ORIGINAL ARTICLE

Aortic valve replacement in pediatric patients with Laubry-Pezzi syndrome

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Objective. **The aim was to evaluate the clinical and surgical results of pediatric patients with Laubry - Pezzi Syndrome (LPS) undergoing cardiac surgery.** ***Methods.*** **An observational and retrospective study was carried out. Patients diagnosed with LPS undergoing cardiac surgery from January 1, 2004 and March 31, 2021, were included; preoperative characteristics and conditions were considered.** ***Results.*** **Six patients were included, with a mean age of 16.3 ± 0.8 years, being 66.7% women. Had a previous surgery 33%. In 83.3% of the cases, mechanical aortic prostheses were used, with an average size of 23 ± 0.8 mm. Perioperative complications included arrhythmias (83.3%), pleural effusion (83.3%), and major bleeding (16.7%). Overall survival was 66.7% and 16.7% reoperation.** ***Conclusions.*** **The closure of the ventricular defect and replacement of the aortic valve in pediatric patients with LPS provides a therapeutic option in patients where aortic valve repair is not possible or has been unsuccessful.**

Key words: **Aortic valve; Aortic regurgitation; Ventricular septal defect; Cardiac surgical procedure; Congenital heart disease.**

Objetivo. **Evaluar los resultados clínicos y quirúrgicos de los pacientes pediátricos con Síndrome de Laubry - Pezzi (SLP) sometidos a cirugía cardiaca.** ***Métodos.*** **Se realizó un estudio observacional y retrospectivo en el que se incluyeron pacientes con diagnóstico de SLP sometidos a cirugía cardiaca, 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 6 pacientes, con edad promedio de 16.3 ± 0.8 años; 66.7% fueron mujeres. Tuvieron un procedimiento quirúrgico previo 33.3% de los pacientes. En 83.3% de los casos se utilizaron prótesis aórticas mecánicas, con tamaño promedio de 23 ± 0.8 mm. Las complicaciones perioperatorias incluyeron trastornos del ritmo (83.3%), derrame pleural (83.3%) y sangrado mayor al habitual (16.7%). La sobrevida global fue 66.7% y la reoperación se realizó en el 16.7% de los casos.** ***Conclusiones.*** **El cierre del defecto interventricular y reemplazo de la válvula aórtica en pacientes con SLP en edad pediátrica ofrece una opción en el tratamiento de pacientes donde la plastia aórtica no es posible o ha resultado fallida.**

Palabras clave: **Válvula aórtica; Insuficiencia aórtica, Comunicación interventricular; Cirugía cardiaca; Cardiopatía congénita.**

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Laubry-Pezzi syndrome (LPS) was first described by Charles Laubry and Cesare Pezzi in 1921, characterized by a ventricular septal defect (VSD) with aortic regurgitation caused by aortic valve prolapse into a subjacent VSD due to Venturi effect [1,2].

Aortic valve regurgitation is found in over 5% of children with VSDs, so surgical VSD closure is essential and aortic valvuloplasty when needed [3]. However, aortic valve repair in patients with a ventricular septal defect is still considered a challenging surgical issue [4,5].

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This study aimed to evaluate the clinical and surgical results of pediatric patients with LPS undergoing cardiac surgery.

METHODS

An observational and retrospective single-center study included patients under 18 years diagnosed with Laubry-Pezzi syndrome who underwent cardiac surgery from January 1, 2003 to March 31, 2020. The exclusion criteria were aortic valvuloplasty without prosthetic aortic valve implantation and patients who underwent cardiac surgery in another institution. Medical records were reviewed in detail, including clinical and surgical notes. Demographic, primary diagnosis, functional class according to the

New York Heart Association [6], and previous interventions of the aortic valve and ventricular septal defect were collected and analyzed. Surgical data included: date of admission, date of surgery, type of lesion and indication for aortic valve replacement, and morbidity. In addition, the type, size, and technique of insertion of the prosthetic aortic valve and concomitant procedures were recorded. The following mechanical aortic valve prostheses were used: St. Jude (St. Jude Medical Inc, St Paul, Minneapolis, USA), ATS (ATS Med. Inc., Minneapolis, USA), Carpentier-Edwards (Edwards Lifesciences, Irvine, California, USA), and CarboMedics (Sorin SpA, Milan, Italy). For VSD closure bovine pericardial patch INC (Instituto Nacional de Cardiología, Ciudad de México, México) was used. Patients were followed at the outpatient clinic at 1, 3, 6, and 12 months after surgery and then once per year unless earlier follow-up was required. The duration of follow-up was calculated based on the most recent clinic visit in March 2020. The diagnosis was made with transthoracic echocardiograms and confirmed intraoperatively by the surgeon (**Fig.1**) The nature of the 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 management of patients with valvular heart disease [7]. Aortic valve reintervention was defined as a surgical procedure for replacing the prosthetic valve, evidenced by clinical and/or echocardiographic dysfunction findings. Early mortality was defined as death from all causes within 30 days of surgery.

Surgical technique

Surgery was performed through a median sternotomy under cardiopulmonary bypass using aortic and bicaval cannulation. Left ventricular venting was inserted in the upper right pulmonary vein. Aortic cross-clamping under moderate hypothermia and antegrade cardioplegia solution was utilized. Partial transverse aortotomy was performed, and VSD closed via transatrial approach using a bovine pericardial patch. The morphology of the aortic valve cusps was examined, and the valve was then excised in a standard fashion. The annulus is sized, and an appropriately sized prosthesis is selected for replacement of the aortic valve. The aortic valve replacement is done using an interrupted suture supra-annular technique with a Teflon pledget. All the patients were assessed with intraoperative transesophageal echocardiograms after weaning off cardiopulmonary bypass.

Statistical analysis

Descriptive statistics were used for the demographic variables. Frequencies and percentages were used to describe categorical variables, while mean ± standard deviation (±SD) or median (interquartile range [IQR]) were used for quantitative variables, according to the data distribution. The software used was SPSS version 24.0, SPSS Inc., Chicago, IL.

RESULTS

Clinical-demographic characteristics

We included six patients during the study period. Four (66.7%) were female, with a mean age of 16.3 ± 0.8 years, mean weight of 54.6 ± 8.3 kg, and a mean height of 165 ± 5.4 cm. Two (33.3%) patients underwent previous surgery, and

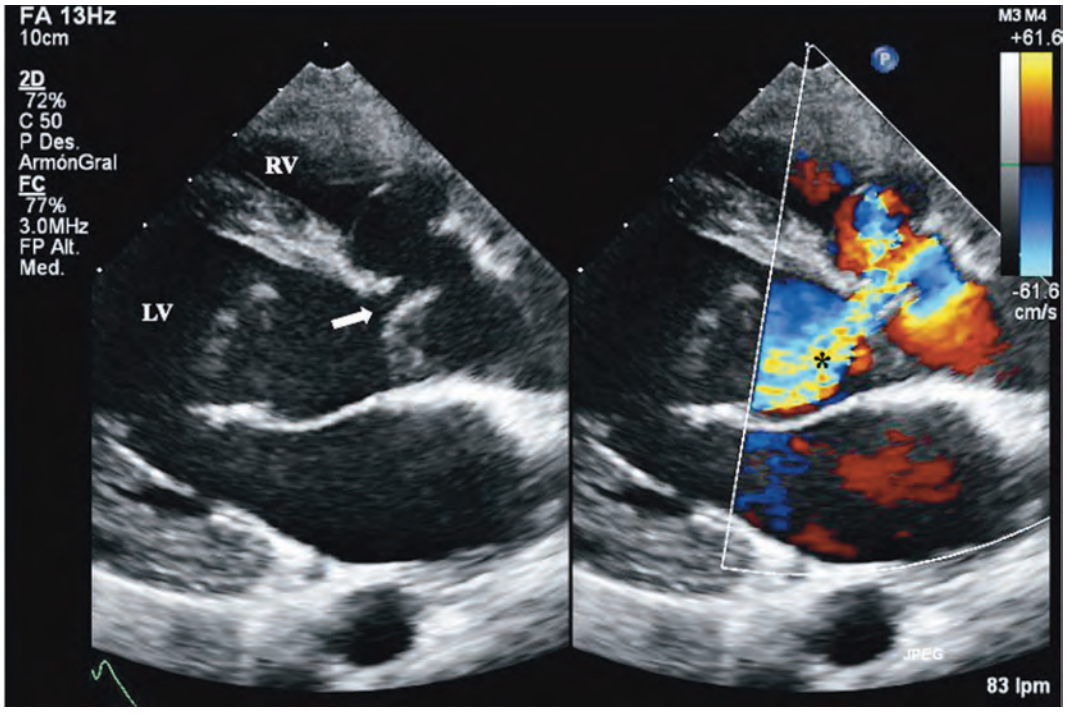

Figure 1. Transthoracic echocardiogram shows the ventricular septal defect (arrow) and aortic regurgitation (*). LV: left ventricle; RV: right ventricle

Table 1. Overall patient characteristics.

Characteristics	Total, n = 6
Gender, n (%)	
Male	2 (33.3)
Female	4 (66.7)
Age (years), median (IQR)	16.5 (15.7 - 17)
Weight (kg), median (IQR)	55.5 (45 - 62.6)
Height (cm), median (IQR)	164.5 (162.3 - 168)
BSA (m2), median (IQR)	1.6 (1.4 - 1.7)
Previous surgeries, n (%)	
Yes	2 (33.3)
No	4 (66.7)
Nature of aortic valve lesion, n (%)	
Stenosis	1 (16.7)
Regurgitation	5 (83.3)

BSA: body surface area; IQR: interquartile range.

none had a cardiac catheterization. Besides aortic regurgitation and VSD, there was one (16.7%) patient with severe tricuspid regurgitation and one (16.7%) with rupture of the right coronary sinus of Valsalva. In 83.3% (n=5) patients, preoperative echocardiogram shown severe aortic regurgitation (**Table 1**).

Surgical characteristics

All patients underwent VSD bovine pericardial patch closure, and the most used type of valves were mechanicals (83.3%, n=5), and 50% (n=3) were St. Jude (Table 3). The mean size of the aortic valves placed was 23 ± 0.8 mm; in one (16.7%) patient, an additional prosthetic valve was required without an associated procedure. Myocardial protection was performed with anterograde crystalloid cardioplegia (Custodiol®) in 83.3 % (n=5) of the cases, while for one (16.7%) patient, Del Nido cardioplegia was used. The mean cardiopulmonary bypass time was 150.3 ± 39.8 minutes, with a mean aortic cross-clamp time of 108.5 ± 23.7 minutes (**Table 2**). All the patients were assessed with intraoperative transesophageal echocardiograms after weaning off cardiopulmonary bypass showing good prosthetic valve function, and no residuals shunt.

Table 2. Surgery characteristics.

Characteristics	Total, n = 6
Type of prosthetic implanted, n (%)	
Mechanical prosthesis	5 (83.3)
Bioprosthetic valves	1 (16.7)
Cardiopulmonary bypass time(min), median (IQR)	160.5 (104 - 183.8)
Aortic cross-clamping time (min), median (IQR)	109.5 (83.3 - 133.3)
Mechanical ventilation (min), median (IQR)	21.5 (12.5 - 68.5)
PICU LOS, median (IQR)	3 (2 - 4.8)

IQR: interquartile range; LOS: length of stay; PICU: pediatric intensive care unit.

Early results

The mean stay in the pediatric intensive care unit was 3.5 ± 1.9 days, remaining with mechanical ventilation for a mean time of 39.5 ± 17.9 hours. Perioperative complications included arrhythmias (83.3%, n=5), pleural effusion (83.3%, n=5), and major bleeding (16.7%, n=1) who required reoperation. There were no early deaths.

Follow-up

The mean follow-up time was 142.2 ± 7.2 months, and during this period, there were 2 (33.3%) late deaths, one (16.7%) patient from cardiogenic shock, and one (16.7%) from septic shock. One (16.7%) patient was reoperated for dysfunction of the valve prosthesis. The remaining patients show no prosthesis dysfunction or residual shunts during follow-up. One (16.7%) patient had arrhythmia after discharge from the hospital, requiring medical therapy. The overall survival was 66.7%. One patient with a mechanical prosthesis and another with a biological prosthesis died (**Table 3**).

DISCUSSION

LPS is characterized by an aortic regurgitation caused mainly by two factors: the Venturi effect [2,4] and a lack of continuity between the ventricular septum and the aortic sinus [4,8,9]; this lack of support beneath the right coronary/noncoronary commissure, seen mostly in the setting supracristal (infundibular) VSDs [2,4,8,9]. The restrictive and

Table 3. Procedures and follow-up.

			Prosthetic implanted		NYHA Functional Class				
Patient	Age (years)	Surgery	Brand	Size (mm)	Preoperative	Postoperative	Reoperation	Death	Follow-up (months)
1	17	VSD closure + AVR	ATS	23	II	I	no	no	60
2	16	VSD closure + AVR + TVR	St. Jude	23	II	II	yes	yes	88
3	17	VSD closure + AVR	St. Jude	23	I	I	no	no	138
4	15	VSD closure + AVR	Edwards	23	II	I	no	yes	35
5	17	VSD closure + AVR	St. Jude	25	II	I	no	no	36
6	16	VSD closure + AVR + Valsalva sinus repair	CarboMedics	23	I	I	no	no	35

AVR: aortic valve replacement; NYHA: New York Heart Association; TVR: tricuspid valve replacement; VSD: ventricular septal defect.

high-velocity shunting through the VSD creates a low-pressure zone that impacts the adjacent aortic valve cusp, resulting in aortic valve prolapse and subsequent aortic regurgitation [2,8]. Surgical closure of the VSD with a patch and aortic intervention is indicated to prevent major complications [10]; even though there is not a consensus about when is the ideal time to do this intervention, surgical correction is suggested as soon as the aortic regurgitation is detected, even before aortic valve prolapse occurred to prevent future complications [10-12].

We agree with Jung et al., who reported that early closure (before four years) prevented 95.1% of patients from progressing to severe aortic regurgitation[10], in addition to being a noble procedure with no mortality reported during or after the procedure; also, Amano et al., found that in 92.7% of the patients there was no progression when performing the VSD closure; however, if there was a postoperative residual shunt, it was considered a risk factor for late aortic regurgitation ($p < 0.01$)[12].

Aortic valve prolapse is one of the complications that are sought to be avoided since the absence of the anatomical muscular support that is located just below the valve determines that in medium- or different long-term degrees of aortic regurgitation, by the deformation of the valves due to the Venturi effect already mentioned. In this matter, it is essential to have a complete evaluation of the morphology and functionality of the aortic valve to determine the appropriate surgical plan, being the current trend to attempt valve repair; but since it is not possible or if it fails, aortic replacement is necessary; there are currently a few data, especially in the pediatric population, because there is still no consensus on the use of prosthetic valves at this age. These findings coincide with the strategies reported by other centers in the management of VSDs [5,10], avoiding valve deterioration and, on the other hand, in our center, the initial management of the aortic regurgitation has been the replacement, considering that in all cases it was not possible to repair. Finally, it is important to mention that the trend is to perform aortic repair, but when the use of a valve prosthesis is necessary and with the advent of new technologies in the manufacture of these, the new generations of prostheses could be a better option by ruling out the need of anticoagulation and would allow the adjustment of the size of the valve prosthesis according to the somatic growth of the patients.

We can conclude that VSD surgical closure and aortic valve replacement in children with LPS provides an alternative treatment in patients where aortic valvuloplasty cannot be done or fails. It is important to consider reoperation in this population and the risk of a new procedure; on the other hand, a variety of prostheses with new technologies in a short or medium-term period could be implemented to reduce or avoid new procedures in these patients.

Limitations

The study is subject to the usual limitations of a retrospective, unicentric, non-randomized study. In addition, the study included a small cohort of patients with few adverse outcomes. However, we believe that this first report of our experience brings important information about the management of these patients in our country. This information is important to identify prognostic factors that can be modified, implemented, and/or complemented with new therapeutic options.

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