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High Overweight and Obesity in Fontan Patients: A Twenty-Year History

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Abstract

Background: The prevalence of obesity in long-term survivors with complex congenital heart disease may be increasing, and little is known about the timing and onset of weight gain and growth patterns in these high-risk patients.

Methods and Results: Prevalence rates of overweight/obesity and longitudinal changes in body mass index (BMI) with age were determined in 606 patients with Fontan circulation seen at a tertiary care cardiology center from 1992 – 2012. The number of clinic encounters (n) was stratified by age group (n=401, 2–5y; n= 333, 6–11y; n=217, 12–19y; and n=129, >20y). Among adults, 39% were overweight/obese at last clinic visit; 22% overweight and 17% obese. Childhood anthropometric data were available for 82 adults; of which 15% (n=12/82) were overweight/obese in childhood. The likelihood of being overweight/ obese as an adult was 3 times higher if there was a BMI 85th percentile in childhood (CI 2.1–4.5, p <0.01). Overweight/obesity in adulthood was associated with lower heart failure rates (4% vs. 19%, P=0.03). Pediatric rates of overweight/ obesity were comparable to national data (NHANES 2011–2012) in every age group: at 2–5y, (25 vs. 23%), 6–11y (26 vs. 34%), and 12–19y (15 vs. 35%). Systolic blood pressure was higher in overweight/obese children as young as 2–5 years of age.

Conclusions: Childhood and adult survivors with Fontan circulation have high rates of overweight/obesity. Childhood obesity is a strong predictor of future adiposity and is linked to changes in systolic blood pressure at a very young age.

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Disclosures

JNH had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. STC and JNH conceptualized and designed the study, collected the data, interpreted and analyzed the results, wrote the manuscript and approved the final version as submitted. BH, LP, CJP contributed to data acquisition and analysis, critically reviewed and revised the manuscript and approved the final version as submitted.

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Keywords

heart defect; congenital; obesity; pediatrics; Fontan procedure; growth

Introduction

Obesity is an increasingly recognized comorbidity in pediatric heart disease that further increases risk for cardiovascular morbidity [1,2]. Among children with congenital heart disease, those with complex single ventricle disease were reported to be at lowest risk for obesity, as they often experienced growth failure resulting from cyanosis, low cardiac output, and heart failure [3]. However, advances in medical and surgical techniques, including staged single ventricle palliative surgery culminating in Fontan circulation, have dramatically altered the outcome in these children [4]. Lower mortality rates and improved functional status have resulted in many children with Fontan circulation surviving into adulthood [5–8].

Contemporary analyses of adolescent and adult patients with Fontan circulation, which demonstrated improved quality of life and function, have shown that the proportion of overweight/ obesity may be increasing in older children and adults [9–11]. Long-term survivors of Fontan surgery may be particularly susceptible to excess weight gain due to a combination of rapid catch-up growth and social and environmental factors [12]. Although the exact etiology of increased risk for obesity has not been extensively investigated in patients with severe congenital heart disease, rapid infantile weight gain and sedentary lifestyle are known independent predictors of childhood and adult-onset obesity [13–16]. Children with complex heart disease often receive nutritional supplementation to help alleviate poor weight gain and failure to thrive, and the combination of rapid catch-up growth and physical activity restriction in early childhood may increase their risk for obesity later in life [17–19].

Obesity and its associated comorbidities are concerning especially in children with Fontan circulation, as the associated increased afterload could expose the limited ventricular reserve capacity in survivors [5,20–22]. Despite these concerns, there are no long-term, systematic assessments of growth and body mass index (BMI) trajectories in children or adults with Fontan circulation. In this report we determined prevalence rates of overweight/ obesity and longitudinal trends in weight, height and BMI among children and adults with Fontan circulation over a 20-year period.

Methods

The protocol was approved by the Baylor College of Medicine Institutional Review Board for Human Subjects Research. A retrospective analysis was performed of all patients aged 2 to 50 years of age who underwent Fontan corrective surgery at Texas Children's Hospital and had a clinic visit between 1992 and 2012. Patients were identified from ICD-9 diagnosis codes for Fontan operation: Fontan Operation Atrio-pulmonary; Fontan Operation Atrioventricular, Fontan Operation Unspecified, Fontan Operation Cavopulmonary, Fontan Cavo-pulmonary fenestration, Fontan revision and Fontan procedure. Patient records were

categorized by age groups as used in the 2011–2012 National Health and Human Survey (NHANES) [23]: children 2–5 years, 6–11 years, 12–19 years and adults > 20 years.

There were 7416 encounters for 752 patients. After exclusion of duplicate and missing anthropometric records, complete anthropometric data was available in 606 patients: 129 adults and 395 children (Figure 1). Within the adult cohort, 82 of 129 patients had at least one clinic visit, with documented height and weight data, in childhood. Within the pediatric cohort, anthropometric data from the last clinic visit within each age category were used for cross-sectional analysis, and the number of clinic encounters by age category was as follows: 401 (2–5 years), 333 (6–11 years), 217 (12–19 years) and 129 (> 20 years). Seventeen percent of children (68/395) had documented consecutive serial height and weight measurements during the 3 age groups (2–5 years, 6–11 years, 12–19 years, Figure 1).

Electronic and paper charts were reviewed and the following data collected for the last clinic visit within the age category: height, weight, date of visit, gender, age, race and ethnicity, cardiac diagnosis, and systolic and diastolic blood pressure. The following additional medical information was collected for adult patients: diagnosis of heart failure, date of transplantation and morphology of single ventricle (i.e. right, left or biventricular disease).

Weight and height z-scores were calculated from NHANES pediatric growth reference charts using the United States Department of Agriculture, Agricultural Research Service (USDA/ARS) Children's Nutrition Research Center Body Composition Laboratory calculator (<https://www.bcm.edu/bodycomlab>). Body mass index was calculated as weight in kilograms divided by the square of height in meters (kg/m^2). In children, BMI percentiles were tabulated according to Center for Disease Control (CDC) reference criteria and weight status classified as: underweight (BMI percentile < 5th), overweight (BMI percentile 85th but < 95th), and obese (BMI percentile 95th). In adults, weight status was classified as follows: underweight (BMI < 18.5 kg/m^2), overweight (BMI 25–29.9 kg/m^2) and obese (BMI 30 kg/m^2). Prevalence rates of overweight and obesity were calculated within each age group.

Statistical Analyses

Means (standard deviation) and percentages were calculated, and analyses of variance (ANOVA) for continuous variables, and chi-square analysis for categorical variables were performed. Non-parametric data (systolic blood pressure, age) were logarithmically transformed for analyses. P values < 0.05 were considered significant. All statistical analyses were done using SPSS for Windows, (SPSS Inc, version 22, Chicago, IL).

Results

Adult cohort

Cross-sectional evaluation in adults > 20 years of age (n=129)—Adult patients were 27.8 (6.8) years of age; male (55%) with single ventricular congenital heart disease. Most adult patients had single left ventricle (82%), while single right ventricle and biventricular heart disease were less common (12% and 6% respectively). The average age

at Fontan operation was 11.6 (9.4) years. Among the adult cohort, 18% (23/129) of patients had been diagnosed with heart failure while 5% (6/129) had undergone orthotopic heart transplant at 19.2 (5.3) years of age (range 11.5 – 26.6 years).

The average height was 170.3 (9.8) cm and 162.3 (14.7) cm, and weight 69.7 (14.1) kg and 65.9 (15.4) kg, for men and women respectively. The average BMI was 24.4 (9.5) kg/m² with no difference in BMI by gender (data not shown). The demographic and anthropometric characteristics stratified by weight status are shown in Table 1. Thirty-eight percent of adults (49/129) were overweight or obese while 8% (10/129) were underweight (Figure 2). There were no race or gender differences between overweight/obese and normal weight adults. Overweight/obesity were associated with lower rates of heart failure, $p = 0.03$ (Table 1). All of the 6 patients who underwent a heart transplant over the 20 year period were normal weight at the time of evaluation, BMI 21.1 (2.1) kg/m².

Longitudinal weight trends from childhood to adulthood (n=82)—Among the adult cohort, a subset had repeated height and weight measurements available. The prevalence of overweight and obesity within the adult subgroup who had serial childhood data was also 40% (overweight/ obesity, $n = 33/82$; 17 overweight and 16 obese adults). There were no race or gender differences between normal weight and overweight/obese adults. One third of these overweight/obese adults had BMI 85th centile in childhood (13/33). Over fifty percent of the obese adults had BMI 85th centile in childhood (9/16, $p = <0.001$). The presence of childhood overweight/obesity was associated with a 3-fold increased odds of overweight/obesity in adulthood (OR = 3.0, 95% CI 2.1– 4.5, $p < 0.01$).

There were no associations between overweight/obesity in childhood and age at Fontan procedure [8.8 (5.9) vs. 9.8 (7.0) years, $p = 0.6$] or diagnosis of heart failure (19% vs. 8%, $p = 0.4$, normal vs. overweight/ obese respectively). Within the adult cohort, 4 of 6 patients who underwent heart transplant had recorded height and weight data between 12–19 years, and BMI in these 4 adolescents was 23 (5.9) kg/m² (range 7–64th centile).

Pediatric Cohort

Cross-sectional evaluation in children 2–19 years of age (n=395)—

Anthropometric characteristics and blood pressure by age and weight category are shown in Table 2. The overall prevalence rate of overweight/ obesity for Fontan patients aged 2–19 years was 22% and differed by age group, $P < 0.001$ (Figure 2). Rates of overweight/obesity were comparable to national NHANES 2011–2012 data: at 2–5 years, (25 vs. 23%), at 6–11 years (26% vs. 34%), but lower at 12–19 years (15% vs. 35%) in the Fontan cohort vs. NHANES respectively. The percentage of Fontan children who were underweight (<5th centile) in each age category was: 2–5 years; 9% (35/401), 6–11 years; 4% (12/333) and 12–19 years; 16% (35/217).

Systolic blood pressure was significantly higher in overweight/obese children compared to underweight children ($P = 0.01$) (Figure 3). This was even evident in the youngest age group, 2–5 years old ($P = 0.001$), as well as in adolescence ($P = 0.02$), with a similar pattern noted in the 6–11 year-old cohort. There was no difference in diastolic blood pressure by weight status (Table 2).

Longitudinal weight trends in childhood (n=68)—Since the analysis of the adult data showed childhood obesity to be a strong predictor of adult obesity in Fontan patients, we examined BMI patterns of developing obesity in adolescence. Serial height and weight data were available in 68 children for each of the 3 age ranges studied (age 2–5 years, 6–11 years, 12–19 years, Figure 1). Among adolescents (12–19 years of age) in this group, 20% (14/68) were overweight/obese, and 16% (11/68) were underweight. Of the 14 overweight/obese adolescent patients identified, over half of children (8/14) were already overweight/obese at age 2–5 years and the remainder of children showed a striking rise in BMI by 6–11 years (Figure 4).

Discussion

This report is the first to characterize long-term weight trends in children and adults with complex congenital heart disease over a twenty-year period. Overweight and obesity were common in adults with Fontan circulation, affecting 40% of adults older than 19 years of age. This high rate of overweight/obesity challenges previous reports suggesting that obesity is uncommon in patients with complex congenital heart disease [1,2,24] [25]. Those prior investigations focused on pediatric clinics and were limited by their cross-sectional study design and smaller cohorts of children with complex congenital heart disease. More recently, a cross-sectional evaluation of 54 adolescent and adult Fontan patients (15–50 years) indicated that the prevalence of overweight/obesity may be higher, affecting ~ 1 in 5 long-term Fontan survivors [9]. The current study offers further insight into weight trends in a larger group of adults with Fontan circulation and demonstrated that adult survivors with Fontan circulation have at least a 2-fold higher risk of obesity than previously anticipated [9]. The greatest risk for obesity is in adulthood, which follows the overall national trend of increasing adiposity with age [23].

In order to further elucidate the pattern of increased weight gain, we examined serial trends in weight and growth. Notably, overweight/obese adolescents had documented increased weight in early childhood (2–5 years, Figure 4). Moreover childhood-onset overweight/obesity was a prominent feature in overweight adult patients. Elevated BMI in childhood was a strong predictor of future adiposity, associated with a 3-fold increased risk for overweight/obesity in adulthood. Therefore, in this large, longitudinal Fontan data set, we identified a bimodal pattern of increased obesity: in early childhood and in adulthood.

In our Fontan cohort, childhood overweight/obesity was up to 1.5 fold higher than in previous estimates of children with complex congenital heart disease [1,2,26]. Although our rates of childhood obesity were lower than in the general pediatric population (Fontan 22% vs. NHANES 32%), this contemporary assessment of children with Fontan circulation suggests that increased adiposity is becoming a more prevalent cardiometabolic risk factor in this high-risk population. It is well known that childhood obesity is a major public health concern associated with increased morbidity and risk for cardiometabolic disease in adolescence and adulthood [27–29]. Within the realm of congenital heart disease, obesity confers additional risk for morbidity and mortality [30–32]. In addition to the risk related to obesity-associated complications, obese patients with Fontan circulation may endure added cardiovascular morbidity. Obesity, hypertension and heart failure may further complicate the

management of the Fontan patient, who as an adult is already susceptible to arrhythmias, thromboembolism, and hepatic dysfunction [33].

In the current era of improved long-term survival for single ventricle heart disease, obesity clearly matters. Our current findings suggest that in patients with Fontan circulation, overweight/obesity was associated with higher systolic blood pressure, even at very young ages. Single ventricle physiology is unique, and this population of patients is vulnerable to physiologic disturbances such as high systemic blood pressure. Little has been published regarding the longstanding effects of systemic arterial hypertension in Fontan patients, as the majority of studies have focused on the elevation in systemic venous tone[34,35], pulmonary vascular resistance, or the response in Fontan patients to selective pulmonary vasodilators [36,37]. Yet from a ventricular function standpoint, both systemic and pulmonary vascular resistances are equally important and valid considerations. In the normal circulation, a systemic (left) ventricle pumps blood through the systemic capillary bed, while a pulmonary (right) ventricle pumps through the pulmonary capillary bed. In the Fontan circulation, both the systemic and the pulmonary vascular resistances are present in series, and are therefore additive. Given a constant pulmonary vascular resistance, an increase in systemic vascular resistance has the effect of increasing the net ventricular afterload, leading to a potentially higher negative impact on cardiac function than in a patient with two-ventricle circulation. Our study indicates that obese children have higher systolic blood pressure, even at very young ages, and this could represent an elevation in systemic vascular resistance [38] and the potential for increased cardiovascular risk. Further study, however, is required to determine the impact of overweight/obesity on blood pressure and ventricular function in the long-term outcome of Fontan patients [24].

Interestingly, the current study also demonstrates that overweight/obese adults had lower rates of heart failure when compared to normal weight patients, and there was no increased risk for heart transplant. Furthermore, growth (height velocity and final height) was normal in both overweight/obese and normal weight adults (Table 1) and children (Table 2). These findings extend previous growth data from a smaller series of Fontan patients, in which normal childhood growth was documented in children who were ~ 8 years post total cavopulmonary connection [25].

The normal growth and lower rates of heart failure observed in overweight/obese patients compared to underweight patients in our Fontan cohort could signify increased adiposity as a marker of positive nutritional balance and an indicator of improved cardiac health. An optimistic interpretation would be that adult Fontan survivors are able to live longer because of improved function and quality of life. These adults are also susceptible to environmental influences, and their positive nutritional balance may indicate proof of a “normal”, comparatively speaking, lifestyle. Alternatively, overweight/ obesity may indicate less severe disease in patients who had the most successful outcomes from Fontan palliative procedure. Prospective longitudinal analyses are needed to further elucidate the association between obesity and increased risk for cardiovascular morbidity in this at-risk population.

The retrospective nature of this study permitted sampling of a large representative cohort of patients who underwent Fontan surgical procedure at a single institution. However, since this

cohort was selected from a regional tertiary referral center, selection bias could have resulted in over-representation of severely ill patients. Similarly, in our role as a referral center, complete death records were not available to us, and nor were complete data on specific clinical markers such as hypoalbuminuria, edema, or medication history. Therefore we cannot offer insight into the predictors of obesity in this population or whether known obesity modulators, such as birth weight, physical activity, nutritional intake and family history play a role the development of obesity. Nevertheless, the current report demonstrates obesity is prevalent even in a cohort of patients with the most complex single ventricle heart disease.

We also found that adolescents 12–19 years of age had the lowest rates of obesity across all age groups and that these adolescents were least likely to have complete anthropometric data when compared to other age categories (Figure 1). Factors which could explain these low rates include: poor compliance with follow-up visits [39], increased mortality, or clinician focus on other patient data. It was striking to find that nearly 20% of patients did not have a single set of concurrent height and weight data recorded with which to calculate BMI. While there are controversies regarding the validity of BMI in defining obesity, it is a simple, low-cost, and readily available screening tool. Although the cardiologist may be primarily focused on the complexities of managing survivors with single ventricle circulation, they are also ideally suited to recognize the newly emerging concerns of obesity in these patients with chronic disease thereby empowering the patient and subspecialties' in the prevention and treatment of obesity.

Finally, in our adult cohort, the average age at Fontan procedure was 11½ years. Although the optimal timing of Fontan operation is still controversial, many contemporary centers aim to complete Fontan surgery in early childhood [40–43]. Older age at Fontan operation is associated with lower exercise capacity [44,45] which could increase risk for excess weight gain. Therefore it is important to note that the high obesity rates in our adult Fontan cohort could be related to their older age at completion of their Fontan procedure. Since this is a retrospective cohort, we were unable to evaluate the effect of functional exercise capacity on obesity, and the high obesity rates in our series may not be generalizable to a younger contemporary population. Nevertheless, by confirming higher childhood overweight/ obesity rates than were previously reported in the literature, in our pediatric Fontan cohort analysis we highlight the importance of obesity and weight gain in contemporary Fontan survivors.

Conclusion

Patients with Fontan circulation have a high rate of overweight and obesity. Childhood obesity is a strong predictor of future adiposity and is also linked to changes in systolic blood pressure at a very young age. Since patients with Fontan circulation are among the highest- risk for cardiovascular mortality, further investigation is needed to determine whether obesity modifies this risk. Guidelines for primary and secondary prevention of obesity in Fontan survivors should specifically address carefully selected nutritional, physical activity, and lifestyle interventions that can be implemented in children and adolescents.

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Figure 1:
Study population of Fontan clinic patients seen between 1992 – 2012.

Figure 2:
Prevalence of Overweight and Obesity in the Fontan Cohort between 1992–2012.

Figure 3:

Systolic blood pressure by age and weight status in children with Fontan circulation. Box and whisker plots for age groups A: 2–5 years, B: 6–11 years, C: 12–19 years. * $P = 0.001$; ** $P = 0.02$ vs. underweight for all comparisons.

Figure 4:
Longitudinal BMI trajectory throughout childhood in overweight/obese adolescents with Fontan circulation (n=14).

Table 1

– Adult Fontan Demographic and Anthropometric Characteristics

	Underweight n = 10	Normal n = 70	Overweight/obese n = 49	P value [*]
Male	50	60	51	0.6
Age (years)	26.8 (5.9)	27.3 (7.3)	28.6 (6.4)	1.0
Ethnicity				
Non-Hispanic white	70	74	67	0.6
Hispanic	10	11	20	
Non-Hispanic black	10	3	4	
Height (cm)	168.2 (6.4)	166.9 (10.3)	166.3 (8.9)	0.7
Weight (kg)	49.8 (4.6)	60.9 (8.4)	81.8 (11.7)	<0.001
BMI (kg/m²)	17.6 (0.5)	21.8 (1.6)	29.6 (3.6)	< 0.001
Age at Fontan (years)	15.3 (8.1)	12.2 (10.4)	9.9 (7.8)	0.1
Heart Failure	40	21	8	0.03
Transplant history	10	7	0	0.3
Systolic BP(mmHg)[†]	114.5 (14.9)	114.4 (13.1)	119.7 (20.7)	0.4
Diastolic BP(mmHg)[†]	70.5 (2.1)	66.3 (8.1)	69.9 (13.2)	0.3

Data presented are mean (SD) or percent.

^{*} P values are for the comparison between all 3 groups.[†] Measurements available for 65% of adults. BMI: body mass index; BP: blood pressure.

Table 2

– Children Age 2–18 Years, Anthropometric Characteristics and Blood Pressure

	Underweight	Normal	Overweight/Obese
2–5 years (n=401)			
Weight z-score	–2.2 (0.9)	–0.8 (1.0)	0.8 (1.2) [*] , [†]
Height z-score	–1.1 (1.0)	–1.0 (1.2)	–0.8 (1.4)
Systolic BP (mmHg) [§]	89 (10)	97(11) [‡]	101 (11) [*]
Diastolic BP (mmHg)	57 (6)	59 (9)	61 (8)
6–11 years (n=333)			
Weight z-score	–2.4 (1.0)	–0.6 (2.4)	1.1 (1.0) [*] , [†]
Height z-score	–1.2 (1.0)	–0.5 (9)	–0.4 (1.4)
Systolic BP (mmHg) ^{//}	101 (1)	106 (12)	109 (11)
Diastolic BP (mmHg) ^{//}	60 (7)	61 (8)	63 (9)
12–19 years (n=217)			
Weight z-score	–2.6 (2.6)	–0.7 (1.0)	1.1 (0.9) [*] , [†]
Height z-score	–1.1 (1.9)	–0.9 (1.4)	–0.4 (1.5)
Systolic BP (mmHg) [§]	105 (5)	111 (12)	117(15) [‡]
Diastolic BP (mmHg) [§]	64 (8)	63 (1)	61 (9)

Data presented as means ± SD, n= number of clinical encounters,

^{*} P 0.001 vs. underweight,[†] P<0.05 vs. normal,[‡] P=0.02 vs. underweight,[§] measurements available for 50% of encounters,^{//} measurements available for 80% of encounters. BP: blood pressure