Research Square

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Nutritional Status Trajectory in Children and Adolescents With Repaired Tetralogy of Fallot: A Retrospective Longitudinal Cohort Study From a Latin American Tertiary Center

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Abstract

Purpose

Improved survival in repaired tetralogy of Fallot (rToF) has shifted attention to long-term comorbidities, notably obesity, a modifiable risk factor for adverse remodeling and mortality. We hypothesized that children with rToF show a significant upward body mass index Z-score (zBMI) trajectory during follow-up despite a lower prevalence of excess weight than the general pediatric population.

Methods

Retrospective longitudinal cohort of 70 patients with rToF aged 5–18 years followed at a Chilean tertiary center between 2015–2024. Excess weight was defined as zBMI ≥ + 1 (WHO 2007). Baseline and final assessments were compared with Wilcoxon signed-rank tests; subgroups (sex, anatomy, type of repair) with Mann-Whitney U or Kruskal-Wallis tests. Subgroup analyses were exploratory and unadjusted for multiplicity.

Results

Mean follow-up was 3.6 ± 2.4 years. Final prevalence of excess weight was 31.4% (95% CI 21.8–43.0), lower than the Chilean national estimate of 51.4%. Median zBMI rose from − 0.09 (IQR − 0.71 to 0.80) to 0.31 (IQR − 0.27 to 1.23; p = 0.003), and 12.9% (95% CI 6.9–22.7) moved from normal weight or underweight to excess weight. Patients with pulmonary atresia and major aortopulmonary collateral arteries had lower baseline zBMI (p = 0.02) but higher final left ventricular end-diastolic diameter Z-scores (p = 0.03). Only the complex-repair subgroup showed a significant zBMI increase (p = 0.04). No differences were found by sex.

Conclusion

Children with rToF had a lower prevalence of excess weight than the general population but a significant upward zBMI trajectory, supporting longitudinal nutritional surveillance in routine rToF follow-up.

Introduction

Tetralogy of Fallot (ToF) is the most prevalent cyanotic congenital heart disease, representing 7–10% of congenital heart diseases worldwide [1]. ToF encompasses an anatomical spectrum of increasing complexity, from pulmonary stenosis (PS) to pulmonary atresia (PA), with or without major aortopulmonary collateral arteries (MAPCAs); definitive repair correspondingly ranges from a transannular patch (TAP) or valve-sparing procedure (VSR) to more complex reconstructions involving a right ventricle–to–pulmonary artery conduit and unifocalization of MAPCAs [1]. Surgical repair of ToF has significantly reduced mortality, achieving a 50-year survival rate of 71%, increasing up to 84% when 30-day post-surgical mortality is excluded in patients undergoing repair before age 15 [2]. This improved survival, alongside stable birth prevalence, has resulted in a growing population living with repaired ToF (rToF) [2, 3].

Concurrently, the prevalence of excess weight (overweight and obesity) in the global pediatric population has risen, which represents a critical secondary challenge for the growing rToF population [4, 5]. This trend is particularly evident in Chile, where the prevalence reached 51.4% nationwide in 2023 [6]. For children with a repaired congenital heart defect, the superposition of excess weight creates a clinical double hit. The rToF myocardium, already compromised by surgical scarring, residual right ventricular outflow tract (RVOT) dysfunction, and chronic volume or pressure overload, must adapt to the systemic demands of obesity [1, 7, 8]. Excess adiposity leads to increases in circulating blood volume, altered peripheral vascular resistance, and subclinical chronic inflammation, all of which demand sustained increases in cardiac output [5, 9]. In an already vulnerable right and left ventricle, this chronic hemodynamic stress is associated with a higher risk of metabolic syndrome and a significantly lower threshold for tachyarrhythmias [10, 11]. Furthermore, it drives accelerated adverse myocardial remodeling, which manifests as biventricular dilation, ventricular hypertrophy, impaired systolic function, and reduced exercise capacity [9, 12, 13]. Therefore, monitoring nutritional trajectories in the rToF population is more than an epidemiological concern; it is a fundamental cardiovascular imperative [5, 8].

Despite this clear cardiovascular imperative, evidence regarding the longitudinal evolution of nutritional status in patients with rToF remains scarce. Studies have shown a prevalence of overweight and obesity in patients with congenital heart disease similar to that of the general population [4, 7, 14]. Given the rising prevalence of excess weight in the pediatric population, particularly in Chile, it is essential to analyze whether this trend is also present in children with rToF. Understanding the nutritional trajectory of these patients will allow for the optimization of clinical management strategies and the prevention of future metabolic complications.

The objective of this study was to determine the prevalence of excess weight (overweight and obesity) in pediatric patients with rToF and to describe its trajectory over time. We hypothesized that this population would show a significant upward zBMI trajectory during follow-up.

Methods

Study Design. A retrospective longitudinal cohort study was conducted in pediatric patients with rToF followed at the UC-Christus Healthcare Network between 2015 and 2024. The study is reported in accordance with the STROBE statement for observational studies.

Participants and sample size. The source population consisted of 116 patients with a confirmed diagnosis and rToF. For the purposes of this study, rToF was defined as the completion of intracardiac repair, comprising surgical closure of the ventricular septal defect (VSD) together with relief of right ventricular outflow tract (RVOT) obstruction, either as a primary repair or following prior palliative procedures. Inclusion criteria were age between 5 and 18 years and the availability of anthropometric data from clinical visits starting at 5 years of age. A total of 70 patients met the inclusion criteria and were included in the final analysis. Patients with incomplete anthropometric records (n = 31), those with only a single clinical encounter at the center (n = 14), and those with atypical rToF variants (n = 1), such as ToF and atrioventricular septal defect or absent pulmonary valve syndrome, were excluded. The study sample corresponded to a convenience sample including all eligible patients followed at our institution during the study period.

Data Collection and Anthropometric Assessment. Anthropometric data were obtained from echocardiography reports. In our echocardiography laboratory, all patients are weighed and measured by a licensed vocational nurse or a registered nurse using a Seca® 700 scale and stadiometer, following World Health Organization (WHO) international recommendations. Body Mass Index (BMI) was calculated as weight (kg) divided by height squared (m^2). Nutritional status was classified according to the 2007 WHO BMI Z-score (zBMI) cut-off points: obesity was defined as a Z-score ≥ +2, overweight as a Z-score between +1 and +1.99, and normal weight as a Z-score between -0.99 and +0.99 [15]. Excess weight (overweight and obesity combined) was defined as a Z-score ≥ +1 and used as the primary composite outcome. To characterize nutritional trajectories during childhood and adolescence, anthropometric and echocardiographic variables were compared between the first available assessment (since age 5) and the most recent follow-up. This methodology standardizes the evaluation of discrete physiological states, mitigating bias inherent in the irregular follow-up intervals of retrospective cohorts. By anchoring the analysis on these clinical endpoints, the focus was placed on long-term outcomes while minimizing noise from intermediate visit variability.

Clinical variables were extracted from patient medical records, and included age, sex, original cardiac anatomy (ToF with PS or PA, with or without MAPCAs), age at surgical repair (months), type of repair: Transannular Patch (TAP), Valve-sparing Repair (VSR) or Complex repair, history of prior palliative intervention (categorized as none, systemic-to-pulmonary shunts [specifically the modified Blalock–Taussig–Thomas], or alternative modalities [including ductal or right ventricular outflow tract (RVOT) stenting]), and the presence of genetic testing results. For analytic purposes, the “Complex repairs” group encompassed patients who did not undergo TAP or VSR and who instead required right ventricle–to–pulmonary artery conduit placement, unifocalization of MAPCAs, or both — procedures reserved for the most anatomically complex variants (PA and PA-MAPCAs). These interventions reflect a higher baseline disease burden and a longer perioperative course than TAP or VSR, which is relevant for the interpretation of subsequent nutritional trajectories.

Echocardiographic parameters were extracted from echocardiography reports and included: right ventricular outflow tract (RVOT) diameter and RVOT Z-score (reflecting the degree of residual right-sided obstruction or dilation), Tricuspid Annular Plane Systolic Excursion (TAPSE; a marker of right ventricular longitudinal systolic function), left ventricular end-diastolic diameter (LVEDD) Z-score (a measure of left ventricular chamber size indexed to body surface area), and shortening fraction (SF; a marker of left ventricular systolic function).

Statistical Analysis: Statistical analyses were performed using SPSS v25 and Python with Matplotlib. Data distribution was assessed for normality using the Shapiro-Wilk test. Due to non-normal distributions and modest subgroup sizes, non-parametric methods were applied uniformly to all continuous variables to ensure internal consistency. Accordingly, continuous variables are presented as median (interquartile range), and categorical variables as frequencies (percentages).

Longitudinal changes in nutritional and echocardiographic parameters were evaluated using the Wilcoxon signed-rank test. Between-subgroup differences were assessed using the Mann-Whitney U test or the Kruskal-Wallis test, as appropriate. To increase statistical power for secondary analyses, clinically related subgroups were pooled (PS+PA vs. PA-MAPCAs; TAP+VSR vs. complex repairs) and compared using the Mann-Whitney U test. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate. A p-value < 0.05 was considered statistically significant.

Ethics: This study was approved by the Scientific Ethics Committee of the School of Medicine of the *Pontificia Universidad Católica de Chile* (Protocol Nº 240711008), in accordance with the Declaration of Helsinki. Informed consent was waived, due to the retrospective nature of the study and minimal risks to participants.

Results

Study Population and Surgical Characteristics

The 70 analyzed rToF patients (44.3% female) had a median age at first evaluation of 7.70 years (IQR 5.84–11.15), and a median age of 12.38 years (IQR 9.48–14.64) at last follow-up. The clinical, anthropometric, and echocardiographic characteristics of the cohort are summarized in Table 1. Baseline cardiac anatomy comprised ToF with PS (57.1%), PA (22.9%), and PA-MAPCAs (20.0%). At baseline, weight, height and zBMI did not differ significantly across the three anatomical groups (Kruskal-Wallis, p = 0.07 for zBMI). Final LVEDD Z-score differed significantly across subgroups (p = 0.03), while RVOT Z-score, TAPSE and SF remained within normal ranges and showed no significant longitudinal changes.

Surgical and genetic characteristics by anatomical subtype are detailed in Table 2. The median age at definitive surgical repair for the entire cohort was 6.25 months (IQR 3.95–15.82), but this timing varied significantly across all anatomical subtypes (p < 0.001). Patients with pulmonary atresia underwent repair at the earliest age, followed by those with pulmonary stenosis, whereas the MAPCAs subgroup underwent definitive correction at a significantly later age, presenting a median of 36.50 months (IQR 16.12–65.40). Transannular patch was the most frequent repair (48.6%) and predominated in PS (70.0%), whereas complex repairs were required in 68.8% of PA and 92.9% of PA-MAPCAs patients, most often involving right ventricle–to–pulmonary artery conduit placement and unifocalization. Palliative surgery [Blalock–Taussig–Thomas Shunt / RVOT stent) was performed in 25.7% of the cohort prior to definitive repair, reaching 62.5% in PA (p = 0.001). Genetic testing (Fluorescence in situ hybridization and/or Multiplex ligation-dependent probe amplification) was performed in 44.3% of patients; 22q11.2 deletion was identified in 8.6% overall, with the highest prevalence in PA-MAPCAs (21.4%).

Nutritional Status and Trajectory

A total of 461 echocardiographic and nutritional follow-up assessments were available for the 70 patients, with a mean of 6.59 evaluations per participant (range 2-20). The mean follow-up duration was 3.6 ± 2.4 years, and 57.1% of the cohort had at least 3 years of follow-up.

At the end of the follow-up period, 10 patients (14.3%; 95% CI 7.9-24.3) were classified as underweight, 38 (54.3%) as normal weight, and 22 (31.4%; 95% CI 21.8-43.0) as having excess weight, including 19 patients (27.1%; 95% CI 18.1-38.5) with overweight and 3 (4.3%; 95% CI 1.5-11.9) with obesity. The prevalence of excess weight was significantly lower than the 51.4% reported for the general Chilean pediatric population (one-sample binomial test, p = 0.001). The median zBMI increased significantly from -0.09 [IQR -0.71 to 0.80] at baseline to 0.31 [IQR -0.27 to 1.23] at the final assessment (p = 0.003). During the follow-up, 9 patients (12.9%; 95% CI 6.9-22.7) transitioned from normal weight or underweight to excess weight. The trajectory of zBMI over time is summarized in Figure 1.

Trajectory of body mass index Z-score (zBMI) in 70 patients with repaired tetralogy of Fallot (rToF), 2015–2024. Each grey line represents an individual patient trajectory; the bold blue line represents the cohort median trend. The shaded light blue area indicates the 95% confidence interval of the median. Overall, median zBMI increased significantly from -0.09 (IQR: -0.71 to 0.80) at baseline to 0.31 (IQR: -0.27 to 1.23) at final follow-up (Wilcoxon signed-rank test, p = 0.003). A p-value < 0.05 was considered statistically significant. zBMI was calculated using the WHO 2007 reference. IQR: Interquartile Range; rToF: Repaired tetralogy of Fallot; zBMI: Body Mass Index Z-score.

Echocardiographic Parameters

In the overall cohort, longitudinal analysis showed that both ventricular dimensions and systolic function parameters remained stable throughout the follow-up period. There were no statistically significant changes from baseline to final evaluation in the RVOT Z-score (p = 0.20) or LVEDD Z-score (p = 0.63). Biventricular systolic function also remained preserved, with no significant longitudinal changes in TAPSE (p = 0.38) or left ventricular SF (p = 0.12) (Online Resource 1).

Comparative Analysis

When stratified by sex, no clinically significant differences were observed in zBMI trajectories (males: 0.13 to 0.23; females: -0.11 to 0.38; p = 0.73 and p = 0.38, respectively). Similarly, longitudinal echocardiographic parameters showed no significant differences between sexes.

Anatomical subgroup analysis across the three distinct categories revealed a trend toward baseline variations in zBMI, though it did not reach strict statistical significance (p = 0.07). However, when evaluating specific phenotypes, patients with PA-MAPCAs had significantly lower initial zBMI values (-0.56; IQR: -1.65 to 0.03) compared to other subtypes (PS+PA pooled: 0.10; IQR: -0.65 to 1.05; p = 0.02 via Mann-Whitney U test), although this nutritional difference was no longer statistically significant by the end of follow-up (pooled p = 0.07). Despite this, significant differences emerged in echocardiographic parameters, with the MAPCAs group exhibiting higher final LVEDD Z-scores compared to patients with PS or PA (p = 0.03). No significant differences were found between anatomical groups regarding biventricular systolic function (TAPSE and SF) at any point during the study.

Regarding surgical repair, initial zBMI differed significantly across subgroups (TAP: 0.35, VSR: -0.15, complex: -0.40; p = 0.039). While this three-group difference did not persist (p = 0.14), pooled analysis showed patients with complex repairs maintained significantly lower zBMI than

TAP+VSR patients both initially (p = 0.012) and at final follow-up (p = 0.048). Longitudinally, only the complex repair group exhibited a significant zBMI increase over time (p = 0.040).

Stratification by the presence of palliative surgery showed no significant differences in either initial or final zBMI (p = 0.71 and p = 0.75, respectively). Finally, no significant differences in zBMI were found between patients with and without genetic testing results. The comparative analysis between anatomy groups is summarized in Figure 2.

Trajectory of body mass index Z-score (zBMI) stratified by anatomical complexity. Grey lines represent individual patient trajectories. Coloured lines represent group median trends: green, pulmonary stenosis and pulmonary atresia pooled cohort (PS+PA); purple, pulmonary atresia with major aortopulmonary collateral arteries (MAPCAs). At baseline, median zBMI was significantly lower in the MAPCAs group compared with the pooled PS+PA cohort (Mann-Whitney U test, p = 0.02), although this difference did not reach statistical significance by the end of follow-up (p = 0.07). A p-value < 0.05 was considered statistically significant. zBMI was calculated using the WHO 2007 reference. MAPCAs: Major Aortopulmonary Collateral Arteries; PA: Pulmonary Atresia; PS: Pulmonary Stenosis; zBMI: Body Mass Index Z-score.

Discussion

The prevalence of excess weight (overweight and obesity) in our study cohort was 31.4%, a figure considerably lower than the 51.4% reported in the general Chilean pediatric population [6]. This comparison should be interpreted as descriptive rather than as a matched comparison: the national estimate derives from a school-based census of predominantly publicly funded schools, with an age range, measurement setting and socioeconomic composition that differ from those of a tertiary-referral cardiology cohort. Within these constraints, the difference may reflect factors related to rToF itself (chronic disease burden, surgical history, intensive longitudinal follow-up) as well as the socioeconomic profile of our cohort. Our finding is nonetheless consistent with Perin et al. [14], who reported a comparable prevalence of excess weight (35.4%) in a pediatric population undergoing intervention for various congenital heart diseases, including rToF.

When evaluating the nutritional trajectory, we observed a statistically significant increase in zBMI from -0.09 to 0.31 (p = 0.003). Although the cohort remained, on average, within the normal-weight range, this significant upward trend suggests a progressive shift in nutritional status over time. Notably, 12.9% of patients transitioned from a normal-weight or underweight status to excess weight during the follow-up period (3.6 ± 2.4 years). These findings reinforce international evidence regarding the progressive increase of obesity in rToF, which is linked to adverse ventricular remodeling, biventricular dilation, and worsened biventricular systolic function [9, 12].

Patients with rToF and excess weight face a higher risk of metabolic syndrome, atherosclerotic cardiovascular disease, and type 2 diabetes [10]. Mayourian et al. found obesity (BMI ≥ 30 kg/m²) to be an independent and modifiable risk factor for mortality in adult rToF, conferring a 1.7-fold increase in risk [13], with additional associations to myocardial remodeling, systolic dysfunction, arrhythmias, and reduced exercise capacity [9, 11, 12]. Identifying at-risk patients early is therefore essential for timely intervention.

Anatomical subgroup analysis revealed significant differences in patients with PA-MAPCAs compared with those with PS and PA. Patients in the MAPCAs group exhibited persistently lower zBMI values, likely due to the higher complexity of the heart disease, which is associated with an increased number of surgical interventions and prolonged hospital stays [16-18]. Similarly, complex-repair patients maintained persistently lower zBMI than the TAP+VSR cohort, reflecting prolonged metabolic stress (Online Resource 2). However, only this complex-repair group showed a significant longitudinal zBMI increase over time (p = 0.040).

A further observation was a difference in final LVEDD Z-scores across anatomical subgroups (p = 0.03), driven primarily by the higher final values in the PA-MAPCAs group (n = 12). This left ventricular dilation is pathophysiologically distinct from the right ventricular changes typically monitored in rToF. In patients with PA-MAPCAs, definitive repair is highly complex, often involving extensive unifocalization and multiple surgical stages [19]. The elevated final LVEDD Z-scores may reflect chronic left-sided volume overload. This is frequently caused by residual aortopulmonic collateral flow or systemic-to-pulmonary shunts that were not completely ligated during the staged reparative process [1, 19]. Over time, this subclinical left ventricular dilation could compromise biventricular mechanics, particularly when coupled with a progressive upward nutritional trajectory [9, 12]. Given the small size of this subgroup and the exploratory nature of the comparison, this mechanism remains hypothetical and requires confirmation in larger cohorts with dedicated assessment of residual collateral flow.

Regarding baseline demographics, no significant differences in nutritional status or zBMI trajectories were observed between sexes. These findings are consistent with the Chang et al. cohort, which reported comparable BMI-for-age distributions between males and females [20]. Nevertheless, existing literature suggests important sex-specific differences in body composition, with males exhibiting lower fat mass indices despite similar zBMI values [20]. Furthermore, evidence indicates that excess weight in the general pediatric population has cardiac effects that are clinically more relevant in females, where it is associated with ventricular hypertrophy and diastolic dysfunction [21]. Therefore, female patients with rToF and excess weight may warrant special attention for early nutritional intervention.

Echocardiographic Trajectory and Subclinical Remodeling

In our longitudinal analysis, both ventricular dimensions (RVOT and LVEDD Z-scores) and biventricular systolic function parameters (TAPSE and left ventricular SF) remained stable throughout the follow-up period. This apparent echocardiographic stability contrasts with established literature indicating that increased adiposity in rToF is associated with progressive biventricular dilation and worsened biventricular systolic function [9, 13]. Several factors may explain this finding. First, although we identified a significant upward trend in zBMI, the cohort on average remained within the normal-weight range. The relatively short follow-up time may not have been sufficient for obesity-related maladaptive remodeling and gross systolic dysfunction to fully manifest. Furthermore, Z-score stability (RVOT p = 0.20; LVEDD p = 0.63) should be interpreted with caution, as BSA-indexed metrics may numerically normalize pathological chamber growth in patients with excess weight, masking subclinical progression [22,23].

Although cardiac dimensions are routinely indexed to body surface area (BSA) to account for somatic growth, standard BSA calculations become heavily skewed by excess weight [22]. Consequently, indexing raw cardiac dimensions to an inflated BSA artificially decreases the resulting Z-score, potentially masking pathological ventricular dilation and remodeling, leading to a false clinical reassurance of stability [8, 9, 12, 19]. Compounding this, conventional functional indices such as TAPSE and SF are insensitive to early, obesity-mediated systolic impairment in rToF, which is detectable predominantly through myocardial deformation imaging (speckle-tracking echocardiography or strain cardiac MRI), a technique that quantifies regional myocardial shortening (e.g., global circumferential strain) and detects subtle contractile dysfunction before changes in ejection fraction or SF become apparent [5, 8, 23]. Echocardiographic stability in the present cohort should therefore be regarded as hypothesis-generating rather than reassuring. To prevent diagnostic delay, future longitudinal protocols should consider incorporating ideal body surface area (iBSA), lean body mass, or height-based allometric scaling alongside strain-based functional assessment when evaluating rToF patients with an upward zBMI trajectory [9, 12, 19, 22, 23].

Clinical Implications

Overall, our findings underscore that obesity is a major yet modifiable risk factor in pediatric patients with rToF, that demands targeted intervention. The high prevalence of excess weight, together with the concerning upward trajectory of zBMI over time, serves as a call to action for pediatric practices [7, 8]. Multidisciplinary strategies, including early nutritional counseling and tailored cardiac rehabilitation programs focused on weight management and physical fitness, should be integrated into routine rToF follow-up care early, before obesity fully manifests [9, 10]. Prospective studies are required to evaluate whether timely weight interventions can effectively reverse adverse ventricular remodeling, improve exercise tolerance, and enhance patients' quality of life.

Limitations and Future Directions

This study has several limitations. As a single-center retrospective analysis, selection bias cannot be excluded, though the broad referral pattern of UC-Christus partially mitigates this risk. Missing echocardiographic data may overrepresent patients requiring closer monitoring. Additionally, genetic testing was driven by anatomical complexity rather than systematic screening. Subgroup analyses were exploratory and unadjusted for multiplicity; mixed-effects models could better account for the hierarchical data structure (461 visits in 70 patients). Measurements were not blinded, and heterogeneous follow-up windows introduce variability in exposure duration.

BMI is an indirect proxy for adiposity and may underestimate true body composition [20]; future studies should incorporate waist circumference, waist-to-height ratio, or bioelectrical impedance.

Prospective multicenter studies with longer follow-up (>10 years), advanced imaging including myocardial deformation analysis, and structured evaluation of nutritional and physical activity interventions are warranted to clarify whether early multidisciplinary care can mitigate the cardiovascular consequences of excess weight in rToF [7, 8, 21].

Conclusion

In this cohort of pediatric patients with repaired tetralogy of Fallot (rToF), the prevalence of excess weight (31.4%) was lower than that reported in the general Chilean pediatric population. However, longitudinal analysis revealed a concerning nutritional trajectory with a statistically significant increase in zBMI (p = 0.003) during follow-up, and 12.9% of patients transitioned from a normal-weight or underweight status to excess weight.

This subgroup represents a population at increased clinical risk. Given that obesity is an independent and modifiable risk factor for mortality in patients with rToF, and has been associated with adverse myocardial remodeling, systolic dysfunction, arrhythmia and metabolic syndrome, these findings carry high clinical implications [9–13].

Our findings support longitudinal monitoring of zBMI trajectories to identify rToF patients shifting toward excess weight [5]. Whether early intervention in this subgroup mitigates long-term cardiovascular and metabolic risk remains to be established and warrants prospective multicenter study.

Declarations

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Competing Interests: The authors have no relevant financial or non-financial interests to disclose.

Ethics Approval: This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Pontificia Universidad Católica de Chile (September 2024 / No 240711008).

Consent to Participate: Informed consent was waived by the Scientific Ethics Committee of the School of Medicine, Pontificia Universidad Católica de Chile, due to the retrospective design of the study and the use of de-identified clinical data with minimal risk to participants.

Consent to publish: Not applicable.

Data Availability: The de-identified datasets generated and analyzed during the current study are available from the corresponding author on reasonable request, subject to institutional data-sharing policies.

Contributions:

All authors contributed to the study conception and design. Material preparation and data collection were performed by Guillermo Larios and Daniel Amato. Analysis was performed by Marianne Niklitschek, Vicente Mayol and Martin Niklitschek. The first draft of the manuscript was written by Marianne Niklitschek and Vicente Mayol. Critical revision of the manuscript was done by Guillermo Larios. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1: Clinical, Anthropometric, and Echocardiographic Characteristics of the Study Population.

	Total	Stenosis	Pulmonary Atresia	PA with MAPCAs	P-Value
	n=70	n=40 (57.1%)	n=16 (22.9%)	n=14 (20%)	
Age at first evaluation, years	7.70 (5.84–11.15)	7.75 (5.76–10.91)	8.07 (6.45–10.78)	6.27 (5.51–12.46)	0.64
Age at last follow up, years	12.38 (9.48–14.64)	11.94 (9.32–14.33)	12.88 (11.40–14.37)	13.22 (8.40–16.34)	0.52
Female sex, n (%)	31 (44.3%)	18 (45.0%)	7 (43.7%)	6 (42.8%)	
Initial weight, kg	24.5 (20.0–35.5)	27.50 (21.0–37.3)	24.5 (22.5–34.3)	21.0 (19.0–28.6)	0.18
Final weight, kg	43.0 (30.3–51.8)	41.5 (31.8 – 52.2)	47.3 (42.3–52.3)	34.2 (25.4–46.1)	0.22
Initial height, cm	122.0 (116.3–143.0)	122.0 (117.0–145.0)	127.0 (117.0–139.5)	118.0 (112.6–137.5)	0.43
Final height, cm	149.0 (128.5–158.0)	150.5 (127.0–159.0)	151.50 (141.5–155.8)	139.5 (125.3–158.0)	0.79
Initial BMI Z–Score	-0.09 (-0.71–0.80)	0.06 (-0.67–1.17)	0.17 (-0.59–0.90)	-0.56 (-1.65 – -0.03)	0.07
Final BMI Z–Score	0.31 (-0.27–1.23)	0.43 (-0.27–1.45)	0.49 (0.04–1.18)	-0.07 (-1.15–0.56)	0.19
Initial RVOT diameter, mm (n=27)	17.20 (15.35–19.30)	17.25 (16.67–18.80) [n=20]	11.40 (11.30–12.70) [n=5]	n = 2	—
Final RVOT diameter, mm (n=27)	19.00 (16.00–20.15)	19.00 (17.20–20.07) [n=20]	16.00 (12.00–20.00) [n=5]	n = 2	—
Initial RVOT Z–Score (n=27)	-0.98 (-2.06–0.13)	-0.94 (-1.47–0.11) [n=20]	-3.17 (-3.71 – -2.21) [n=5]	n = 2	—
Final RVOT Z–Score (n=27)	-0.96 (-2.35–-0.34)	-0.99 (-2.11– -0.75) [n=20]	-2.53 (-3.15 to -0.84) [n=5]	n = 2	—
Initial TAPSE, cm (n=60)	1.60 (1.30–1.80)	1.60 (1.34–1.80) [n=35]	1.42 (1.30–1.75) [n=14]	1.40 (1.30–1.77) [n=11]	0.85
Final TAPSE, cm (n=60)	1.60 (1.40–1.80)	1.60 (1.40–1.80) [n=35]	1.55 (1.40–1.88) [n=14]	1.40 (1.29–1.62) [n=11]	0.15
Initial LVEDD Z–Score (n=60)	-0.17 (-1.03–0.67)	-0.30 (-1.15–0.66) [n=34]	-0.16 (-0.67–0.29) [n=14]	0.13 (-1.08–1.03) [n=12]	0.78
Final LVEDD Z-Score (n=60)	-0.20 (-0.91–0.74)	-0.30 (-0.98–0.54) [n=34]	-0.27 (-1.58– -0.06) [n=14]	0.88 (-0.48–1.70) [n=12]	**0.03**
Initial shortening fraction, % (n=58)	38.50 (33.00–42.00)	38.00 (32.50–40.00) [n=31]	41.00 (35.00–43.00) [n=15]	40.00 (31.50–44.30) [n=12]	0.61
Final shortening fraction, % (n=58)	36.50 (32.25–40.00)	35.00 (31.00–39.50) [n=31]	38.00 (34.50–41.00) [n=15]	37.50 (34.50–40.00) [n=12]	0.40

Data are presented as median (interquartile range), or frequency (percentage) as appropriate. BMI Z–scores and echocardiographic parameters were compared between anatomy groups with Kruskal-Wallis test (global comparison). Specific pooled subgroup comparisons (e.g., PS+PA vs. PA-MAPCAs) were performed using the Mann-Whitney U test, as detailed in the Results section. P-values in bold indicate statistical significance ($p < 0.05$). To ensure internal validity and consistency across longitudinal comparisons, baseline and final echocardiographic parameters are presented exclusively for the subset of patients with available paired measurements at both time points. BMI: Body Mass Index; LVEDD: Left Ventricular End-Diastolic Diameter; MAPCAs: Major Aortopulmonary Collateral Arteries; PA: Pulmonary Atresia; PS: Pulmonary Stenosis; RVOT: Right Ventricular Outflow Tract; TAPSE: Tricuspid Annular Plane Systolic Excursion; zBMI: Body Mass Index Z-score. RVOT diameter and RVOT Z-score values for the PA-MAPCAs subgroup are not reported owing to insufficient sample size (n = 2); the corresponding p-values were not computed for this stratum.

Table 2: Surgical Procedures and Genetic Findings by Anatomical Subtype.

Surgical Procedure	Total	Pulmonary Stenosis	Pulmonary Atresia	MAPCAs	P-Value
	n=70	n=40 (57.1%)	n=16 (22.9%)	n=14 (20.0%)	
Type of reparative surgery, n (%)					<0.001[a]
Transannular patch (TAP)	34 (48.6%)	28 (70.0%)	5 (31.2%)	1 (7.1%)	
Valve-sparing repair (VSR)	12 (17.1%)	12 (30.0%)	0 (0.0%)	0 (0.0%)	
Complex repair	24 (34.3%)	0 (0.0%)	11 (68.8%)	13 (92.9%)	
Specific surgical interventions, n (%)					
Previous palliative surgery	18 (25.7%)	5 (12.5%)	10 (62.5%)	3 (21.4%)	0.001[a]
Palliative surgery (BTT shunt)	17 (24.3%)	4 (10.0%)	10 (62.5%)	3 (21.4%)	
Palliative surgery (RVOT stent)	1 (1.4%)	1 (2.5%)	0 (0.0%)	0 (0.0%)	
RV-PA conduit	24 (34.3)	0 (0.0%)	12 (75.0%)	12 (85.7%)	<0.001[a]
Unifocalization	7 (10.0%)	0 (0.0%)	1 (6.3%)	6 (42.9%)	<0.001[a]
Collateral ligation	2 (2.9%)	0 (0.0%)	0 (0.0%)	2 (14.3%)	0.016[a]
Age at first intervention, months (IQR)	3.95 (1.50–6.15)	4.45 (2.68–5.93)	0.29 (0.20–0.89)	6.10 (4.25–15.68)	<0.001
Age at definitive repair[b], months (IQR)	6.25 (3.95–15.82)	5.00 (3.45–6.85)	7.17 (5.01–15.68)	36.5 (16.12–65.40)	<0.001
Genetic Testing (FISH/MLPA), n (%)	31 (44.3%)	12 (30.0%)	8 (50.0%)	11 (78.6%)	0.006
22q11 deletion, n (%)	6 (8.6%)	1 (2.5%)	2 (12.5%)	3 (21.4%)	0.076[a]

Data are presented as median (interquartile range) for continuous variables or as frequency (percentage) for categorical variables. Categorical distributions across subgroups were compared using the Chi-square test or Fisher's exact test, as appropriate. [a] denote sparse data (expected frequencies < 5) where exact tests or adjustments were applied. Continuous variables were compared using the Kruskal-Wallis test. [b] Definitive repair is defined as the surgical closure of the ventricular septal defect and relief of right ventricular outflow tract obstruction. BTT: Blalock-Taussig-Thomas; FISH: Fluorescence In Situ Hybridization; MAPCAs: Major Aortopulmonary Collateral Arteries; MLPA: Multiplex Ligation-dependent Probe Amplification; PA: Pulmonary Atresia; PS: Pulmonary Stenosis; RV-PA: Right Ventricle-to-Pulmonary Artery; RVOT: Right Ventricular Outflow Tract; TAP: Transannular Patch; VSR: Valve-Sparing Repair.

Figures

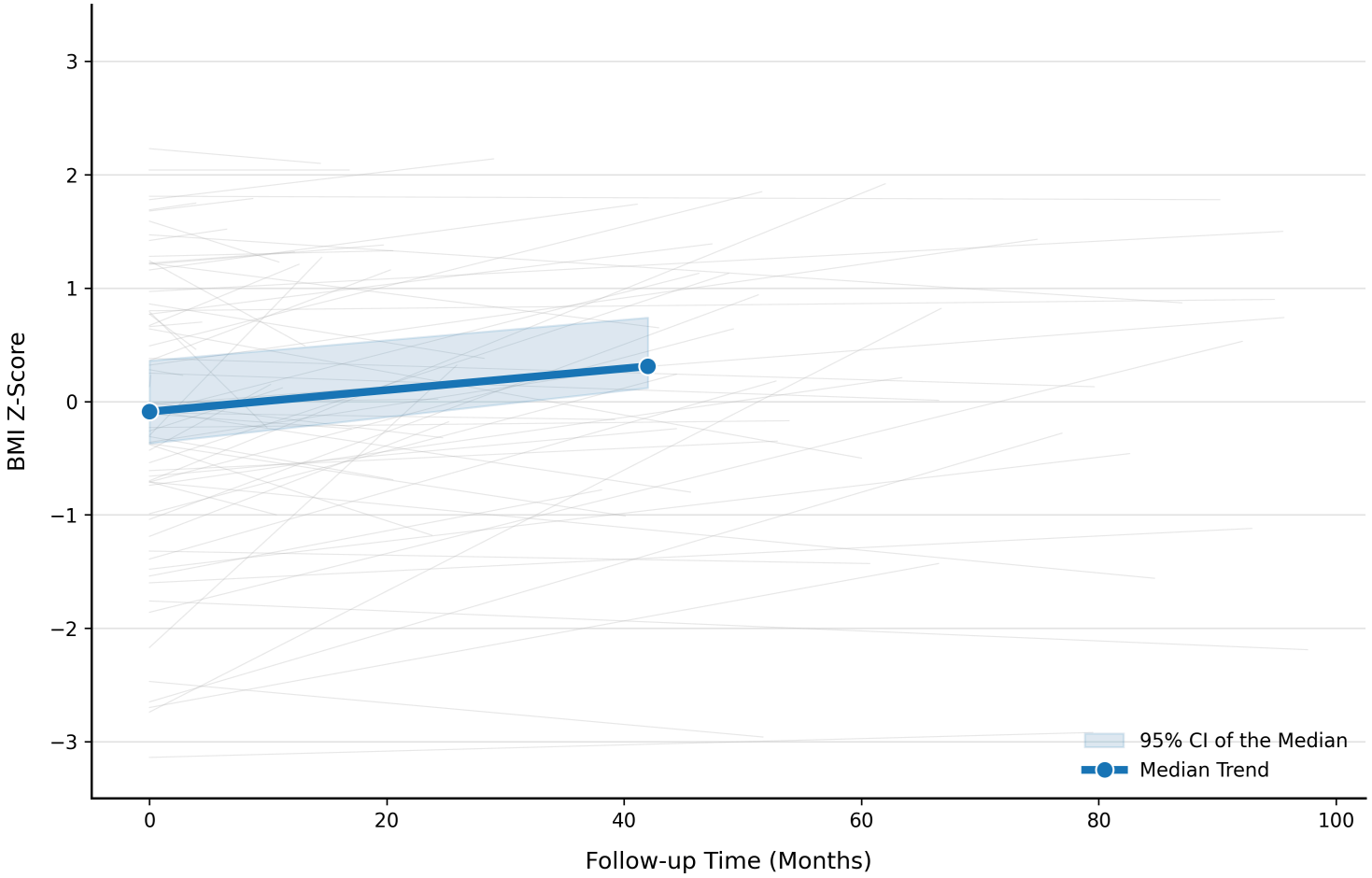


Figure 1

Evolution of BMI Z-Score during Follow-up

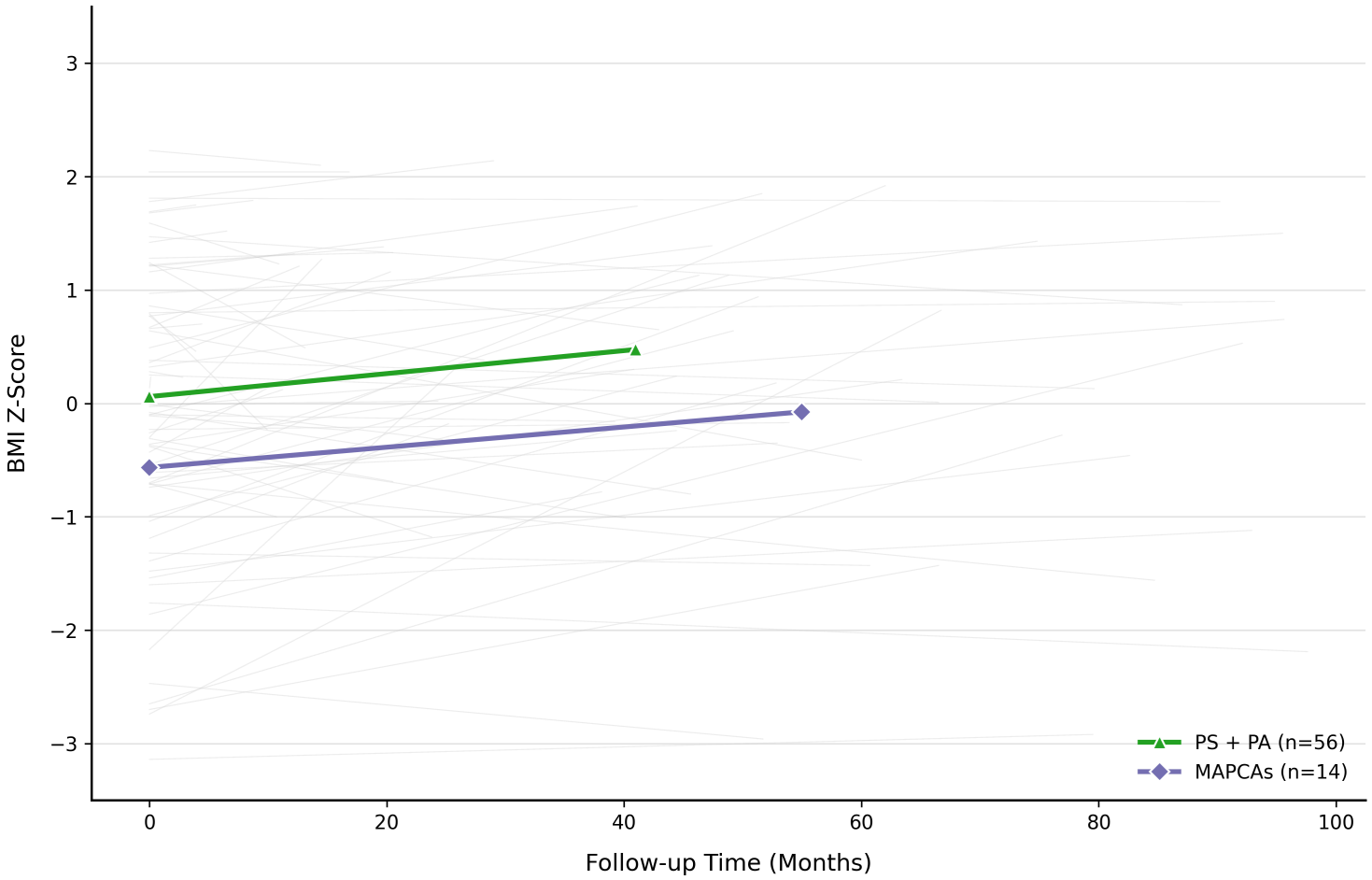


Figure 2

Evolution of BMI Z-Score during Follow-up by Anatomy

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