Aortic stenosis of the neonate: A single-center experience

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ABSTRACT

Objectives: Because data for neonates are limited, optimal management of critical aortic stenosis remains controversial (balloon valvotomy [BV] or open valvoplasty [OV]). In a center with balanced experience in both methods, we hypothesized that OV can provide a better individualized approach than blunt BV and better serve long-term outcomes.

Methods: A retrospective review of data and follow-up (survival, freedom from operation/replacement) of all neonates, suitable for biventricular repair, undergoing aortic valve procedure (1989-2015), was performed.

Results: One hundred three patients were concomitantly treated (BV [n = 51], OV [n = 52]). Median age was 8 days, median aortic annulus Z-score was -1.3 for BV (range, -3.9 to 2.0) and OV (-3.9 to 3.2) groups. Operative mortality after BV or OV was 8% (n = 4) and 4% (n = 2), respectively. With a 13-year median follow-up, 10-year freedom from operation was 36% and 66% after BV or OV, respectively. Valve replacement was ultimately required in 32 patients (n = 20 [39%] in the BV group; n = 12 [23%] in the OV group) within a 5.9-year median time. After OV, tricuspid arrangement of the repaired aortic valve provided a 10-year freedom from operation and replacement of 87% and 95%, respectively. In multivariate analysis, associated left heart malformations, BV, nontricuspid geometry, and inadequate post procedural result were predictive of operation and replacement.

Conclusions: In neonates with critical aortic stenosis, both methods (BV and OV) offer excellent survival benefit. OV significantly minimizes the need for operation, whereas BV did not postpone age of replacement. Clearly superior results are achieved with OV when a post repair tricuspid arrangement is obtained. (J Thorac Cardiovasc Surg 2019;157:318-26)

Freedom from operation after BV/OV; 103 neonates, 1989 to 2015.

Central Message

In a center with equal experience in interventional and surgical care of critical aortic stenosis, open valvoplasty reduces the need for operation with best results for postrepair tricuspid geometry.

Perspective

Optimal management of critical aortic stenosis (ie, interventional vs surgical) remains controversial because the surgical arm of the comparison is dramatically under-represented. In a unique environment of balanced experience, over 26 years, open valvoplasty reduced the need for operation, with optimal long-term preservation of the native valve if a postrepair tricuspid geometry can be restored.

See Editorial Commentary page 327.

Treatment modalities of isolated aortic stenosis (AS) in the neonate include balloon valvotomy (BV) and open valvoplasty (OV), both yielding equivalent results in terms of survival.¹ Both methods are palliative and reintervention

remains frequent. Choice of initial approach is a matter of debate since the first BV in 1983. In the 80s, surgical valvoplasties in the neonate were limited to blunt transventricular dilatation (up to 2000 in some centers²). BV, a similar technique but performed percutaneously, has rationally become, in this era, the intervention of choice in most institutions. Surgical refinements, in the following years (open commissurotomy; improvements of neonatal

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Abbreviations and Acronyms

AS	= aortic stenosis
BV	= balloon valvotomy
CI	= confidence interval
LCOS	= low cardiac output
LV	= left ventricle
OV	= open valvoplasty

surgery), did not reverse this choice. However, since 2000, the advent of new surgical techniques for aortic valve repair in children^{3,4} has questioned the preeminence of BV use. Indeed, whereas most improvements for BV have been focused on—efficiently—reducing periprocedural complications (smaller catheter, guidewires), the process of BV (even with reduced balloon-to-annulus ratio) did not dramatically change over the past decade. Oppositely, whereas approach-related complications (better perioperative management of neonatal cardiopulmonary bypass) have been reduced with OV, the technique of valvoplasty (adding leaflet remodeling to the commissurotomy) has also recently developed.⁵

In our center, both approaches were equally applied. We hypothesized that surgical repair can provide a better individualized approach to valve disturbance than blunt BV, and therefore better serve long-term preservation of the native valve. We retrospectively analyzed our experience with BV or OV in neonates with AS, specifically investigating long-term outcome.

METHODS**Patient Population**

Institutional review board approval was obtained and individual consent was waived. All neonates who underwent aortic valve procedures (1989–2015) were identified (51 BV, 52 OV).

Exclusion criteria were: initial procedure performed elsewhere (13 BV, 15 OV), borderline or hypoplastic left ventricle (LV),⁶ severe subaortic stenosis, requiring early relief with Konno procedure. Preoperative characteristics are listed in Table 1.

Treatment Protocol

Through the largest part of the experience, patients were erratically assigned to BV or OV (Figure 1). Through the first decade, similar rates of LV dysfunction were present in both groups. Since 2000, those patients were preferentially assigned to BV. Since 2013 the protocol was enhanced into a more integrative approach of both techniques.⁷ For patients with LV dysfunction, primary “gentle” BV (<70% of annulus diameter; not as intention-to-treat AS, but only as intention-to-treat LV dysfunction) was favored and OV subsequently performed (within the first month of life) after LV recovery (Video 1). This approach was used in 4 patients, classified as surgical patients.

Our decision-making protocol for uni- or biventricular pathway has been detailed elsewhere.⁶ Fixed morphologic variables (<7 mm or < −2 Z-score mitral annulus, severe LV inflow obstruction, <0.8 left to right ventricular length ratio, a cardiac apex not formed by the LV, massive endocardial fibroelastosis) or functional variables (predominantly reversed flow in ascending aorta) are criteria for univentricular palliation. Our surgical techniques have been published elsewhere.^{4,5} A 2-step strategy was applied:

leaflet remodeling by extensive debridement (shaving, removal of myxomatous nodules) to increase leaflet mobility, then suspending apparatus rehabilitation (commissurotomy, reduction of doming by detaching commissures from aortic wall; Videos 2 and 3). Repair was always performed without additional material. Routine transesophageal echocardiography was performed. Intraoperative revision was required for >30 mm Hg peak gradient and/or greater than mild regurgitation. Concomitant procedures were performed in 13 patients (Table 2). In surgical patients, a post repair tricuspid arrangement was reached in 20 patients.

BV was performed using retrograde femoral access, with the patient under general anesthesia. The median balloon-size-to-aortic-annulus ratio was 1.0 (0.59–1.43).

Follow-up

Follow-up data (up to June 2017) were complete in all patients. Mean follow-up was 11.4 ± 7.1 years (13.3 ± 6.4 [BV], 9.6 ± 7.3 [OV]; $P < .01$). Indications for aortic valve reintervention included > 60 mm Hg echocardiographic peak gradient, greater than mild regurgitation, or >3 LV end-diastolic diameter Z-score. Death occurring in-hospital or within 30 post procedural days was defined as early.

Statistical Analysis

End points were valve operation, replacement, and mortality. Statistical analysis was performed using R 3.1.1 (R-Foundation for Statistical Computing, www.r-project.org). Comparison was achieved with Fisher exact test and Student *t* test. Freedom from event was analyzed using Kaplan–Meier estimates (95% confidence interval [CI]). Univariate analysis was achieved using log rank test and Cox model. Variables with $P < .10$ were included in the multivariate model.

RESULTS**Early Postoperative Course**

Periprocedural characteristics are listed in Table 2. Severe complications occurred in 9 BV patients (6 femoral thrombosis, 2 myocardial perforations, 1 ductus rupture); only 2 of them had preprocedural ventricle dysfunction, 1 died of cerebral bleeding. Complications occurred in 3 OV patients (1 postoperative coarctation, 1 capillary leak syndrome, 1 superior vena cava thrombosis). Inadequate results (>50 mm Hg echocardiographic peak gradient and/or greater than mild regurgitation) was found in 10 BV (all stenosis) and 3 OV (1 stenosis, 2 moderate regurgitations) patients.

Mortality

There were 6 early deaths, all but 1 before 2000. Neonatal mechanical support was not used because of era (4 patients before 1995), contraindication (cerebral bleeding), or postdischarge death. Four patients died after BV (8%). Two patients with isolated AS (<2 kg) with depressed ventricular function, died of low cardiac output (LCOS). One patient with AS associated with severe mitral stenosis died in another center, during a Ross-Konno-mitral procedure 3 weeks after BV. One patient with isolated AS discharged with 20 mm Hg gradient, mild regurgitation, and incomplete right bundle block, died 3 weeks post intervention of rhythm disturbance at home. Two patients died after OV (4%), both isolated AS with depressed ventricular function (intractable postoperative LCOS).

TABLE 1. Preprocedural characteristics of patients

Characteristic	BV patients (n = 51)	OV patients (n = 52)	P value
Median age (range), d	3.0 (0-30)	11.5 (1-30)	.00
Mean weight $\pm$ SD, kg	3.3 $\pm$ 0.8	3.4 $\pm$ 0.7	.44
Congestive heart failure	26 (51)	25 (48)	.84
Low cardiac output syndrome	10 (20)	2 (4)	.01
Mechanical ventilation	13 (25)	4 (8)	.02
Less than 25% left ventricle shortening fraction	23 (45)	7 (13)	.00
Z-score left ventricle end-diastolic diameter >2	8 (16)	7 (13)	.99
Endocardial fibro elastosis	16 (31)	10 (19)	.16
Mean preoperative aortic valve maximal gradient $\pm$ SD, mm Hg	61 $\pm$ 23	74 $\pm$ 29	.02
Mean aortic annulus Z-score (range)	−1.2 (−3.9 to 2.0)	−1.1 (−3.9 to 3.2)	.99
Z-score < -2	15 (29)	15 (29)	.99
Left heart-associated malformations	9 (18)	12 (23)	.62
Arch obstruction	4 (8)	12 (23)	.05
Mitral valve Z-score < -2	5 (10)	1 (2)	
Ventricular septal defect	1 (2)	6 (12)	.11
Cor triatriatum	1 (2)	0 (0)	.99

Data are presented as n (%) except where otherwise noted. Bold indicates significant values. BV, Balloon valvotomy; OV, open valvoplasty; SD, standard deviation.

There were 4 late deaths, 1 in the OV group. Two had AS with associated lesions and died at 1 year of age: 1 had BV followed by 2 OVs with mitral repair for severe stenosis, and died from pulmonary hypertension; 1 had OV and arch repair followed 5 days later by the Ross-Konno procedure and died 1 year later from pulmonary hypertension. Two had isolated AS treated with BV and died at 10 years of age: 1 had BV followed by early OV, and died of a neurologic disorder; 1 had BV followed by late BV and OV and died at Ross-Konno surgery.

The 10-year survival was 88% (95% CI, 78%-97%) after BV and 94% (95% CI, 88%-99%) after OV (Figure 2, A). In multivariate analysis, none of the parameters identified

in univariate analysis (LCOS, low shortening fraction, annulus Z-score < -2) did reach significance.

Operations

Twelve BV (24%) patients had 18 re-BV (not classified as “operation”). In 51 patients (35 in the BV group, 16 in the OV group), an (at least 1) operation was performed after a median of 2.4 years: 37 repair and 14 replacement.

Indications for operation were: stenosis (n = 28; 55%), regurgitation (n = 15; 29%), combined (n = 8; 16%), with a similar pattern in the BV and OV groups (Figure 3). Operations for stenosis (n = 28, 24 repaired) were performed at a median delay of 0.6 years. All had

FIGURE 1. Distribution of procedures over the study period. BV, Balloon valvotomy; neonate without left ventricle (LV) dysfunction; BV+LVdysf, BV; neonate with LV dysfunction; OV, open valvoplasty; neonate without LV dysfunction; OV+LVdysf, OV; neonate with LV dysfunction.

VIDEO 1. A typical situation of failing LV neonatal AS, primarily managed with “gentle” BV (note the further intraoperative leaflet tear shown) and 10 days later, after LV recovery, surgically approached (comment in video). At 4 years of follow-up, patient is free from reoperation, peak gradient is 20 mm Hg and without regurgitation. Video available at: [https://www.jtcvs.org/article/S0022-5223\(18\)32483-8/fulltext](https://www.jtcvs.org/article/S0022-5223(18)32483-8/fulltext).

recurrent fusion of commissures and thickened leaflets. Operations for regurgitation ($n = 14$, 7 repaired) were performed at a median delay of 2.4 years. The mechanisms were tear, leaflet retraction, or elongated/dehiscent commissure. Operations for combined regurgitation and stenosis ($n = 8$, 6 repaired) were performed at median delay of 8.9 years. The mechanisms were tear, retraction, or elongated/dehiscent commissure. Repair techniques are listed in [Table E1](#).

Freedom from operation at 10 years was 36% (95% CI, 22%-51%) after BV and 66% (95% CI, 50%-82%) after OV ([Figure 2, B](#)). Multivariate analysis identified as predictors for operation ([Table 3](#)): left heart malformations, BV, nontricuspid post repair valve arrangement, inadequate postprocedural result, and higher postprocedural gradient.

Replacement

There was no intraoperative conversion to Ross through the whole experience. In 31 patients (19 in the BV group, 12 in the OV group), valve replacement was eventually performed after a median of 5.9 years: 21 Ross, 8 mechanical prosthesis, 2 tissue-engineering valves. Indication pattern was similar to indication for operation (16 stenosis, 9 regurgitations, 5 combined, 1 unknown).

Replacement was performed in the first year of life ($n = 8$; 26%), delayed to more than 9 years ($n = 14$; 45%), or performed between 1 and 7 years of age ($n = 9$; 29%). Operative mortality was 6% (2 Ross procedures at 1 month and 10 years of age).

Freedom from replacement at 10 years was 60% (BV; 95% CI, 45%-75%), 79% (OV; 95% CI, 65%-92%; [Figure 4, A](#)). In OV patients, freedom from replacement was 95% (95% CI, 86%-99%) when a tricuspid morphology of the aortic valve was restored, and 67%

VIDEO 2. A typical situation of unicuspid valve (left and right coronary common cusp with underdeveloped anterior commissure). A thick raphe is restricting leaflet motion. The posterior commissure (non-to-left coronary, located above) is sufficiently highly developed and slightly fused. The anterior commissure (non-to-right coronary) is underdeveloped. Myxoid tissue obstructs outflow. Both commissures are incised, raphe (not illustrated in video) is slimmed down, extensive shaving is performed (video speed, 2×). Leaflets slightly prolapsing at the anterior commissure level are resuspended. Ending geometry is bicuspid but a normal mobility of leaflets and effective orifice area (7 mm; Z-score, -0.9) are restored. Even if bicuspid geometry is at higher risk of reoperation, the diminutive size of the root restrains the use of any supplemental material to restore a trileaflet arrangement. Such repair without material allows for growth of the child to an age when repair—if required—with material can be performed. Surgical strategy is early repair without material, with better outcome if tricuspid geometry could be achieved. At 7 years of follow-up, patient is free from reoperation, peak gradient is 40 mm Hg and regurgitation less than mild. Video available at: [https://www.jtcvs.org/article/S0022-5223\(18\)32483-8/fulltext](https://www.jtcvs.org/article/S0022-5223(18)32483-8/fulltext).

(95% CI, 46%-89%) when not ([Figure 4, B](#)). Multivariate analysis identified as predictors for replacement ([Table 3](#)): left heart malformations, nontricuspid post repair valve arrangement ($P = .06$), inadequate postprocedural result, and higher postprocedural gradient.

Late Function

At final follow-up, 64 patients were surviving with their native valve. Undisturbed valve function was present in 54 patients (peak gradient <40 mm Hg, regurgitation mild or less), whereas 8 had mild stenosis (50 mm Hg peak gradient), 1 had moderate stenosis (60 mm Hg peak gradient), 1 had moderate regurgitation and stenosis. LV function and dimensions were preserved in 97% ($n = 90$) of survivors. LV function was mildly altered in 2 (systolic) and 1 (diastolic).

Discussion

In this retrospective, single-center study, we report the long-term outcomes of neonates with AS initially managed

VIDEO 3. Another unicuspid valve: only the posterior commissure (non-to-left coronary, located above) is sufficiently highly developed; the 2 other commissures are fused and underdeveloped. The right coronary leaflet is small and implanted higher than the usual annulus location. Both fused commissures are spitted (video speed, 2×) and extensive leaflet remodeling with shaving of the 3 leaflets is performed. Ending geometry is tricuspid (offering the best long-term results) with a restored normal leaflet mobility and effective orifice area (7 mm; Z-score, −0.9). At 1 year of follow-up, peak gradient is 20 mm Hg without regurgitation. Video available at: [https://www.jtcvs.org/article/S0022-5223\(18\)32483-8/fulltext](https://www.jtcvs.org/article/S0022-5223(18)32483-8/fulltext).

with BV or OV, over more than 2 decades. This investigation indicates that BV did not efficiently release aortic valve obstruction, compared with OV, in the early and long-term course. Main failure mode, after any procedure, is early stenosis, highlighting the importance of tissue reduction, only provided by OV. Restoring a tricuspid anatomy, only provided by OV, clearly yields superior long-term results for preservation of the native aortic valve.

Reported Cohort

AS in the neonate is rare and surgical valvoplasty has been adopted only in a few centers.^{3,5,8-10} The number of surgically managed neonates in the literature is dramatically unbalanced compared with BV patients: 27 OV versus 105 BV (among 26 institutions) in the Congenital Heart Surgeons' Society (CHSS) multicentric study,¹¹ 121 OV versus 712 BV in a recent meta-analysis.¹ Given the paucity of surgical results, only obsolete data are reported: mortality in 2012 for OV, from the CHSS report¹¹ was 30%. This leads to inadequate conclusions compared with potential performance of up-to-date surgical management. The present report represents a large, up-to-date, adjunct to the published surgical group. Furthermore, most monocentric studies report on 1 modality, or both, but with unequal experience. In this report, both techniques were simultaneously developed leading to balanced experience.

Early Mortality

Early mortality after OV is reported to be between 6% and 19%.^{3,6-9} Our early mortality was 6% with only 1 death after 2000. This is likely the result of setting up a

TABLE 2. Procedural and postprocedural early characteristics

Characteristic	BV patients (n = 51)	OV patients (n = 52)	P value
Procedural			
Mean balloon to annulus ratio (range)	1.0 (0.59-1.43)	NA	
Mean aortic cross-clamp time, min	NA	33.8 ± 15*	
Associated procedure	4 (8)	12 (24)	≤.05
Arch repair	4 (8)	12 (24)	
Ventricular septal defect	0 (0)	5 (10)	
Subaortic stenosis	0 (0)	2 (4)	
Early postprocedural			
Mortality	4 (8)	2 (4)	.68
Median intensive care length of stay, d	2.5 (0-70)	6 (2-65)	.61
Prolonged intensive care stay†	12 (24)	12 (24)	.99
Complication‡	9 (18)	3 (6)	.12
Valve function			
Mild regurgitation	10 (20)	6 (12)	.41
Inadequate result§	10 (20)	3 (6)	.07
Aortic valve maximal gradient, mm Hg	35 ± 12	26 ± 11	.00

Data are presented as n (%) except where otherwise noted. Bold indicates significant values. BV, Balloon valvotomy; OV, open valvoplasty; NA, not available. *Data of patients without intracardiac-associated procedure (n = 43). †Intensive care stay longer than the third quartile for each group. ‡BV group: femoral thrombosis, myocardial and ductus perforations; OV group: postoperative coarctation, capillary leak syndrome, and superior vena cava thrombosis. §Greater than 50 mm Hg echographic peak gradient and/or greater than mild regurgitation.

contemporary univentricular program, leading to redirection of high-risk patients toward the univentricular pathway.⁶ Likewise, Agnoletti and colleagues reported higher mortality (19%), but claimed the absence of a univentricular program for hypoplastic left-heart patients.⁸ Setting up a univentricular palliation program will benefit biventricular patients, as mentioned by Hickey and colleagues.¹² In case of LV dysfunction, we developed a hybrid approach, with an initial “gentle” BV and subsequent OV after LV recovery.⁷ For a dilated LV without recovery, balloon septostomy to further decompress the LV and prostaglandins for ductus patency are used. In the absence of LV recovery, we rather reorient patients in the univentricular pathway (bilateral pulmonary banding, ductus stent, or bailout shunt¹³ or/and Norwood stage 1) to provide patients more time to grow, mature, and “declare themselves” as either 1- or 2-ventricle candidates. However, for nonresponders (no LV recovery), univentricular and biventricular pathways have shown, in our experience, poor results. This specific area is, in our center, under investigation.

The common concept that surgery requires sternotomy and cardiopulmonary bypass thus, carrying a greater risk¹⁴ was not confirmed. With carefully selected patients (LV dysfunction patients assigned to BV), OV did not increase mortality compared with BV. To extend this strategy,

FIGURE 2. Kaplan–Meier survival (A) and freedom from operation (B). Shaded area indicates 95% confidence interval. OV, Open valvuloplasty; BV, balloon valvulotomy.

we developed the hybrid approach: “gentle” BV as an intermittent step to stabilize the patient before OV.⁷

Early Morbidity

The common acceptance that BV is less invasive was not verified. Similar rates of prolonged stay were observed in both groups (Table 2), even for normal shortening fraction (11% vs 20%; $P = .3$, BV vs OV). Second, in a recent United States multicenter report,¹⁵ acute procedural success of BV was evenly distributed, with one third optimal, one third adequate, or one third inadequate results. Similarly, even in an experienced team, 18% of our BV patients had a severe complication and 20% a 50 mm Hg residual gradient.

Furthermore, another common concept on BV was not confirmed: the notable incidence of severe post ballooning regurgitation requiring emergency high-risk (mortality up

FIGURE 3. Pattern of indication among patients who received an operation ($n = 51$) after the initial procedure. BV, Balloon valvulotomy; OV, open valvuloplasty.

to 28%¹⁶) Ross/Ross-Konno procedure. None of our BV neonates developed immediate severe regurgitation. Seven patients (3 after BV, 4 after OV) had Ross-Konno in the following 3 months, for mixed valve dysfunction (4 regurgitations, 3 stenosis). In fact, 2 BV patients developed severe regurgitation a few weeks after the procedure, only 1 died postoperatively after rapid Ross-Konno procedure with mitral replacement in 1994.

Surgical Techniques

Surgical strategy for repair of neonatal AS has considerably evolved in the past decade.^{3,5,6} Recently, in an interventional cardiologist point of view, Benson mentioned unpublished surgical data of Southampton General Hospital (this group previously reported their series in 2001¹⁴). Noteworthy, the mean cross-clamp time was 14 minutes. In our experience, mean time was 34 minutes. The surgical procedure should not be limited to sole commissurotomy, but also include extensive work of leaflet remodeling (shaving). When limited to simple blade commissurotomy, OV long-term results will likely not be able to challenge the BV approach.

Another point arguing for this procedure is the indication for further operation (stenosis in 71% of the patients). This makes the requirement for leaflet remodeling critical. Only surgery can provide this asset.

Long-Term Outcomes

This report clearly established OV superiority to limit the rate of operation for neonates with AS. These results are consistent with the Melbourne experience with a 30% (BV) and 75% (OV) 5-year freedom from reintervention.³ However, unlike this report, renewed BV—18 times in 12 of our patients—was not considered as an end point in our results. Indeed, the choice of reintervention is highly dependent on initial management (after BV, both BV or OV can be subsequently proposed, whereas after OV, BV

TABLE 3. Uni- and multivariable Cox model for risk of operation and valve replacement

Parameter	Freedom from operation			Freedom from replacement		
	Univariable	Multivariable*		Univariable	Multivariable*	
	<i>P</i> value	HR (95% CI)	<i>P</i> value	<i>P</i> value	HR (95% CI)	<i>P</i> value
Age at surgery	.00			.04	1.0 (0.9-1.0)	.31
Weight	.15			.80		
Low cardiac output syndrome	.01	0.7 (0.3-1.8)	.48	.98		
Less than 25% left ventricle shortening fraction	.01	0.9 (0.4-2.3)	.88	.43		
Left heart-associated malformations	.02	3.1 (1.5-6.4)	.00	.08	2.7 (1.2-6.0)	.02
Endocardial fibroelastosis	.05	1.0 (0.4-2.5)	.93	.35		
Aortic annulus Z-score	.03	0.9 (0.7-1.2)	.54	.23		
Procedure: OV	.00	0.4 (0.2-0.9)	.02	.24		
Post-repair valve arrangement: tricuspid	.01	0.1 (0.0-0.5)	.01	.03	0.1 (0.0-1.0)	.06
Balloon to annulus ratio	.18			.99		
Aortic cross-clamp time†	.07	1.0 (1.0-1.1)	.27	.01	1.0 (1.0-1.1)	.25
Intensive care length of stay	.09	1.0 (1.0-1.1)	.13	.04	1.0 (1.0-1.1)	.82
Postprocedural mild aortic regurgitation	.24			.98		
Inadequate postprocedural result‡	.00	5.7 (2.6-12.2)	.00	.00	7.3 (3.1-17.1)	.00
Postprocedural aortic valve maximal gradient, mm Hg	.00	1.0 (1.0-1.1)	.00	.01	1.0 (1.0-1.1)	.01

Bold indicates significant values. HR, Hazard ratio; CI, confidence interval; OV, open valvoplasty. *Parameters with univariable $P < .10$ were included. †Data of patients without associated procedure ($n = 41$). ‡Greater than 50 mm Hg echocardiographic peak gradient and/or greater than mild regurgitation.

will never be proposed). Inclusion of renewed BV would dramatically stress the already significant OV superiority for freedom from reintervention.

Risk Factors

Valve morphology determined the need for reintervention and replacement. As previously reported^{6,9} and found in our experience with older children,⁴ tricuspid post repair arrangement (Video 3) yielded the best outcome (95% 15-year freedom from replacement). A less severe malformation of the valve or better fluid dynamics might account for these results. Because of the obvious inability of BV to restore a tricuspid anatomy, these figures provide evidence of superior long-term outcomes of OV compared with BV regarding preservation of native aortic valve.

Notwithstanding the value of a tricuspid geometry, we did not, in case of only 2 available commissures, construct a third leaflet with material (tricuspidization). Indeed, in our experience with older children,⁴ the use of material in repair at an earlier age (<10 years) led to early reoperation (because of high growth potential at this age) and was not superior to nonmaterial repair. Therefore, neonatal repair was always performed without material (Videos 2 and 3) to bring the child to an age at which repair with material would offer better durability. Later on (optimally after 10 years of age), if surgery is required, tricuspidization (leaflet replacement) offers 80% 8-year freedom from reoperation. Tricuspidization with neocommissure creation seemed promising in non-neonates, whatever age, but experience is limited (20 patients).

Despite the critical importance of morphology, we did not emphasize perioperative echocardiographic findings. First, the study spanned over a long period making the echocardiographic data weaker in the earlier era. In our experience, only surgical view did correctly assess the valve morphology, whereas such accuracy was missing for BV patients. Poor echocardiographic intraoperative correlation illustrates this insight: in the OV group, among 38 available echocardiographic descriptions of valve anatomy, only 19 (50%) matched the operative description. This could, however, be the key of outcome and procedural success. Indeed, none but 1 (left side-associated malformation) of patient-specific data influenced outcomes, highlighting our failure to individually predict outcome.

Three-dimensional echocardiography might increase our ability to understand valve-disturbed geometry, better predict outcome, and also better assign therapy. Up to now, high heart rate and diminutive size of semilunar valve in neonates have exceeded resolution capacity. A key finding is the degree of development of commissures: a well-developed (in height) commissure can be opened, whereas a less (percentage to be determined) developed—thus unsupported—commissure cannot be opened otherwise leaflets will prolapse. OV, unlike BV, can correct leaflet prolapse using commissural resuspension.

Critical AS is not a separate morphological lesion, but rather a spectrum of conditions including different degrees of hypoplasia of left heart structures. Indeed, associated left-side malformation was the only preprocedural patient-specific factor affecting outcomes. Similarly, mitral valve

FIGURE 4. Kaplan–Meier freedom from replacement in (A) all patients (biased; see Discussion) and in (B) OV patients, according to morphology of the valve after repair. Shaded area indicates 95% confidence interval. OV, open valvoplasty; BV+OV, balloon valvotomy followed by open valvoplasty; BV, balloon valvotomy.

hypoplasia is a well identified risk factor affecting outcomes in Ross-Konno patients.¹⁶ Because our capacity to appropriately describe valve hypoplasia is limited (even Z-score was not a predictive factor), associated left-side malformations might be a surrogate to predict outcome in these children.

In our experience with aortic valve repair in older children,⁴ early BV has been identified as a predictor of replacement. However, the 10-year freedom from replacement, although higher in the OV group (78% vs 60%), did not reach significance.

Nevertheless, significant biases hamper comparison of replacement rate after BV or OV (in favor of BV). First, choice of reintervention is highly dependent on initial management (OV patients will never be offered BV). Thus, freedom from replacement after BV is biased by the fact that 50% of BV patients will subsequently be redirected to the other arm of management (ie, OV), making the comparison inadequate. Second, decision-making at surgery is highly influenced by initial procedure: the threshold for replacement is high in BV patients (repair always considered), whereas replacement is not out of scope in OV patients requiring reoperation. Further underlining these biases is the fact that 2 large reference reports on OV and BV comparison^{3,17} did not show any result on freedom from replacement. Last, parental request at a second surgery (after failed OV) also biases the analysis: some demand “definitive” solutions (replacement) instead of repair and risk of renewed surgery. Such a request is never raised at a “first” surgery (after failed BV).

Furthermore, one could hypothesize that the OV superiority shown is artificially created by inferior BV results. First, the BV experience was significantly longer than OV (13.3 ± 6.4 vs 9.6 ± 7.3 ; $P < .01$) thus favoring the former. Then, local experience (patients per year) was 2.5 times higher than national average per center (Table E2).¹⁸ Comparable BV data sets (same age, criteria, follow-up, stable indications [ie, nonmulticentric]) are unexpectedly scarce (Table E2) but the difference in results is thin (even nonsignificant [no available CI]): 11% less freedom from surgery in our data than the average (likely because of aortic repair expertise in our center), with similar freedom from replacement. Surprising is that, for similar experience length, average follow-up (which is critical to assess long-term outcomes) is 6.5 years (2 reports with 3 years), whereas ours is 13.5 years. Finally, only 1 center championed BV¹⁹ (85% 10-year freedom from replacement). However, the rate of subsequent OV after BV were not revealed, and one cannot exclude that results have been improved or biased by an interim OV strategy.

For patients who will inevitably reach replacement, the main goal is to postpone age for this procedure. Indeed, mechanical replacement is associated with lifelong anticoagulation, repeated replacement because of child overgrowth. For autograft replacement, dilatation and autograft failure occur, up to 40%, in the second decade^{20,21} after the Ross procedure. Techniques of supported Ross have developed,²² but can only be applied in mature children. With regard to this time-sparing strategy, BV fails to postpone replacement further than OV (Figure 4, A).

Limitations

These results are achieved in a unique environment of balanced experience with both techniques. Although this equipoise is an asset for comparison, these results might

not be achieved in most centers, where mainly one approach is favored, and therefore expertise developed in that area. Furthermore, as aforementioned, the management of borderline patients in a center with univentricular palliation program influenced the results.

LV function was significantly different between groups. LV function does not affect the risk of operation (in multi-variable analysis) but only the risk of mortality. The end point was freedom from operation, thus not taking death into account.

Retrospective design is associated with several well known biases. Several reports claim for randomized data,¹ but long-term results of such an approach will come in more than a decade—if such results one day come. Indeed, in a recent survey over 13 unselected North American pediatric interventional centers¹³: none would agree to randomize infants in a clinical trial. While awaiting such utopia, the present report adds to the lack of data regarding outcome of neonates with surgically managed AS.

CONCLUSIONS

In a retrospective, single-center study, our results indicate that BV, compared with OV, did neither efficiently release aortic valve obstruction in the early and long-term course, nor postpone the age of replacement. Leaflet remodeling using surgical extensive shaving plays a critical role. Nevertheless, BV remains an important modality for patients with LV dysfunction. Long-term preservation of the native valve is related to valve morphology (ie, tricuspid arrangement) that only OV can offer. In a bicuspid scenario, the initial procedure does not affect preservation of the native valve but, with BV, a high likelihood of earlier surgical repair has to be anticipated.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: critical aortic stenosis, aortic valve repair, neonate, CHD, valve (lesions, repair, replacement), cardiac catheterization/intervention, outcomes (mortality, morbidity, survival)

TABLE E1. Repair procedure at first operation after initial procedure (n = 37)

Procedure	n	%
Commissurotomy, shaving	35	95
Leaflet replacement	11	30
Leaflet extension	6	16
Patch repair of leaflet tear	5	13.5
Neocommissure creation	4	11
Subaortic stenosis resection	8	22

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TABLE E2. Literature review for results of BV in neonates

First author	Year	Time* since first BV, years	n	Age	Median follow-up	Length of experience, years	Patients per year	Freedom from surgery			Freedom from replacement		
								5 Years	10 Years		5 Years	10 Years	
Sullivan ^{E1}	2017	24	76	Neonates	7	20	3.8	NA	NA		75% (no CI)	55% (no CI)	
Maskatia ^{E2}	2011	26	50	Median 3 y	3	24	2.1	NA	NA		84% (no CI) [†]	FU, 3 y [‡]	
Brown ¹⁹	2010	25	113	Neonates	9	23	4.9	NA	NA		92% (no CI)	85% (no CI)	
Fratz ^{E3}	2008	22	68	Neonates	3	18	3.8	65% (no CI)	FU, 3 y [‡]		NA	NA	
Ewert ¹⁸	2011	26	334	Neonates	2.7	21	0.8	70% (no CI)	FU, 2.7 y [‡]		NA	NA	
Present study, BV patients	2018	27	51	Neonates	13.5	26	2.0	53% (39-68)	36% (22-51)		81% (69-92)	60% (45-75)	
Hill ¹	Meta-analysis		282	Younger than 1 y	NA, 6% remain followed at 10 y	NA	NA	57% (50-62) (including renewed BV)	40% (27-45) (including renewed BV)		82% (75-86)	75% (65-80)	
Present study, OV patients	2018	27	52	Neonates	9.2	25	2.1	74% (61-87)	66% (50-82)		87% (76-97)	79% (62-92)	

BV, Balloon valvotomy; NA, not available; CI, confidence interval; FU, follow-up; OV, open valvuloplasty. *Time between first BV and publication date. †Results include 220 non-neonates. ‡Results not mentioned as follow-up are limited.