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Scientific letters

Percutaneous valvuloplasty in neonates with severe and critical aortic stenosis: evolution and poor prognosis prediction

Valvuloplastia percutánea en estenosis aórtica grave y crítica en neonatos: evolución y predictores de mal pronóstico

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To the Editor,

Critical, severe, and congenital aortic stenosis (AS) is challenging regarding the decision-making process, and has high mortality and morbidity rates,[1] being percutaneous treatment the one more commonly used in most centers. The objective of this study was to assess the clinical and echocardiographic progression of congenital ASs treated with percutaneous valvuloplasty (PV), and the predictive factors of worse disease progression.[2,3]

RSevere (peak velocity > 4 m/s or mean gradient > 40 mmHg), and critical ASs (ductus-dependent systemic flow) were included retrospectively based on the first postnatal echocardiography diagnosed during the fetal stage and until the first month of life and then treated with PV in a tertiary center from 2009 through 2019. The criteria established by the Declaration of Helsinki were followed, and the patients' informed consent was waived.

Left ventricular ejection fraction (LVEF), endomyocardial fibroelastosis, flows in ductus, foramen ovale, ascending aorta, aortic arch, mitral regurgitation, and hydrops were all analyzed. The size and shape of the aortic valve, the size, function, and ventricular fibroelastosis at birth, the immediate control after PV and at the follow-up, the hemodynamic gradients of PV, and complications were collected. PV was considered effective with peak residual hemodynamic gradients ≤ 35 mmHg or 50% decrease with normal LVEF. The need for Ross surgery, heart transplant, and death were regarded as unfavorable disease progression. Qualitative variables were expressed as percentages, and the quantitative ones as median and interquartile range [IQR]. The contrast of univariate hypothesis was conducted using the Mann-Whitney *U* test, and Fisher's exact test. Confounding variables distinction was conducted through multivariate analysis using the linear regression inverse verisimilitude method. The significance level of the alpha risk was .05%.

A total of 23 patients were obtained, 6 of whom (26.09%) were women. Overall, 7 patients (30.44%) were associated with aortic coarctation, and 2 (11.39%) with moderate-to-severe mitral stenosis. A total of 6 critical ASs (26.09%) were found, 2 of which (11.39%) were unicuspid, 8 (34.78%) pure bicuspid, and 12 (52.17%) tricuspid; a total of 8 raphes were reported between the non-coronary and right coronary leaflets, and 2 between the right and left coronary leaflets.

Regarding the moment of diagnois, 6 ASs (26.09%) were diagnosed during the prenatal stage and 17 (73.91%) during the neonatal period. A total of 3 ASs (13.05) from the prenatal group had severe dysfunction with grade 4 friboelastosis and flow reversal in the ascending and transverse aortic arch. One of them had hydrops and the other one was treated with an elective fetal valvuloplasty that was performed on week 26.

A total of 6 patients (26.09%) presented with cardiogenic shock at birth. Only in critical ASs systo-diastolic dysfunction was reported with median LVEF of 42.50% [IQR, 40.00-57.25], which was lower compared to the severe ones (P = .011). A total of 10 patients (47.83%) had mitral regurgitation, 2 of them (8.70%) severe.

The PV was performed after a median 42 days of life [IQR, 12.25-56], 7 of which (30.43%) wre performed within the first week of life. The balloon used was the TYSHAK mini or II (NuMED Inc., United States). The balloon/valvular diameter ratio was 1.00 [IQR, 0.91-1.03], which was significantly higher in the unicuspid valve group. The vascular access was the femoral artery. The overall effectiveness rate was 78.26%, 83.33% (n = 5/6) in critical ASs, and 76.5% (n = 13/17) in the severe ones.

After a median follow-up of 4 years [IQR, 3,5-6,25] the survival rate was 92.31%. A total of 15 patients (65.22%) remained reintervention-free. Reinterventions (figure 1) occurred within the first year of life: 4 patients needed a new PV, 3 patients required Ross surgery, and 2 surgical valvulotomy (1 died due to postoperative cardiogenic shock), and 1 heart transplant due to heart failure and pulmonary hypertension (the patients died due to rejection, and pulmonary hypertension).

During the patient's disease progression, a 69.57% rate of aortic regurgitation was reported, 33% moderate and 8% severe (figure 2). No statistically significant differences were seen regarding disease progression into moderate-to-severe aortic regurgitation based on the balloon-to-annulus ratio (P = .435) or on the rate of procedural success (P = .446).

Statistically significant differences were reported in the univariate contrast for the risk factors of unfavorable progression in critical ASs (P = .021), greater systolic transvalvular gradient at birth (P = .027),

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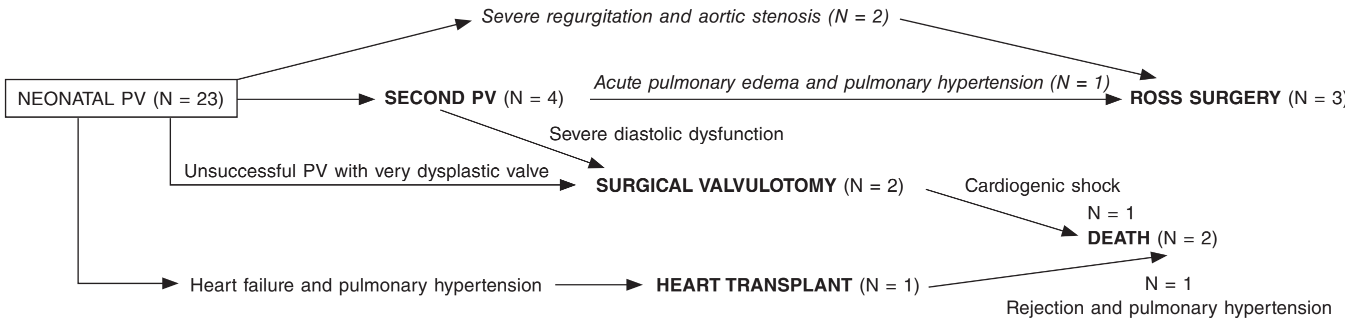

Figure 1. Need for new procedures in individuals after percutaneous valvuloplasty (PV).

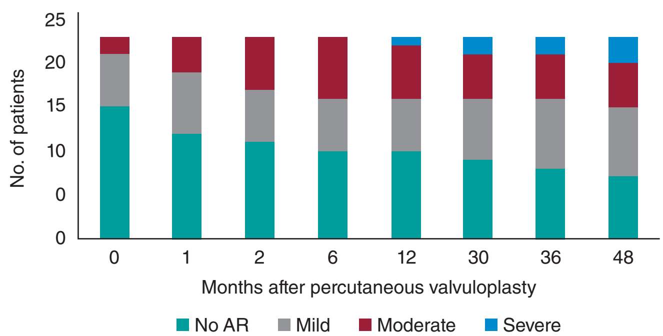

Figure 2. Evolution of aortic regurgitation (AR).

shorter diameter of aortic annulus (P = .017), ductus-dependent systemic flow (P = .003), mechanical ventilation (P = .009), lower weight at birth (P = .001), younger age during the first PV (P = .013), lower LVEF (P = .021), and smaller diameter of the aortic annulus after PV (P = .009). No differences were seen based on valvular morphology (P = 1).

In the multivariate analysis (table 1) of previously significant and clinically relevant variables statistical significance was obtained for a smaller diameter of the aortic annulus (hazard ratio, 2.82; P = .016).

This study—that shows the complexity and heterogeneity of AS—found that after a neonatal aortic PV has occurred some type of

Table 1. Predictors of unfavorable disease progression

	Fisher's exact test or Mann Whitney *U* test	Multivariate test: inverse verisimilitude method of a bivariate analysis			Fisher's exact test or Mann Whitney *U* test	Multivariate test: inverse verisimilitude method of a bivariate analysis	
Variables	***P***	**HR (95% confidence interval)**	***P***	**Variables**	***P***	**HR (95% confidence interval)**	***P***
Critical AS	.021*			Mitral stenosis at birth	.481		
Prenatal diagnosis	.275			Mitral regurgitation at birth	.069		
Unicuspid valve	.462			Z-score of mitral valve annulus at birth	.268		
Affected by aortic coarctation	.369			Z-score of aortic valve annulus at birth	.017*	1.234 (0.436-3.4494)	.692
Affected by Shone syndrome	.146			Z-score of LV end-diastolic diameter	1.000		
LVEF at birth	.101			LV end-diastolic gradient before the PV	.841		
LV S-wave at birth	.222			Inotropic score at birth	.500		
Diastolic dysfunction at birth	.131			Infusion of prostaglandins	.003*		
Mean gradient of AS at birth	.143			Mechanical ventilation	.009*		
Systolic gradient of AS at birth	.027*	0.983 (0.906-1.066)	.676	Lower weight at birth	.001*		
Aortic regurgitation at birth	.481			Age at cardiac catheterization	.013*	0.896 (0.569-1.344)	.596
Aortic annulus diameter at birth	.039*			Aortic systolic hemodynamic pressure before the PV	.687		

(Continues)

Table 1. Predictors of unfavorable disease progression *(continued)*

	Fisher's exact test or Mann Whitney *U* test	Multivariate test: inverse verisimilitude method of a bivariate analysis	
Variables	***P***	**HR (95% confidence interval)**	***P***
Mean aortic hemodynamic pressure before the PV	.622		
Aortic diastolic hemodynamic pressure before the PV	.107		
Mean LV hemodynamic pressure before the PV	.154		
LV systolic hemodynamic pressure before the PV	.424		
Aortic systolic hemodynamic pressure after the PV	.398		
LVEF after the PV	.021*	1.007 (0.896-1.131)	.910
LV S-wave on echocardiography after the PV	.106		
Echocardiographic aortic regurgitation after the PV	.609		
Z-score of the aortic annulus on the echocardiography after the PV	.009*	0.355 (0.153-0.826)	.016*
Monitorization of mitral regurgitation after the PV	.635		
Monitorization of mitral stenosis after the PV	.100		

95%CI, 95% confidence interval; AS, aortic stenosis; HR, hazard ratio; LV, left ventricle; LVEF, left ventricular ejection fraction; PV, percutaneous aortic valvuloplasty:
* Statistically significant variables.

new intervention was required in a third of the patients with similar results to those reported by other series.[4] Due to the complex decision-making process it is important to know which characteristics are associated with grimmer prognosis.[5,6] It has been reported that worse prognosis is associated with lower weight, ductus-dependent systemic flow, and mechanical ventilation, critical AS, and a greater systolic aortic transvalvular gradient at birth, smaller annular sizes, and worse LVEF after the PV. Also, when the latter is performed earlier. These factors are often concomitant. However, only the diameter of the annulus has statistical significance in a multivariate analysis. A larger sample would have probably resulted in more significant variables. Even so, it seems obvious that the group of patients with poor clinical progression often share the same characteristics, indicative that they make up a totally different spectrum of the disease with different therapeutic needs while requiring multidisciplinary and individualized assessments.

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AUTHORS' CONTRIBUTIONS

Freixa-Benavente had the study idea, curated data, analyzed, drafted, and submitted the manuscript. P. Betrián-Blasco supervised the study, recruited patients and data, and analyzed them; also, he reviewed the manuscript final version and gave his approval. F. Rosés-Noguer, and G. Giralt-García reviewed the manuscript, and made significant remarks. Q. Ferrer-Menduiña supervised the study, recruited the patients, data, and drafted the manuscript; also, she reviewed the manuscript final version and gave her approval.

CONFLICTS OF INTEREST

The authors declared no conflicts of interest whatsoever.

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