some practitioners recommend unnecessary exercise restriction due to previous practice and/or outdated literature. Despite guidelines for competitive sports [40], there is no evidence that exercise restriction prevents sudden death in the HD population.

Some unnecessary restrictions may stem from parental anxieties regarding the perceived risk of sudden cardiac death [42]. A large study performed by Jortveit et al. reviewing the Norwegian Birth Registry found that in a population of over 11,000 children with HD born from 1994 to 2009 and followed until 2012, there were no physical activity related sudden deaths. There were two children who experienced sudden cardiac arrests with exercise but both survived and were known to have arrhythmia. Based on this data, the estimated rate of sudden unexpected death related to physical activity in children 2–18 years old with HD is as low as 2 per 100,000 person years [43]. Thus, the rate of sudden death in the HD population is quite low and likely a similar risk to death from a motor vehicle accident. These types of comparisons can sometimes put such risk in perspective.

In some cases, exercise may not be discussed in the outpatient setting or if discussed, recommendations may remain unclear. A study of children after Fontan palliation found that cardiologist, parent, and medical chart reports often disagreed about activity restriction. As a result, one in five children in this study population was unnecessarily restricted from exercise [44]. Exercise restriction may indeed contribute to the development of obesity. Stefan et al. found that those children with CHD who were restricted from competitive sports were more likely to develop overweight and obesity over an 8 year follow up

period compared to those who were allowed to participate [45].

Some issues regarding exercise restriction are related to the children themselves. Qualitative studies of children with CHD have identified low self-efficacy, fear, anxiety regarding inability to keep up with healthy peers, and physical fatigue as self-limiting factors [46,47]. Voss et al. evaluated children with mild, moderate, or severe HD or after heart transplant and found that only 8% met the physical activity guidelines of 60 min of moderate to vigorous physical activity at least 6 days a week that is recommended for children. Even though the overwhelming majority of participants did not meet exercise goals, only 15% were activity restricted by their cardiologist [48].

Ultimately, the benefits of exercise outweigh the risks for the pediatric HD population. Current studies are focusing on physical activity promotion over restriction [49]. In a cohort of patients with CHD, perceived quality of life was markedly better in both physical and psychosocial domains for patients who participated in competitive sports compared to those who were sedentary [50]. Even children who participated in recreational activities had better quality of life compared to the group who did not participate in sports at all [50]. Increasing duration of habitual exercise has been associated with lower BMI in children and adolescents with tetralogy of Fallot, transposition of the great arteries, and Fontan palliation [51]. With regard to Fontan physiology, leg exercise in such activities as cycling, walking and running may have the added benefit of augmenting cardiac output. Cordina et al. reported that increased muscle mass in the lower extremities in a cohort of Fontan patients was associated with improved cardiac filling, stroke volume and exercise capacity [52].

6. Cardiovascular and other sequelae

Children with HD may have structural or functional abnormalities that make them more vulnerable to the development of atherosclerosis. In 2019, the AHA published an updated statement on cardiovascular risk reduction in high-risk pediatric patients [53]. The statement identified several groups of children including subsets of the HD population who are at risk for the development of premature cardiovascular disease including those with Kawasaki disease with persistent or regressed coronary aneurysms, a history of surgical coronary translocation for anomalous coronary arteries or transposition of the great arteries, coarctation of the aorta, aortic stenosis, and cardiomyopathies [53].

Patients who have congenital or acquired abnormalities of coronary blood flow are at especially high risk for the development of premature cardiovascular disease. Studies of patients following arterial switch operation have shown coronary artery abnormalities including decreased coronary artery vasoreactivity, decreased coronary flow reserve, and increased proximal intimal proliferation, a precursor to atherosclerosis [54,55]. Obesity thus poses an additional cardiovascular burden on these patients. Other cardiovascular abnormalities have been reported in obese children who have undergone the arterial switch operation including higher rates of dyslipidemia and hypertension, decreased vascular reactivity and higher left ventricular mass when compared to normal weight children who underwent the arterial switch operation [56].

Patients with a history of coarctation of the aorta also fall into this high-risk category. They are at increased risk of developing hypertension and premature cardiovascular disease regardless of body habitus or successful repair [57,58]. Impaired flow mediated vasodilation and increase carotid intima media thickness, early signs of endothelial dysfunction, have been seen as early as childhood in this population [59]. Alarmingly, the prevalence of overweight/obesity in the repaired coarctation population is extremely high. Smith-Parish et al. found that by age 10 years, 25% of patients who had undergone coarctation repair were overweight or obese; this rate jumped to 63% by age 20 years [60]. It is not clear why these patients have such high rates of overweight and obesity but it warrants further investigation.

In addition to the concerns regarding premature coronary artery disease in this population, obesity poses other cardiac risks to the HD population. In a population with tetralogy of Fallot, obese patients had increased biventricular mass on cardiac MRI with the right side affected more than the left [61]. Moreover, the obese cohort had decreased biventricular end diastolic volume and stroke volume when indexed to body surface area [61]. The long term impact of these changes is unclear but in a population, like tetralogy of Fallot where the right heart is already dilated, these changes may be further deleterious or may result in more re-interventions over a patient's lifetime.

In addition to the effects on the heart itself, obesity has been associated with increased postoperative mortality and hospital utilization in children with CHD [62]. A multicenter study of patients undergoing a congenital heart disease operation in the Society of Thoracic Surgeons Congenital Heart Surgery Database found that obesity was significantly associated with an increased risk of composite adverse outcome (one or more of operative mortality, major adverse event, prolonged hospital length of stay, and wound infection/dehiscence) independent of other risk factors [63].

In the general population, obese children report poorer quality of life and emotional issues related to depression, poor self-esteem, and poor school performance compared to normal weight peers [64]. Children with CHD are known to be at risk for neurodevelopmental impairment, emotional, and behavioral problems [65–67]. This risk may only be compounded but the additional burden of obesity.

7. Conclusions

More than one quarter of children with HD are overweight or obese. Alarmingly, there is evidence to suggest that the prevalence of overweight and obesity continues to rise in this population and impacts more than 50% of adults with CHD [60,68,69]. Unique risk factors such as high calorie diets, tube-feeding in early childhood and exercise restriction likely contribute to these trends. The implications of the obesity epidemic on children with HD are not entirely clear but given the longer life expectancies in this population that have come with cardiac surgical and catheter-based strategies, the obesity epidemic in the HD population warrants further investigation. Pediatric cardiologists can play a role in monitoring their patients with HD who are at risk of developing overweight or obesity. In particular, we as a field need to recognize that exercise restriction may do more damage than good in the long-term health of our patients. Exercise should be introduced as a "prescription" early in routine cardiology outpatient visits and may be one of the most beneficial recommendations we can make for our patients.

Declaration of competing interest

Rachel Shustak, MD: None.
Meryl Cohen, MD: None.

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