The Cardiovascular Effects of Obesity on Ventricular Function and Mass in Patients after Tetralogy of Fallot Repair

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Objectives To determine the cardiovascular effects of obesity on patients with tetralogy of Fallot (TOF) repair.
Study design Ventricular performance measures were compared between obese (body mass index [BMI] ≥95%), overweight (85% ≤BMI <95%), and normal weight subjects (BMI <85%) in a retrospective review of patients with TOF who underwent cardiac magnetic resonance from 2005-2010. Significance was $P < .05$.
Results Of 260 consecutive patients with TOF, 32 were obese (12.3%), 48 were overweight (18.5%), and 180 were normal weight (69.2%). Biventricular mass was increased in obese compared with normal weight patients with right ventricular mass more affected than left ventricular mass. Obese patients demonstrated decreased biventricular end-diastolic volume (EDV) and stroke volume (SV) when indexed to body surface area (BSA) with an increased heart rate when compared with normal weight patients; cardiac index, ejection fraction, and pulmonary regurgitation fraction were similar. When indexed to ideal BSA, biventricular EDV and SV were similar. EDV and SV for overweight patients were nearly identical to normal weight patients with ventricular mass in between the other 2 groups.
Conclusions Approximately 12% of patients after TOF repair referred for cardiac magnetic resonance in a tertiary referral center are obese with increased biventricular mass. Obese patients and normal weight patients have similar cardiac indices, however, when indexed to actual BSA, obese patients demonstrate decreased EDV and SV with increased heart rate and similar cardiac indices. When indexed to ideal BSA, no differences in biventricular volumes were noted. *(J Pediatr 2015;167:325-30)*.

Childhood and adolescent obesity has reached epidemic proportions and is a leading concern in the United States[1]; normal children have an obesity rate of approximately 16%.[2] It not only affects individuals with normal hearts but patients with congenital heart disease (CHD) (13.8% of all patients with CHD)[3]; these children may even be more prone to obesity because of physical limitations.[4] The prevalence of obesity also can vary by disease state (eg, Fontan[3] and transposition of the great arteries after arterial switch operation[5]). The National Heart, Lung, and Blood Institute's Working Group on Obesity and Other Cardiovascular Risk Factors in Congenital Heart Disease has just recently outlined issues related to obesity.[6] It is one of the few modifiable risk factors in this population.

The hearts of children with repaired tetralogy of Fallot (TOF), the most common form of cyanotic CHD, often have pulmonary regurgitation and right ventricle (RV) volume overload. Multiple studies also have documented depressed RV function at rest and with exercise.[7,8] Residual outflow tract obstruction, branch pulmonary artery stenosis, RV hypertension, and arrhythmia are also reported after repair. Superimposition of obesity on these sequelae may burden the cardiovascular system further; it is, therefore, important to study the magnitude of the problem and the cardiovascular effects of obesity in this patient population.

Limited data were available on the functional cardiovascular effects of obesity in pediatric patients with CHD such as TOF. This study assessed the prevalence of overweight and obese TOF patients in a large tertiary referral center and additionally determined the effects on ventricular performance and mass compared with nonobese patients with TOF using cardiac magnetic resonance (CMR) cine and phase encoded velocity mapping.[9] It has been the noninvasive gold standard to measure ventricular mass, volume, and function for many years.[10-12] As CMR is unencumbered by adipose tissue and acoustic windows, which can create challenges in imaging the obese individual, it is an ideal imaging modality to assess ventricular function and mass in these patients. We hypothesized that obesity imposes a functional cardiovascular burden over and above what the normal weight patient with TOF faces. As obesity is one of the few modifiable risk factors,

BMI	Body mass index	iBSA	Ideal BSA
BSA	Body surface area	LV	Left ventricle
CHD	Congenital heart disease	RF	Regurgitant fraction
CMR	Cardiac magnetic resonance	RV	Right ventricle
EDV	End-diastolic volume	SV	Stroke volume
EF	Ejection fraction	TOF	Tetralogy of Fallot
HR	Heart rate		

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establishing baseline information on its prevalence will serve as a stepping stone to assess intervention in the future.

Methods

A search of the CMR database at our institution was performed for all patients 2-18 years of age who underwent TOF repair between 2005 and 2010 and had assessment of ventricular performance. If a patient was evaluated more than once, the first study was used. Patients were screened by echocardiography as well as CMR and were excluded if any of the following were present: RV outflow tract obstruction (≥3 m per second velocity), branch pulmonary artery stenosis evaluated by echocardiography, or CMR or pulmonary hypertension as measured by the tricuspid regurgitant jet. These criteria were used so the confounders of afterload were not present. Patients who underwent pulmonary valve replacement and those with pulmonary atresia or absent pulmonary valves were excluded. This study was approved by the institutional review board.

CMRs were performed on a Siemens 1.5 Tesla Sonata or Avanto MRI system (Siemens Medical Solutions, Malvern, Pennsylvania) with data analyzed using the standard Siemens' analysis package (ARGUS). Ventricular volumes, function, and mass were calculated from the analysis of a contiguous stack of cine steady-state free procession short axis images from base to apex. The septum was included in the RV mass as the RV is most affected in repaired TOF (**Figure 1**; available at www.jpeds.com); trabeculations and papillary muscles were included in the mass if contiguous with the endocardial surface but otherwise was included in the ventricular volume. Phase-encoded velocity mapping across the aortic and pulmonary valves were used to measure cardiac output and pulmonary regurgitation.

All CMR reports were examined for demographics including sex, age, height, and weight. In addition, the most recent clinic note (within 1 year of the CMR) was examined for blood pressures. Patients were classified as normal, overweight, or obese according to their body mass index (BMI) (weight/height^2). For pediatric patients between 2 and 18 years of age, BMI percentile for age and sex were determined by plotting the BMI values on the Center for Disease Control BMI-for-age growth charts.[13] Patients over the 95th percentile were classified as obese, between 85th and 95th percentile as overweight, and those <85th percentile as normal.

RV and left ventricle (LV) end-diastolic volume (EDV), end-systolic volume, stroke volume (SV), heart rate (HR), cardiac index, ejection fraction (EF) and myocardial mass were collected by cine; cardiac index and regurgitant fraction (RF) were collected by velocity mapping. Because of the different views in the literature of how to index ventricular volumes in obesity, data were indexed to body surface area (BSA), BSA$^{1.4}$ [14] and ideal BSA (iBSA) (the height of the patients and the 50th percentile for weight at their age).[15] Mass was indexed to height$^{2.7}$.[16]

Statistical Analyses

Descriptive statistics were performed. The primary comparison was between obese and normal weight patients with TOF. Comparison between obese, overweight, and normal weight patients were made using ANOVA with a multiple comparison test (Tukey method) if normally distributed; if the data were found not to be normally distributed, the Kruskal-Wallis test was used. ANCOVA was utilized to determine differences in the regression line between 2 groups. All values are mean ± SD. P values of <.05 was considered statistically significant.

Results

Two hundred sixty consecutive patients with TOF were found; 32 were obese (12.3%), 48 were overweight (18.5%), and 180 were normal weight (69.2%). Of the obese patients, 18 (56.3%) were male and 14 (43.7%) were female; in the normal group, 110 (61.1%) were male and 70 (38.9%) were female.

In the obese, overweight, and normal group, there were no cases of systolic hypertension. Blood pressures were 111.0 ± 10.2/69.4 ± 8.6 mm Hg, 105.6 ± 11.4/66.7 ± 7.7 mm Hg, and 107.6 ± 12.6/68.6 ± 10.1 mm Hg, respectively (P = .87).

Table I lists ventricular function and mass for all groups. BSA and BMI of obese patients were significantly higher than those of normal patients, however, there was no difference between the ages or height. No difference was noted in cardiac index or EF, however, the obese group demonstrated a significant decrease in both RV and LV indexed EDV and SV with a concomitant significant increase in HR. Both RV and LV mass were increased in the obese group, however, the mass/volume ratio was similar between the normal and obese groups in either ventricle. No difference was noted in pulmonary RF between groups. No significant differences were noted between main pulmonary artery flow or aortic flow as measured by phase contrast velocity mapping whether comparing between normal and obese patients (**Table I**) or comparing main pulmonary artery and aortic flows within the normal group (P = .58) or within the obese group (P = .53).

In the overweight group, as expected, BSA and BMI were in between the obese and normal weight patients, however, their HRs were nearly identical to the normal weight patients. Cardiac index, RV, and LV EF and pulmonary RF were very similar to both the obese and normal weight patients. For both RV and LV, however, EDV and SV for overweight patients were nearly identical to normal weight patients with measured ventricular mass in between the other 2 groups.

Another method of indexing ventricular volumes is based on cardiac output by using BSA$^{1.4}$; if this is used, no change in the results was noted from indexing to BSA (**Table II**; available at www.jpeds.com). It has been suggested that because indexing to BSA in overweight and obese patients will lower ventricular volumes because of the larger values