Research Square

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Natural history of trivial and mild aortic regurgitation in children with normal trileaflet aortic valves

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Abstract

Background

Aortic regurgitation (AR) in trileaflet valves carries important morbidity in adults but is rare in children; its natural history, particularly for mild AR, is poorly defined.

Objective

To describe the natural history of trivial and mild AR in children with normal trileaflet aortic valves and normal aortic dimensions.

Methods

Retrospective cohort study at a single tertiary center (2011–2022). Children 0–17 years of age with normal trileaflet aortic valves and AR on at least two echocardiograms were included; structural or functional heart disease, genetic and metabolic syndromes, dilation of the aortic annulus or root, and inadequate image quality were exclusion criteria. Aortic and left ventricular (LV) dimensions were measured per American Society of Echocardiography guidelines; AR severity was graded by the interpreting cardiologist, and progression was assessed by side-by-side comparison of serial studies.

Results

Of 671 reports listing AR, 42 patients (45% trivial, 55% mild) met criteria. Median age was 9.6 years; median interval between studies was 35 months. AR was unchanged in 62% (26/42), improved in 33% (14/42), and worsened in 5% (2/42); in both children in whom AR worsened the aortic and LV dimensions remained normal. No child developed more than mild-to-moderate AR.

Conclusions

Trivial and mild AR in children with normal trileaflet valves and normal aortic dimensions was stable or improved in 95% over a median 35-month follow-up. Surveillance every 2–4 years is supported by our findings, with closer follow-up for children with concomitant heart disease or in those who develop aortic dilation.

Introduction

In adults, the prevalence of aortic regurgitation (AR) in normal trileaflet valves increases with age, and AR is associated with morbidity that often leads to aortic valve replacement [1], with an estimated

population prevalence of 4.9% [2]. In the pediatric population, trivial regurgitation of the tricuspid and pulmonary valves is commonly observed [3], whereas AR in a normal trileaflet valve is rare, with an estimated prevalence of 0.3–0.4% [4, 5]. Even at birth, AR is uncommon: in a population-based cohort of 25,590 newborns, AR was detected in 1.3%, and non-trivial AR was associated with subtly larger aortic dimensions and a higher prevalence of bicuspid aortic valve, prompting the authors to call for longitudinal data to distinguish children at risk of progression from those in whom AR reflects physiologic variation [6]. When trivial or mild AR is detected on echocardiogram in health children with trileaflet valves, there is no consensus regarding the appropriate intensity of surveillance.

AR may arise from primary aortic valve abnormalities or from abnormalities of the aortic root. In developing countries, rheumatic heart disease is the most common cause of valvar AR. In developed countries, bicuspid aortic valve is the most common cause: although bicuspid valves more often produce aortic stenosis, impaired leaflet mobility and coaptation predispose the valve to regurgitation [7]. The pathology and clinical implications of bicuspid aortic valve disease are well described [8, 9]. In contrast, AR in normal trileaflet aortic valves has been poorly studied because of its rarity.

The natural history of AR in pediatric trileaflet valves has received little study. Joyce et al. retrospectively reviewed 60 children and adolescents with trivial AR and structurally normal hearts; among the 36 with follow-up studies (median 2.1 years), AR resolved in 28% and none worsened [10]. However, that cohort was limited to trivial AR and to older children (median age 14.8 years). Colan and Sleeper documented substantial temporal variation in the presence and severity of valvar regurgitation among 200 healthy children, but AR was present in only about 3% of participants and serial aortic dimensions were not examined [11]. Accordingly, the natural history of mild AR, the serial behavior of aortic dimensions in children with AR, and the clinical characteristics that distinguish children at risk of progression remain undefined. Given the morbidity associated with AR in adults and the rarity of this finding in children, we aimed to describe the natural history of trivial and mild AR in normal trileaflet aortic valves at our institution, with particular attention to change in AR severity over time and to serial aortic dimensions.

Material and methods

Study design and population

We performed a retrospective descriptive study at a single tertiary care center. The pediatric echocardiography database was searched for the terms "aortic regurgitation" and "aortic insufficiency" in the diagnosis field to identify echocardiogram reports from 2011 through 2022. Inclusion criteria were pediatric patients (0–17 years of age) with a normal trileaflet aortic valve and AR on echocardiogram who had at least one follow-up echocardiogram. Exclusion criteria were structural or functional heart disease (including bicuspid aortic valve, subaortic membrane, patent ductus arteriosus, membranous, outlet, or inlet ventricular septal defect [VSD], major conotruncal abnormalities, and coarctation of the aorta), history of rheumatic fever or suspected rheumatic heart disease, Kawasaki disease, autoimmune disease, connective tissue disease, cardiomyopathy, mucopolysaccharidoses, bacteremia or fungemia

during the study period, genetic or metabolic syndromes associated with aortic disease (including Williams and Noonan syndromes), prior pacemaker insertion, and inadequate image quality. We additionally excluded patients with dilation of the aortic annulus, root or ascending aorta (z-score > + 2.5) at the baseline study, because AR arising on a dilated aorta was felt to reflect an underlying aortopathy-mediated predisposition — analogous to aortic root disease in Marfan syndrome — rather than primary valvar AR; one patient was excluded on this basis (see Discussion). Given the rarity of the finding, a small number of patients with minor, hemodynamically insignificant lesions (e.g., secundum atrial septal defect (ASD), small muscular VSD) were intentionally retained to preserve sample size; a sensitivity analysis excluding these patients was performed (see Results).

Clinical data

The following clinical information was obtained from the electronic medical record: height, weight, body mass index (BMI), blood pressure, heart rate, cardiac examination findings, personal medical problems, family history. Elevated blood pressure was defined per current pediatric guidelines [12].

Echocardiographic measurements and grading of AR

The degree of AR was determined by the interpreting pediatric cardiologist based on careful color Doppler interrogation of the aortic valve in multiple planes; quantitative measures such as vena contracta width were not routinely recorded, and severity was therefore based on reader assessment consistent with routine clinical practice. Severity was categorized as none, trivial, trivial-to-mild, mild, or mild-to-moderate. Measurements of the aortic annulus, aortic root (sinuses of Valsalva), sinotubular junction, and ascending aorta were obtained in accordance with American Society of Echocardiography guidelines [13]. Left ventricular end-diastolic volume (LVEDV) was calculated by the 5/6 × area × length ("bullet") method. All z-scores were calculated based on body surface area using the Boston Children's Hospital z-score calculator [14]. Progression of AR was determined by side-by-side comparison of interval studies using similar views and Doppler color technique. We did not re-classify studies with a single blinded reader because the interpreting physicians had access to prior images and reports during clinical interpretation; we considered this longitudinal, side-by-side comparison more informative for determining temporal progression than isolated re-reading.

Statistical analysis

Data were compiled in the HIPAA-compliant database REDCap (Vanderbilt University). Continuous variables are reported as median (range), and categorical variables as counts (percent) with Wilson 95% confidence intervals (CIs). Given the small sample size, formal comparative statistics were not performed.

The Institutional Review Board of New York University Grossman School of Medicine approved this study (protocol no. i21-01134).

Results

The database search yielded 671 echocardiogram reports with a diagnosis of AR. After excluding 554 with structural and/or functional heart disease, 25 with genetic or metabolic syndromes associated with aortic disease, 1 with baseline aortic annular and root dilation (z-scores + 3.5 and + 3.3, respectively) consistent with an underlying aortopathy, 2 with inadequate image quality, and 47 from those with only a single echocardiogram. This left 42 with AR, normal trileaflet aortic valves, and more than one echocardiogram. A median of 2.3 echocardiograms were performed on our final cohort of 42 children.

The cohort comprised 21 males (50%) and 21 females (50%). The median age at initial diagnosis was 9.6 years (range 0–17), and the median interval between the first and last echocardiograms was 35 months (range 3–124). Baseline characteristics and echocardiographic measurements are summarized in Table 1. At baseline, 45% (19/42) of children had trivial AR and 55% (23/42) had mild AR.

Table 1
Demographic and baseline characteristics of the study cohort (N = 42)

Characteristic	Value
Male sex, n (%)	21 (50)
Female sex, n (%)	21 (50)
AR severity at baseline, n (%) — Trivial	19 (45)
AR severity at baseline, n (%) — Mild	23 (55)
Age at diagnosis (years)	9.6 (0–17)
Height percentile	45 (0–99)
Weight percentile	52 (0–99)
BMI percentile	56 (2–99)
Aortic annulus — z-score	0.1 (− 2.1 to 1.28)
Aortic root — z-score	−0.2 (− 2.2 to 2.33)
Ascending aorta — z-score	0.2 (− 1.4 to 2.5)
LVEDV — z-score	0.0 (− 3.3 to 1.7)

Continuous variables are median (range). AR aortic regurgitation; BMI body mass index; LVEDV left ventricular end-diastolic volume. Z-scores calculated from body surface area [14].

Figure 2 shows the change in AR severity for each child. Among the 19 children with trivial AR, 26% (5/19) had complete resolution and 74% (14/19) had no change; none progressed. Among children with mild AR, 26% (6/23) had complete resolution, 13% (3/23) decreased to trivial, 52% (12/23) had no

change, and 9% (2/23) progressed from mild to mild-to-moderate. Overall, AR was unchanged in 62% (26/42; 95% CI 47–75%), improved in 33% (14/42; 95% CI 21–48%), and worsened in 5% (2/42; 95% CI 1–16%); 95% (40/42; 95% CI 84–99%) were unchanged or improved. No child developed more than mild-to-moderate AR, and none developed LV dilation or interval aortic root enlargement.

Table 2 summarizes the two children whose AR worsened. Both had trivial congenital heart disease — subject 1, with a secundum ASD successfully repaired, and subject 2, with a small apical muscular VSD that closed spontaneously — and in both, the z-scores of all aortic dimensions and LV volumes remained within normal limits at both evaluations. Excluding these two patients, AR was unchanged or improved in all remaining 40 children (100%).

Table 2
Characteristics of the two children with interval worsening of aortic regurgitation

Variable	Subject 1	Subject 2
Sex	Female	Male
Age at baseline (years)	7.7	0
Age at final study (years)	12.2	1.8
Interval between studies (months)	54	22
[a]AR severity, baseline → final	Mild → mild-to-moderate	Mild → mild-to-moderate
Concomitant cardiac finding	Secundum [b]ASD, surgically repaired	Small apical muscular [c]VSD, closed spontaneously
Aortic annulus z-score, baseline → final	+1.2 → +0.6	−1.1 → +0.7
Aortic root z-score, baseline → final	+1.4 → −0.2	−1.1 → −0.8
Sinotubular junction z-score, baseline → final	+0.3 → +0.5	−0.7 → −1.2
Ascending aorta z-score, baseline → final	+0.1 → −0.6	+1.4 → −0.9
[d]LVEDV z-score, baseline → final	−0.8 → −0.6	−0.8 → +0.1

[a]AR aortic regurgitation; [b]ASD atrial septal defect; [c]VSD ventricular septal defect; [d]LVEDV left ventricular end-diastolic volume. Z-scores calculated from body surface area [14].

Discussion

In this cohort of 42 children with normal trileaflet aortic valves, normal aortic dimensions, and trivial or mild AR — more than half of whom had mild AR, a group not previously studied longitudinally — AR was stable or improved in 95% (40/42; 95% CI 84–99%) over a median follow-up of 35 months, and no patient developed LV dilation or interval aortic enlargement. The two children who progressed both had relatively trivial congenital heart disease; and neither exceeded mild-to-moderate AR. Among children with otherwise entirely normal hearts, AR was uniformly stable or improved (100%).

Prior longitudinal data have been limited to trivial AR. Joyce et al. observed no worsening among 36 children with trivial AR followed for a median of 2.1 years [10], and our trivial subgroup is consistent with that experience: trivial AR resolved in 26% (5/19) and was unchanged in 74% (14/19), with no progression. By contrast, the 22 children with mild AR in our cohort represent, to our knowledge, the first longitudinally followed group with mild AR and trileaflet valves: AR resolved in 27%, decreased in 14%, was stable in 55%, and progressed to 5% (1/22). Colan and Sleeper similarly found that new-onset trace or mild valvar regurgitation in healthy children frequently resolves and cannot be assumed to represent incident valve pathology [11].

A central rationale of our study design was the separation of primary valvar AR from AR arising on a dilated aorta. We excluded children with baseline annular, root or ascending aortic dilation because AR in that setting was more likely to reflect a possible aortopathy-mediated predisposition, rather than primary valvar disease. The course of the single patient excluded on this basis supports this distinction: over 64 months, the child's AR progressed from mild to mild-to-moderate, in parallel with further annular dilation (z-score + 3.5 to + 4.8). These observations align with newborn data from the Copenhagen Baby Heart cohort, in which non-trivial AR was associated with subtly larger aortic dimensions irrespective of valve morphology [6]. Baseline aortic dimensions likely distinguish the small subset of children whose AR reflects an underlying aortopathy and warrants dedicated evaluation and closer surveillance, from the vast majority in whom trivial and mild AR with normal aortic dimensions behaved uniformly benignly.

Based on these observations, we propose that children with trivial or mild AR, normal trileaflet aortic valves, normal aortic dimensions, and otherwise normal hearts can be surveilled with echocardiography every 2–4 years, with earlier reassessment for new symptoms, a changing murmur, systemic hypertension, or other clinical concern. Progression in our cohort occurred only in the two children with congenital heart disease, albeit relatively trivial heart disease. Nevertheless, our numbers are too small to define a separate interval for such children, but closer follow-up may be reasonable. Children with aortic dilation were excluded by design and should be managed according to their underlying aortic pathology rather than the paradigm described here.

Joyce et al. found trivial AR more prevalent in adolescents, males, taller individuals, and those with higher BMI [10], and aortic root dimensions are known to be greater in males and to increase with body surface area and age [16]. Our sample was not powered for subgroup comparisons, and we did not observe an obvious sex, BMI, or height predilection; we therefore draw no inferences about demographic or genetic risk factors.

Study limitations

Our study has several limitations. First, the sample size was small, reflecting the rarity of AR in trileaflet pediatric valves; of 671 identified reports, 554 were excluded for structural or functional heart disease — most commonly bicuspid aortic valve — 47 for lack of follow-up imaging, and 1 for baseline aortic dilation, and the small final sample precluded multivariable analysis and yielded wide confidence intervals. Second, this was a retrospective, single-center study subject to referral and ascertainment bias. Third, AR severity was graded by multiple interpreting cardiologists over time rather than by blinded re-adjudication against quantitative criteria such as vena contracta width [17]; although this reflects real-world practice and preserves longitudinal comparison, inter-reader variability cannot be excluded, and intermediate grades (trivial-to-mild, mild-to-moderate) were uncommon. Fourth, children with aortic dilation were excluded by design, so our findings do not apply to that population, in which AR may behave differently. Fifth, the median follow-up of 35 months may be too short to capture progression driven by adult-onset risk factors. Finally, two patients had minor congenital lesions; a sensitivity analysis excluding them did not materially alter our conclusions (100% unchanged or improved among the remaining 40 patients).

In conclusion, our findings support trivial and mild AR in children with normal trileaflet aortic valves and normal aortic dimensions as a benign finding that does not progress over a median follow-up of approximately 3 years. Progression was uncommon, clinically subtle, and confined to two children with concomitant congenital heart disease. We support surveillance echocardiography every 2–4 years for children with otherwise normal hearts, with closer attention to children with concomitant heart disease and separate management of those with aortic dilation.

Declarations

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Competing interests: The authors have no competing interests to declare that are relevant to the content of this article.

Ethics approval: This retrospective chart review study involving human participants was performed in accordance with the ethical standards of the institutional and national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The Institutional Review Board of the New York University Grossman School of Medicine approved this study (protocol no. i21-01134).

Consent: The requirement for individual informed consent was waived by the Institutional Review Board owing to the retrospective nature of the review of existing clinical records.

Data availability: The datasets analyzed during the current study are not publicly available owing to patient privacy but are available from the corresponding author on reasonable request.

Author Contribution

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Chriselle Ebreo. The first draft of the manuscript was written by Chriselle Ebreo, and all authors commented on previous versions of the manuscript. James Nielsen edited all data tables, figures and manuscript text. James Nielsen added and edited INTRO and DISSICUSSIONS sections. All authors read and approved the final manuscript.

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None.

Data Availability

The datasets analyzed during the current study are not publicly available owing to patient privacy but are available from the corresponding author on reasonable request.

References

1. Roberts WC, Ko JM, Moore T, Jones W (2006) Causes of pure aortic regurgitation in patients having isolated aortic valve replacement at a single US tertiary hospital (1993 to 2005). Circulation 114:422–429. https://doi.org/10.1161/CIRCULATIONAHA.106.622761
2. Singh JP, Evans JC, Levy D et al (1999) Prevalence and clinical determinants of mitral, tricuspid, and aortic regurgitation (the Framingham Heart Study). Am J Cardiol 83:897–902. https://doi.org/10.1016/S0002-9149(98)01064-9
3. Maciel BC, Simpson IA, Valdes-Cruz LM et al (1991) Color flow Doppler mapping studies of physiologic pulmonary and tricuspid regurgitation: evidence for true regurgitation as opposed to a valve closing volume. J Am Soc Echocardiogr 4:589–597. https://doi.org/10.1016/S0894-7317(14)80218-6[verify DOI — legacy format]
4. Thomson JDR (2000) Left sided valvar regurgitation in normal children and adolescents. Heart 83:185–187. https://doi.org/10.1136/heart.83.2.185
5. Clark BC, Krishnan A, McCarter R, Scheel J, Sable C, Beaton A (2016) Using a low-risk population to estimate the specificity of the World Heart Federation criteria for the diagnosis of rheumatic heart disease. J Am Soc Echocardiogr 29:253–258. https://doi.org/10.1016/j.echo.2015.11.013

6. Farooqui AF, Norsk JB, Raja AA et al (2026) Prevalence of congenital aortic valve regurgitation in a newborn cohort. Pediatr Cardiol 47:3484–3491. https://doi.org/10.1007/s00246-025-04149-0
7. Akinseye OA, Pathak A, Ibebuogu UN (2018) Aortic valve regurgitation: a comprehensive review. Curr Probl Cardiol 43:315–334. https://doi.org/10.1016/j.cpcardiol.2017.10.004
8. Michelena HI, Della Corte A, Evangelista A et al (2021) International consensus statement on nomenclature and classification of the congenital bicuspid aortic valve and its aortopathy, for clinical, surgical, interventional and research purposes. J Thorac Cardiovasc Surg 162:e383–e414. https://doi.org/10.1016/j.jtcvs.2021.06.019
9. Spaziani G, Girolami F, Arcieri L et al (2022) Bicuspid aortic valve in children and adolescents: a comprehensive review. Diagnostics (Basel) 12:1751. https://doi.org/10.3390/diagnostics12071751
10. Joyce JJ, Joyce TR, Ferns SJ (2024) Trivial aortic valve regurgitation in children and adolescents with structurally normal hearts: physiologic or pathologic? Cardiol Young 34:131–136. https://doi.org/10.1017/S1047951123001270
11. Colan SD, Sleeper LA (2020) Longitudinal variation in presence and severity of cardiac valve regurgitation in healthy children. J Am Soc Echocardiogr 33:1400–1406. https://doi.org/10.1016/j.echo.2020.05.023
12. Flynn JT, Kaelber DC, Baker-Smith CM et al (2017) Clinical practice guideline for screening and management of high blood pressure in children and adolescents. Pediatrics 140:e20171904. https://doi.org/10.1542/peds.2017-1904
13. Lopez L, Colan SD, Frommelt PC et al (2010) Recommendations for quantification methods during the performance of a pediatric echocardiogram: a report from the Pediatric Measurements Writing Group of the American Society of Echocardiography Pediatric and Congenital Heart Disease Council. J Am Soc Echocardiogr 23:465–495. https://doi.org/10.1016/j.echo.2010.03.019
14. Boston Children's Hospital Heart Center Echocardiographic Z-score calculator. https://zscore.chboston.org. Accessed [JAN-AUG 2022]
15. Rahimi K, Mohseni H, Kiran A et al (2018) Elevated blood pressure and risk of aortic valve disease: a cohort analysis of 5.4 million UK adults. Eur Heart J 39:3596–3603. https://doi.org/10.1093/eurheartj/ehy486
16. Devereux RB, de Simone G, Arnett DK et al (2012) Normal limits in relation to age, body size and gender of two-dimensional echocardiographic aortic root dimensions in persons ≥ 15 years of age. Am J Cardiol 110:1189–1194. https://doi.org/10.1016/j.amjcard.2012.05.063
17. Zoghbi WA, Adams D, Bonow RO et al (2017) Recommendations for noninvasive evaluation of native valvular regurgitation. J Am Soc Echocardiogr 30:303–371. https://doi.org/10.1016/j.echo.2017.01.007

Figures

Image not available with this version

Figure 1

Legend not included with this version

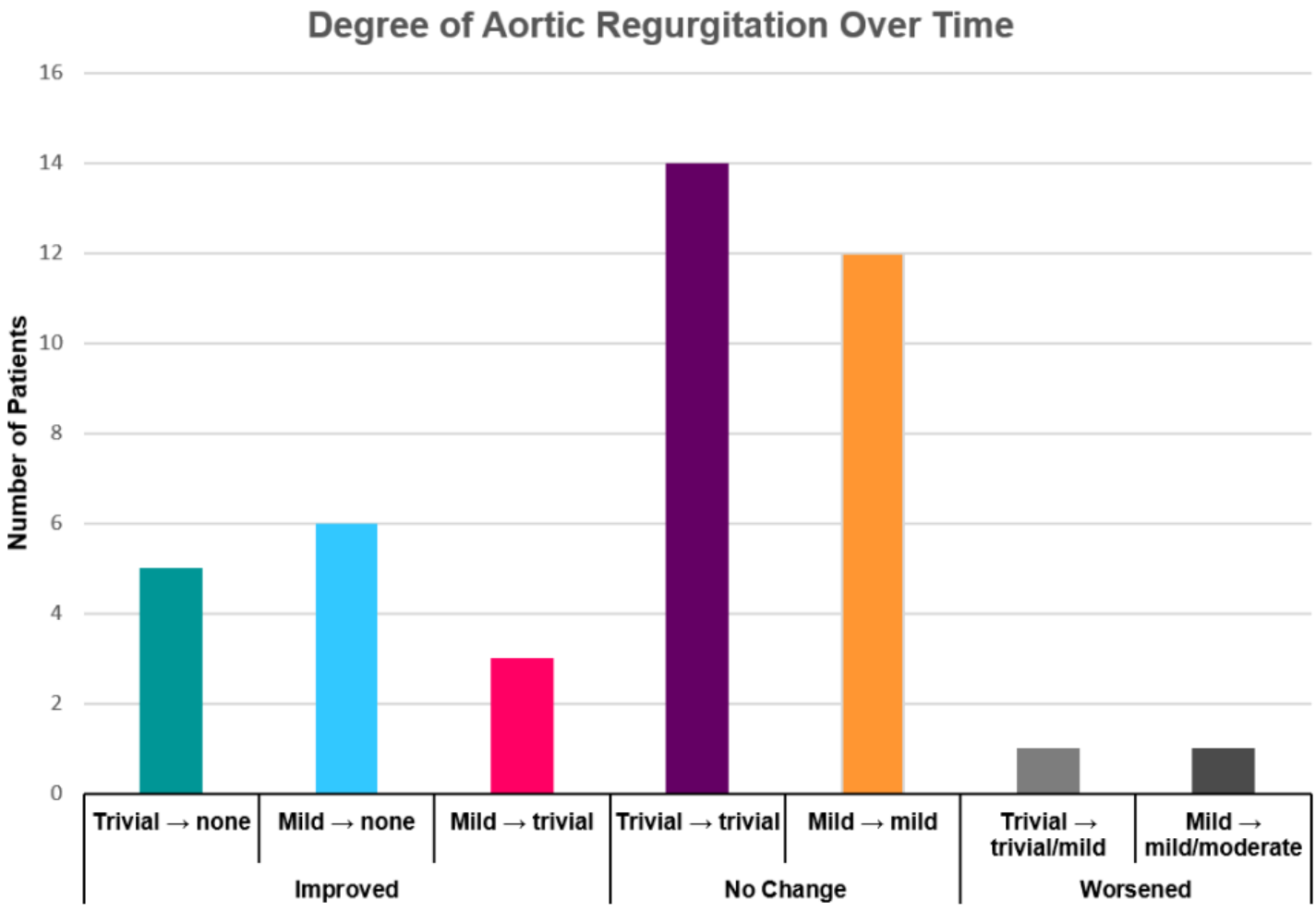


Figure 2

Degree of Aortic Regurgitation Over Time