ORIGINAL ARTICLE

# Surgical outcome of pediatric patients undergoing aortic annular enlargement.

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***Objective.*** **The aim of the study was to evaluate the clinical and surgical outcomes of pediatric patients undergoing enlargement of the aortic valve annulus.** ***Methods.*** **A retrospective study was carried out in which patients undergoing enlargement of the aortic annulus were included in our institution between January 1, 2003 and March 31, 2020. Demographic characteristics and perioperative conditions were described.** ***Results.*** **Fifty-two patients were included, with an average age of 11 ± 4.4 years; 55.8% male. The most frequent diagnosis was congenital aortic stenosis (38.8%) and enlargement of the aortic annulus was mainly performed by the Manougian procedure (40.4%). In 90.4% of the cases, mechanical aortic prostheses were used, with an average size of 20.8 ± 2.3 mm. No significant risk factors associated with mortality were found. The overall survival was 86.5%, with a better outcome in those who underwent the Manougian procedure.** ***Conclusions.*** **The results after enlargement of the aortic annulus in the pediatric population are excellent in the short and long term, regardless of the use of mechanical or biological prostheses and valvular size.**

***Key words:*** **Bicuspid aortic valve disease; Congenital heart disease; Left ventricular outflow tract obstruction; Cardiac surgical procedure**

***Objetivo.*** **Evaluar los resultados clínicos y quirúrgicos de los pacientes pediátricos sometidos a ampliación del anillo aórtico.** ***Métodos*****: Se realizó un estudio retrospectivo en el que se incluyeron pacientes sometidos a ampliación del anillo aórtico en nuestra institución, entre el 1 de enero de 2003 y el 31 de marzo de 2020. Se describieron las características demográficas y condiciones perioperatorias.** ***Resultados*****: Se incluyeron 52 pacientes, con edad promedio de 11 ± 4.4 años; siendo 55.8% hombres. El diagnóstico más frecuente fue estenosis aórtica congénita (38.8%) y se realizó principalmente la ampliación del anillo aórtico con el procedimiento de Manougian (40.4%). En 90.4% de los casos se utilizaron prótesis aórticas mecánicas, con tamaño promedio de 20.8 ± 2.3 mm. No se encontraron factores de riesgo significativos asociados a mortalidad. La sobrevida global fue 86.5%, con mejor desenlace en quienes se realizo el procedimiento de Manougian.** ***Conclusiones*****: Los resultados después de la ampliación del anillo aórtico en la población pediátrica son excelentes a corto y largo plazo, independientemente del uso de prótesis mecánicas o biológicas y el tamaño valvular.**

***Palabras clave:*** **Enfermedad valvular aórtica bicúspide; Cardiopatía congénita; Obstrucción del tracto de salida del ventrículo izquierdo; Cirugía cardiaca.**

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Aortic valve disease is one of the most common congenital heart diseases, occurring in 5% of pediatric patients with heart disease [1]. Along with this malformation may be associated with obstruction of the left ventricular outflow tract due to a dysplastic aortic valve, hypoplastic aortic annulus or subvalvular fibromuscular stenosis [2].

Initial treatment may consist of balloon valvuloplasty, open valvulotomy, subvalvular muscle resection or a combination of these procedures; however, aortic valve replacement combined with enlargement of the aortic annulus may be the definitive treatment to improve obstruction, stenosis due to lack of growth of the prosthetic ring and valvular regurgitation in cases undergoing failed aortic valve repair [2,3].

Several strategies have been developed for aortic root enlargement [4] such as Nicks technique [5], Konno-Rastan procedure [6,7] and Manouguian procedure [8], all of them with the aim of reducing pressure and volume overload in the left ventricle, relieving symptoms and improving survival in these patients [4,9,10].

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This study describes the experience in a national reference center, whose main objective was to evaluate the clinical and surgical outcomes of pediatric patients undergoing aortic annular enlargement.

## MATERIAL

The study was approved by the local institutional review board, waving the need for patient consent due to the nature of the study. A descriptive, observational, retrospective and retrolective study was conducted that included patients under 18 years of age who underwent enlargement of the aortic annulus from January 1, 2003 to March 31, 2020 at our institution. Patients with valve replacement without aortic annular enlargement, aortic valve repair, patients with rheumatic valve disease and patients with extra-institutional surgery were excluded. Variables of interest were collected from clinical and surgical records. Demographic data, primary diagnoses, functional class according to the classification of the New York Heart Association [11], previous interventions of the aortic valve, including surgical ones such as cardiac catheterization, and echocardiographic data were recorded. Surgical variables included date of admission, date of surgery, surgical indication, morbidity and any complications before discharge. In addition, the type of procedure, type and size of the valve prosthesis were recorded, as well as the concomitant procedures. The following mechanical aortic valve prostheses were used: St Jude (St Jude Medical Inc, St Paul, Minneapolis, USA), ATS (ATS Med. Inc., Minneapolis, USA), Edwards (Edwards Lifesciences, Irvine, California, USA) and CarboMedics (Sorin SpA, Milan, Italy). Bovine pericardium patch INC (National Institute of Cardiology, Mexico City, Mexico) was used. Patients were followed in the outpatient clinic at 1, 3, 6 and 12 months after surgery, and then annually, unless earlier follow-up was necessary. The follow-up was documented as the last visit in March 2020. The diagnosis was confirmed by transthoracic echocardiogram and corroborated by the surgeon during the transoperative period. The nature of aortic valve pathology was defined as stenosis, regurgitation or mixed valve disease, according to the 2020 American College of Cardiology and American Heart Association guideline for the treatment of patients with heart valve disease [12]. The aortic valve reoperation was defined as a surgical procedure for the replacement of the valve prosthesis by clinical and/or echocardiographic evidence of dysfunction. The main outcomes to be assessed were mortality and aortic annular enlargement, while secondary outcomes were postoperative complications.

### *Statistical analysis*

Descriptive statistics were performed for demographic variables. Frequencies and percentages were used to describe the categorical variables, while for the quantitative variables, average or medians were used, according to the distribution of the data. To compare proportions, the Chi square test was used. Survival was analyzed using the Kaplan-Meier method. A $p$-value < 0.05 was considered significant. The software used was SPSS version 24.0, SPSS Inc., Chicago, IL.

## RESULTS

### *Clinical-demographic characteristics*

We included 52 patients during the study period. 55.8% were male and 44.2% female, with an average age of 11 ± 4.4 years, an average weight of 37.6 ± 16.3 kg and an average height of 139.7 ± 20.3 cm (**Table 1**). Ten (19.2%) patients underwent previous surgery, mainly subaortic membrane resection (5.8%, n=3) and coarctectomy (5.8%, n=3). Nine (17.3%) patients underwent a cardiac catheterization procedure, with balloon aortic valvuloplasty predominating (13.5%, n=7). The most frequently reported primary diagnosis was congenital

**TABLE 1. Overall patients characteristics**

| Characteristics, n (%) | Total, N= 52 |
|---|---|
| Gender, n (%) | |
| Male | 29 (55.8) |
| Female | 23 (44.2) |
| Age (years), median (IQR) | 11.5 (8-14) |
| Weight (kg), median (IQR) | 46.5 (24-49.6) |
| Height (cm), median (IQR) | 142.5 (125-153) |
| BSA (m2), median (IQR) | 1.2 (0.9- 1.4) |
| NYHA Preoperative | |
| I | 13 (25) |
| II | 29 (55.8) |
| III | 7 (13.4) |
| IV | 3 (5.8) |
| Previous catheterization, n (%) | |
| None | 43 (82.7) |
| 1 | 9 (17.3) |
| Previous surgeries, n (%) | |
| None | 42 (80.8) |
| 1 | 10 (19.2) |
| Native aortic valve anatomy, n (%) | |
| Bicuspid | 49 (94.2) |
| Tricuspid | 3 (5.8) |
| Primary diagnosis, n (%) | |
| Congenital aortic stenosis | 20 (38.8) |
| Aortic stenosis + other valve disease | 2 (3.8) |
| Aortic regurgitation | 6 (11.5) |
| Aortic regurgitation + other valve disease | 2 (3.8) |
| Mixed valve disease | 1 (1.9) |
| Mixed valve disease + other valve disease | 5 (9.6) |
| Connective tissue disease | 1 (1.9) |
| LVOTO | 6 (11.5) |
| Infective endocarditis | 6 (11.5) |
| Conotruncal anomalies | 1 (1.9) |
| Prosthetic valve dysfunction | 2 (3.8) |
| Nature of aortic valve lesion, n (%) | |
| Stenosis | 26 (50) |
| Regurgitation | 13 (25) |
| Mixed valve disease | 11 (21.2) |
| Prosthesis dysfunction | 2 (3.8) |

***BSA: body surface area, IQR: interquartile range, LVOTO: left ventricular outflow tract obstruction, NYHA: New York Heart Association.***

**TABLE 2. Operative characteristics**

| Characteristics, n (%) | Total, N= 52 |
|---|---|
| Aortic root enlargement, n (%) | |
| Manougian | 21 (40.4) |
| Konno-Rastan | 19 (36.5) |
| Nicks | 12 (23.1) |
| Associated procedures, n (%) | |
| Subaortic membrane resection | 7 (13.5) |
| Morrow procedure | 3 (5.8) |
| Bentall-Bono procedure | 1 (1.9) |
| RV-PA conduit | 1 (1.9) |
| Type of valve, n (%) | |
| Mechanics | 47 (90.4) |
| Biological | 5 (9.6) |
| Valve implanted, n (%) | |
| St. Jude | 40 (76.9) |
| ATS | 6 (11.5) |
| Edwards | 4 (7.7) |
| CarboMedics | 2 (3.9) |
| Other prostheses placed, n (%) | |
| Mitral | 6 (11.5) |
| Pulmonary | 2 (3.8) |
| Mitral ring | 1 (1.9) |

*PA: pulmonary artery, RV: right ventricle.*

aortic stenosis (38.8%, n=20), followed by aortic regurgitation (11.5%, n=6), left ventricular outflow tract obstruction (11.5%, n=6) and infective endocarditis (11.5%, n=6); in addition, in 2 (3.8%) patients, dysfunction of the valve prosthesis was found (**Table 1**).

### *Surgical features*

Fifty-two enlargements of the aortic ring were performed (**Table 2**), with the Manougian procedure being more frequent

**TABLE 3. Table 3. Risk factors for mortality (univariate analysis)**

| VARIABLE | OR | CI 95% | | *p* |
|---|---|---|---|---|
| | | Lower | Upper | |
| Previous surgery | 1.85 | 0.30 | 11.29 | 0.50 |
| Previous catheterization | 0.83 | 0.73 | 0.95 | 0.19 |
| Preoperative intubation | 0.86 | 0.76 | 0.96 | 0.56 |
| Preoperative infection | 0.84 | 0.74 | 0.95 | 0.26 |
| Mechanical valve | 0.58 | 0.05 | 6.15 | 0.65 |
| Biological valve | 1.70 | 0.16 | 17.96 | 0.65 |
| Del Nido cardioplegia | 3 | 0.56 | 15.86 | 0.18 |
| Crystalloid cardioplegia | 0.33 | 0.06 | 1.76 | 0.18 |
| Major bleeding | 1.33 | 0.13 | 13.46 | 0.80 |
| Reoperation | 3.20 | 0.48 | 21.07 | 0.20 |
| Early arrhythmia | 4.12 | 0.79 | 21.33 | 0.07 |
| Postoperative infection | 2.33 | 0.20 | 26.22 | 0.48 |
| Late arrhythmia | 4.12 | 0.79 | 21.33 | 0.07 |

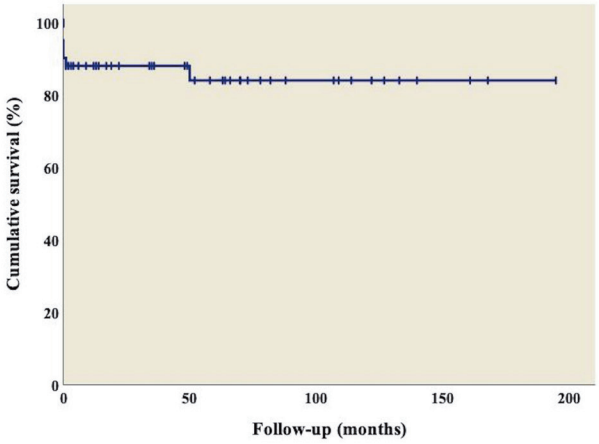


*Figure 1. Kaplan-Meier survival plot representing overall survival.*

in 21 (40.4%) patients and other procedures were associated, mainly subaortic membrane resection (13.5%, n=7). The most used types of valves were St. Jude in 40 (76.9%) patients and ATS in 6 (11.5%) patients, mostly mechanical (90.4%, n=47). The average size of the aortic valves placed was 20.8 ± 2.3 mm, while the average size of the other valve prostheses was 26.1 ± 3.1 mm, being mostly mitral prostheses (**Table 2**). Myocardial protection was performed with anterograde crystalloid cardioplegia (Custodiol®) in 76.9% (n=40) of the cases, while for the other patients Del Nido cardioplegia was used. The average cardiopulmonary bypass time was 182.4 ± 65.7 minutes with an average aortic cross clamp time of 133.6 ± 48.1; in one patient, circulatory arrest of 61 minutes was used.

### *Early results*

The average time to hospitalization was 33.9 ± 14.7 days. The average stay in the pediatric intensive care unit was 4.8 ± 4.8 days, remaining with mechanical ventilation an average time of 59.8 ± 37.1 hours. Perioperative complications included rhythm disorders (28.8%, n=15), pleural effusion (19.2%, n=10), major bleeding (11.5%, n=6), sepsis (1.9%, n=1) and mediastinitis (1.9%, n=1). Reoperation was necessary in 7 patients, 6 (11.5%) for major bleeding and 1 (1.9%) for mediastinitis. There were 5 (9.6%) early deaths, 4 (7.6%) from cardiogenic shock (1 (1.9%) patient died in the first 24 hours) and 1 (1.9%) from multiple organ failure.

### *Follow-up*

During follow-up, there were 2 (3.8%) late deaths, all from cardiogenic shock. One (1.9%) patient was reoperated for dysfunction of the valve prosthesis. The average follow-up time was 166.1 ± 10.2 months and during this period 14 (26.9%) patients were lost.

Univariate analysis was performed, contrasting the variables: previous surgery, previous cardiac catheterization, preoperative intubation, preoperative infection, type of valve, type of cardioplegia, major bleeding, reoperation, early and late arrhythmias and postoperative infection, without identi-

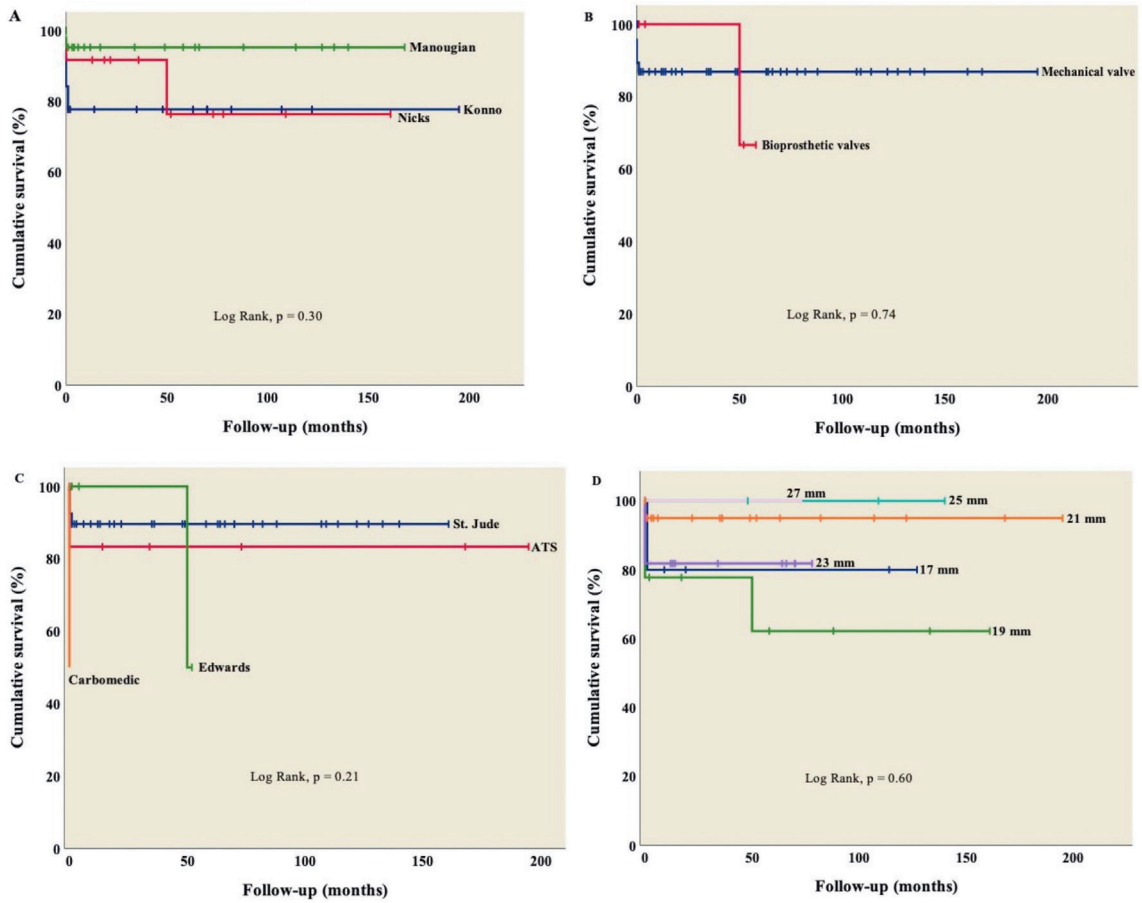


***Figure 2. Kaplan–Meier curves: (A) according to type of enlargement of the aortic ring, (B) according to type of prosthetic, (C) according to prosthetic valve brand, (D) according to valve annulus***

fying factors associated with mortality (**Table 3**). Multivariate analysis was not carried out due to no significant associations were found and the limited number of deaths

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Overall survival was 86.5% (**Fig. 1**), with a better outcome in patients undergoing the Manougian procedure (95.2%) compared to the other types of aortic ring enlargement (p = 0.30) (**Fig. 2A**). In cases where mechanical valves were placed, survival reached 87.2%, with better results than in patients with biological prostheses (p = 0.74) (**Fig. 2B**). Patients with St. Jude valves survived longer (90%), with acceptable results in patients using ATS and Edwards valves (p = 0.21) (**Fig. 2C**). The size of the valve placed showed no significant variations in survival (p = 0.60); however, patients with 25 mm valve prostheses had better results (**Fig. 2D**).

## DISCUSSION

Congenital aortic valve disease is common in children [1], frequently requiring some type of intervention and although advances in percutaneous and surgical interventions have allowed treatment with valvuloplasty in many patients, aortic valve replacement is usually required in children with irreparable valves or with significant destruction after repairs or failed interventions [13].

Pediatric patients with a small aortic ring, it is still debated whether to use a small prosthetic valve (≤21 mm in diameter) or to enlargement of the aortic ring; however, when the aortic ring is extremely small and valve replacement cannot be achieved even with a 19 mm prosthetic valve, a ring enlargement procedure should be considered [14], whereas at this age, it is associated with several challenges despite the fact that both morbidity and mortality have decreased markedly due to advances in perioperative care, surgical techniques and cardioplegia [15]; but with a hypoplastic aortic ring, the procedure can be complicated, requiring the use of an additional technique to insert a prosthesis of adequate size [4].

These techniques have different levels of complexity, allow variable degrees of enlargement and are not totally risk-free [3], with controversies in those of conventional enlargement of the aortic ring procedures as the potential risk of mitral

dysfunction associated with the Manouguian procedure or lesions of the main septal coronary arteries and conduction systems with the Konno-Rastan procedure has not been clarified [14].

Although aortic ring enlargement procedures have been in use for more than four decades, data on long-term outcomes in the pediatric population are scarce; however, our results show that patients who underwent aortic ring enlargement had a duration of postoperative ventilatory support and intensive care unit stay similar to that reported by Peterson et al. [16]. On the other hand, Sommers et al. [17], presented data on 98 patients, demonstrating that enlargement of the aortic ring had an increased operative mortality compared to aortic valve replacement (7.1% vs. 3.5%), coinciding with Dhareshwar et al. [18], who reported higher mortality in patients undergoing aortic ring enlargement (5.6%; p = 0.03); but that, through multivariate analysis, this was not an independent risk factor for mortality.

In our study, overall mortality was 13.5%, with a worse outcome in patients undergoing the Nicks procedure and a smaller valve prosthesis was placed, which despite not finding statistical significance (**Fig. 2**), the results of other series relate the smaller size of the valve prosthesis as an important risk factor for operative mortality [19].

Finally, we must emphasize that the benefits of aortic ring enlargement should be analyzed according to the total number of procedures throughout the life of each patient and thus avoid a new procedure or surgery in the short term.

***Limitations***

The study is subject to the usual limitations of a retrospective, unicentric, non-randomized study. Despite gathering a complete set of variables for study, there may be other non-measures that were not considered to determine the outcome. Nevertheless, we believe that it offers very valuable information about what happens to these patients in hospitals in our country and the region. This information is important to identify prognostic factors that can be modified, implemented and/or complemented by new therapeutic options.

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