

Long-Term Results of Balloon Valvuloplasty as Primary Treatment for Congenital Aortic Valve Stenosis: a 20-Year Review

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Abstract In the presence of new surgical techniques, the treatment of congenital valvular aortic stenosis is under debate. We reviewed the results and late outcomes of all 93 patients aged 1 day to 18 years, treated with balloon valvuloplasty (BAV) as first-line therapy for congenital aortic valve stenosis in our center from January 1991 to May 2012. Mean age at procedure time was 2.4 years; 37 patients underwent BAV at age ≤ 30 days (neonates), 29 patients at age ≥ 1 month and < 1 year (infants), and 27 patients were older than 1 year (children). The invasive BAV peak-to-peak aortic valve gradient (mean 59 ± 22 mmHg) was immediately reduced (mean 24 ± 12 mmHg). The observed diminution of gradient was similar for each age group. Four patients had significant post-BAV AI. Mean follow-up after BAV was 11.4 ± 7 years. The last echo peak aortic gradient was 37 ± 18 mmHg and mean gradient was 23 ± 10 mmHg, and two patients had significant AI. Actuarial survival for the whole cohort was 88.2 and 72.9 % for the neonates. All infants, except one, and all children survived. Sixty-six percent of patients were free from surgery, and

58 % were free from any reintervention, with no difference according to age. Freedom from surgery after BAV at 5, 10, and 20 years, respectively, was 82, 72, and 66 %. Our study confirms that BAV as primary treatment for congenital AS is an efficient and low-risk procedure in infants and children. In neonates, the prognosis is more severe and clearly related to “borderline LV.”

Keywords Congenital valvular aortic stenosis · Balloon valvuloplasty · Outcome · Shone’s syndrome

Introduction

Congenital valvular aortic stenosis (AS) is relatively common (1.1–4.3 per 10,000 live births) [3, 8]. Since 30 years, balloon aortic valvuloplasty (BAV) is the first-line treatment in most centers worldwide [6, 9]. There is still debate, however, concerning what is the most appropriate treatment, especially in the context of new surgical techniques such as aortic valve reconstruction or the Ross procedure. We reviewed the results of all the patients treated with BAV as first-line therapy in our center, and we analyzed the results and late outcomes of the procedure.

Materials and Methods

We reviewed the medical records of all patients aged 1 day to 18 years, treated with BAV from January 1991 to May 2012 in the *Cliniques Universitaires Saint Luc*, UCL, Brussels. Age, weight, gender, echocardiographic and hemodynamic data, and need for re-intervention, and/or surgery were collected.

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Transthoracic echocardiography (TTE) was used to evaluate the anatomy of the aortic valve, with Doppler-derived pressure gradients and insufficiency degree assessed before and after the procedure. Left ventricular shortening fraction (LVSF) and left ventricular end-diastolic diameter (LVDD) were collected. Peak and mean aortic valve gradients were measured using the modified Bernoulli equation. AS was considered significant if the peak gradient exceeded 70 mmHg, without LV dysfunction. Aortic insufficiency (AI), detected by means of color Doppler, was classified from 0 to 4, with grades 3–4 or 4 considered significant AI.

Percutaneous BAV was performed under general anesthesia usually via retrograde femoral artery access. Peak-to-peak gradient through the aortic valve, presence of AI, and annulus size were all assessed before and after the procedure. Balloon sizes ranged from 4 to 25 mm, never exceeding a balloon diameter to aortic annulus ratio of 0.9.

Patients with sub- or supra-valvular aortic stenosis, or those exhibiting hypoplastic left heart syndrome (HLHS), were not included in the study. In addition, those who had undergone surgical aortic valvuloplasty as an initial treatment were excluded from analysis.

SPSS statistical software was used for data analysis. Categorical variables were reported as absolute numbers and percentages. Continuous variables were expressed as either mean $\pm$ standard deviation (SD) or median values and ranges. For all tests, a *p* value <0.05 was considered statistically significant. Actuarial survival and freedom from reintervention were calculated using the Kaplan–Meier method.

The study was conducted in accordance with the Belgian regulatory requirements. Due to its retrospective study design, neither IRB approval nor patient written informed consent was required.

Results

From January 1991 to May 2012, 93 patients with congenital AS were referred to our center to undergo primary BAV. Figure 1a depicts the distribution and frequency over time. A description of the population and results can be found in Table 1 and Fig. 1b. The mean age at procedure time was 2.4 years, with 37 patients undergoing BAV aged ≤ 30 days (neonates), 29 aged between 1 month and 1 year (infants), and 27 aged over 1 year (children). The population was 18 % female and 82 % male. Isolated bicuspid aortic valve was diagnosed in 58 % of the cohort, with 16 % exhibiting Shone's syndrome. After reviewing patient data and evolution, nine patients who had been selected for BAV on account of an adequately sized left ventricle were diagnosed as having multiple small left

ventricular structures, such as the mitral or aortic valve and the aortic arch.

Prior to BAV, the Doppler-derived peak and mean aortic valve gradients were 71 ± 18 and 44 ± 12 mmHg, respectively. The mean LVSF was 42 ± 11 %, with LV dysfunction (LVSF < 30 %) reported in only three patients, all neonates.

During catheterization, the pre-BAV peak-to-peak aortic valve gradient, measured invasively, was 59 ± 22 mmHg. The post-BAV peak-to-peak gradient was immediately reduced to 24 ± 12 mmHg. The observed decrease in gradient was similar in all age groups. Only one patient (neonate) exhibited a post-BAV peak-to-peak gradient exceeding 50 mmHg, which was considered a failure. Yet a spontaneous decrease in gradient was revealed on TTE during follow-up, decreasing to 15 mmHg after 12.3 years, despite no other procedure having been performed. Angiographic nonsignificant AI (grade 1 or 2) was present in eight patients before the procedure and in 37 patients after the procedure, considered significant in four patients (grade 3 or 4).

Echocardiographic reports were available for follow-up in 88 patients (94.6 %), with five lost to late follow-up. At the last echo, the peak aortic gradient was 37 ± 18 mmHg and mean gradient was 23 ± 10 mmHg, with a higher residual gradient observed in the children group (42 ± 18 mmHg). AI was reported in 52 patients (59 %), with only two cases considered significant (one neonate and one infant).

Mean follow-up duration after BAV was 11.4 ± 7 years, with a maximum of 21.7 years. A total of 48 patients (51 %) were followed up for over 10 years. The Kaplan–Meier method showed an actuarial survival for the whole cohort of 88 % at last follow-up (Fig. 2a). Only 72.9 % of the neonates were still alive, whereas all the children survived and all the infants, except one, who died from surgical complications (Fig. 2b).

Out of the entire patient population, 66 % were free from surgery at last follow-up, with no significant difference observed according to age (Table 1), and over half (58 %) were free from any reintervention.

A second intervention (additional BAV or surgery) was performed in 35 patients (37 %) after a mean time of 3.4 years. The results are presented in Table 2. A second intervention was significantly more common in the children, yet took place earlier in the neonate group. No differences were observed in the reintervention type among the three groups. A second BAV was performed in six children (22 %) after a mean time of 5.7 years, in six infants (20.7 %) after a mean time of 4.7 years, and in six neonates (16 %) after a mean time of 0.6 years. Surgery was performed as a second intervention in 17 patients (18.2 %): six children (22 %) after a mean time of 6 years,

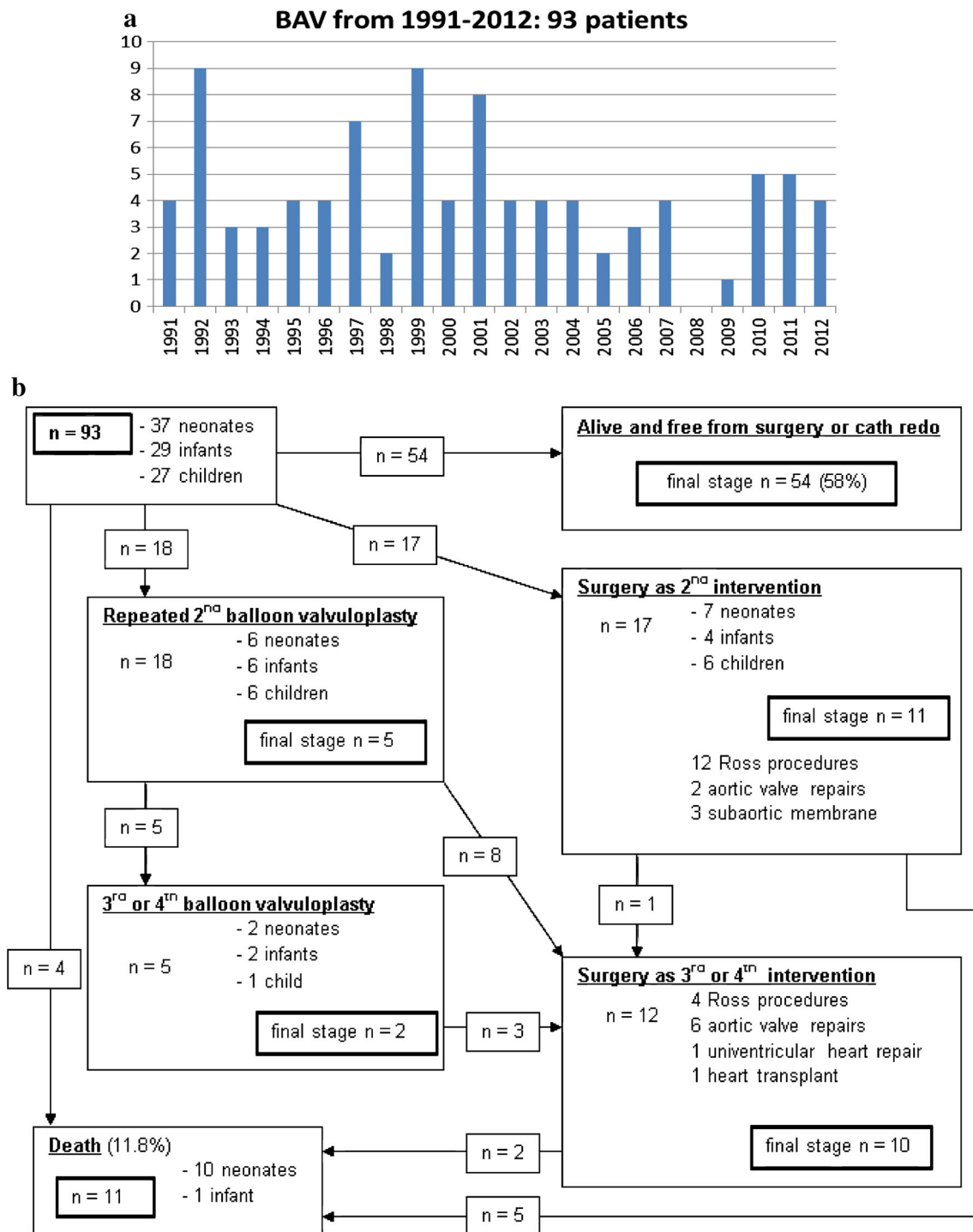


Fig. 1 **a** Congenital AS distribution and frequency in *Cliniques Universitaires Saint-Luc* over study period, **b** flowchart of patient evolution

four infants (13.8 %) after a mean time of 2.8 years, and seven neonates (18.9 %) after a mean time of 1.1 years. A Ross procedure was performed on 12 patients, a surgical aortic valvuloplasty on two, and sub-aortic membrane resection on three. Within this patient group, one 15-year-old patient required LV assistance and a heart transplant

following the Ross procedure, performed due to predominant aortic stenosis. This patient exhibited good final evolution.

Repeat BAV procedures (≥ 3 percutaneous interventions) were conducted in five patients (5.4 %), comprising two neonates, two infants, and one child. For three of these

Table 1 Population data and BAV results in the whole cohort by age group

	Total	Neonates	Infants	Children	<i>p</i>
Patients (<i>n</i>)	93	37	29	27	
Age at BAV	2.4 years	6.7 days	2.7 m ± 1.8	2.4 years	
Gender (m/f)	76/17	32/5	22/7	22/5	
Weight (kg)	10 ± 1.1	3.2 ± 0.5	4.7 ± 1.4	31.7 ± 17	
Pre-BAV TTE					
LVSF (%)	42 ± 11	40 ± 8	46 ± 10	46 ± 9	
LVDD (mm)	23 ± 0.8	18.8 ± 5	22.7 ± 4	38 ± 10	
Balloon aortic valvuloplasty					
Pre-BAV LV–AO gradient (mmHg)	59 ± 22	65 ± 24	52.3 ± 15.4	57 ± 21	
Post-BAV LV–AO gradient (mmHg)	24 ± 12	25 ± 12	21 ± 12	28.6 ± 10	
Aortic annular diameter (mm)	9.8 ± 4.4	6.7 ± 1.1	8.9 ± 1.5	17 ± 3.5	
Pre-BAV AI (1–4/4)	8	3	1	4	
Post-BAV significant AI (≥3/4)	4	2	1	1	
Mean follow-up (years)	11.4 (0.014–27.1)	7.4 (0.014–18.6)	10 (0.14–21.5)	18.2 (3.7–27.1)	
TTE peak LV–AO gradient (mmHg)	37 ± 17.7	37.6 ± 17.8	31.6 ± 15	42.5 ± 18.7	
TTE mean LV–AO gradient (mmHg)	23 ± 9.7	21.5 ± 8.3	20.7 ± 10.5	28 ± 9.5	
Significant AI (≥3/4)	2	1	1	0	
Overall survival	83 (89.2 %)	27 (72.9 %)	28 (97 %)	27 (100 %)	<i>p</i> < 0.01
Free from surgery	62 (66.7 %)	22 (72.9 %)	22 (75.8 %)	18 (66.7 %)	
Free from reintervention	54 (58 %)	20 (54 %)	19 (65.5 %)	15 (55.5 %)	

patients (one neonate and two infants), surgery was eventually performed.

Surgery was performed as third or fourth intervention in 12 patients (12.9 %), consisting of four Ross procedures (in two neonates, one infant, and one child), six aortic valvuloplasty (three infants and three children), one univentricular palliation (in one neonate, who died during surgery), and one heart transplantation (in the previously mentioned 15-year-old patient with severe LV dysfunction following the Ross procedure).

The indications for reinterventions in the 24 patients operated on the aortic valve (16 Ross, eight aortic valve repairs) were aortic stenosis in ten patients, insufficiency in seven patients, and mixed stenosis and regurgitation in seven patients, with aortic valve surgery performed mainly to treat significant AI in 14 of those 24 patients (Fig. 1b).

Patient deaths (Table 3) concerned 10 neonates who had undergone BAV at under 30 days of age, and one infant who underwent BAV at 41 days old and died from post-operative complications (Patient 10). Of the 10 neonates who died, two (20 %) had presented with LV dysfunction prior to BAV and eight either exhibited Shone's syndrome or were diagnosed as having multiple small or abnormal left heart structures. Seven patients died within the 2 months following BAV, and only two patients died after 1 year of age.

In four patients, death was related to catheterization complications: Two patients developed significant AI

following BAV (one infant [Patient 3] died 7 days after a rescue Ross procedure and the other [Patient 5] 2 weeks following BAV), one patient died from a mitral tear resulting in severe regurgitation during a second BAV procedure (Patient 8), and the fourth died from cerebral hemorrhage during streptokinase treatment for femoral artery thrombosis (Patient 9).

Three patients died from surgical complications, consisting of aortic dissection during coarctation repair (Patient 4), air embolism (Patient 10), and stroke during extracorporeal life support following a heart transplant (Patient 11).

In eight neonate patients, death was at least partially related to inadequate LV or left heart structure dimensions (Table 3). One of the eight neonates died following a rescue Norwood procedure (Patient 7), one from LV fibroelastosis revealed during the Ross procedure (Patient 6), and one from persistent LV diastolic dysfunction 6.8 years after a Ross procedure (Patient 11 who died from cerebral hemorrhage following a heart transplant).

Discussion

Our study presents the results and outcomes from a 20-year experience with BAV as an initial treatment for congenital AS in a pediatric population. BAV is an efficient procedure, demonstrated by the significant decrease in aortic

gradient we observed immediately after the procedure and at late follow-up in all groups. Our survival analysis, with a mean follow-up of 11.4 ± 7 years, revealed that 88 % of

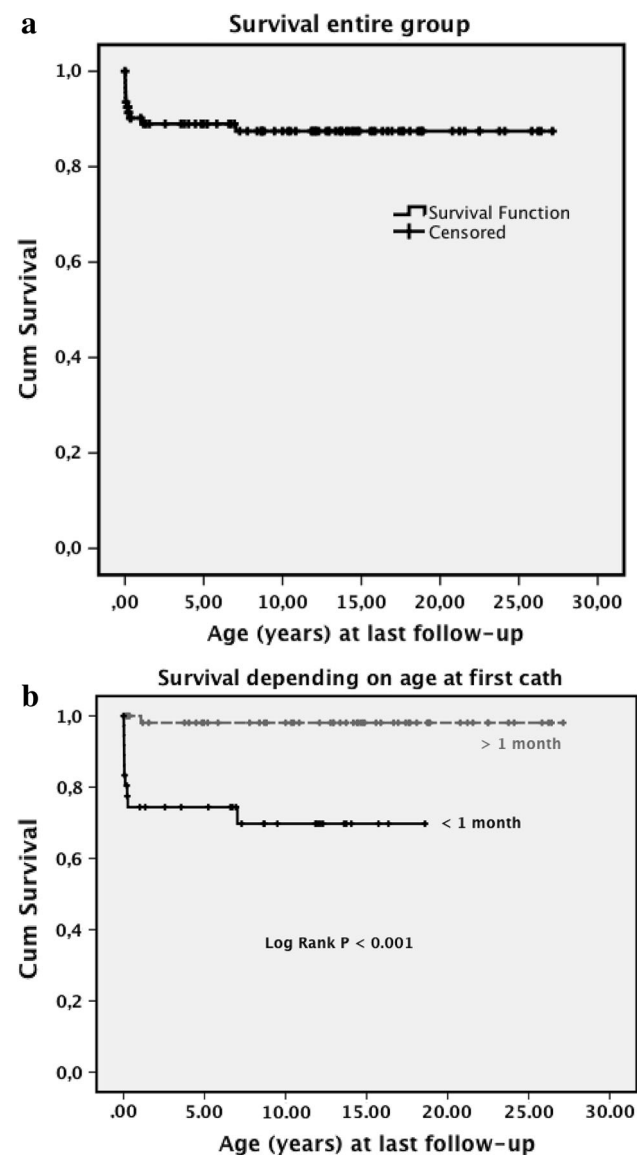


Fig. 2 **a** Patient survival at last follow-up was 89.2 %, **b** patient survival by age at first catheterization. Except one infant who died at 1 year of age from air embolism during surgical aortic valvuloplasty (patient 10, Table 3), all infant and children were alive (98 % survival rate); 72.9 % of the neonates were alive

patients were alive at 20 years of age, with two-thirds of the cohort free from surgery and over half free from any reintervention. These findings are in line with the literature [1, 6, 9]. Nevertheless, a second intervention (either surgery or BAV—36 % in our series) appeared unavoidable in a third of patients in the long term [7, 12, 13].

The mortality rate was 11.8 % for the whole cohort and 27 % for the neonate subgroup. The 73 % survival reported in neonates with critical aortic stenosis in our series was similar to the 72 % survival at 5 years reported in the Congenital Heart Surgeons' Society multicentric study [10]. In our series, all deaths involved neonates, except one. The causes of death were multifactorial: In four cases, death was considered secondary to BAV complications, and in eight cases (8/11—72 %), patients were finally diagnosed with a “borderline LV” with abnormal left heart structures or non-compliant LV, clearly associated with an increased risk of poor results and death [14]. When neonates are diagnosed with a “borderline LV,” predicting which is suitable for biventricular repair remains a substantial challenge [2, 5, 11] and the presence of endocardial fibroelastosis with LV diastolic dysfunction appears to be a more significant risk factor than LV volume or dimensions [14]. LV systolic dysfunction preceding BAV also tended to be associated with poor survival. Although as it concerned only three patients in our study, this assessment should be interpreted with caution.

Another relevant observation was the fact that 66.7 % of the whole population was free from surgery at the last follow-up. The freedom from surgery after BAV of 82, 72, and 66 % at 5, 10, and 20 years of follow-up, respectively, is even more appealing for physicians in charge of young children (Fig. 3).

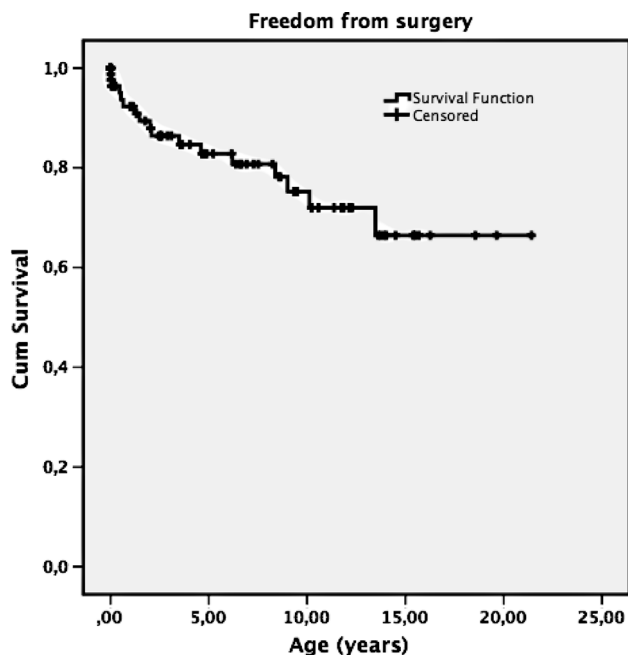
This result should be compared to the 50 % freedom from surgical reintervention and valve replacement at 10 years that was recently reported in a pediatric population following aortic valve repair performed by the most skilled surgeons [4]. The graphs published in this actual surgical study demonstrated 70 % freedom of reintervention at 10 years after aortic valve repair with no cusp extension, yet only 30 % freedom of reintervention when cusp extension was performed. For neonates with critical aortic stenosis, the prospective non-randomized study by

Table 2 Second intervention

	Total	Neonates	Infants	Children	<i>p</i>
Secondnd intervention	35 (37.3 %)	13 (35.1 %)	10 (34.5 %)	12 (44.4 %)	<i>p</i> < 0.05
Mean time after first BAV (years)	3.4	0.7	4.4	5.6	<i>p</i> < 0.05
Cath	18 (19.3 %)	6 (16 %)	6 (20.7 %)	6 (22 %)	
Mean time after first BAV (years)	3.7	0.6	4.7	5.7	<i>p</i> < 0.05
Surgery	17 (18.2 %)	7 (18.9 %)	4 (13.8 %)	6 (22 %)	
Mean time after first BAV (years)	3.3	1.1	2.8	6	

Table 3 Data of the patients who died

Patient	Age at first BAV (days)	Age at death (days)	Date of birth	Causes of death	Death related to abnormal LV	Death related to cath complication	Postoperative death
1	2	6	1991	Severe mitral regurgitation, Shone syndrome	LV		
2	2	8	2012	Severe LV dysfunction, Shone syndrome	LV		
3	3	10	1992	Cath complication, AO regurg, postop death (Ross—day 1)		AO regurgitation	Ross procedure
4	2	13	1993	Shone syndrome, postop death (COA repair—day 1)	LV		COA repair under bypass
5	3	18	1999	Cath complication, severe AO regurg	LV	AO regurgitation	
6	1	16	2007	Fibroelastosis, postop death (Ross-Kono, day 1)	LV		Ross procedure
7	1	36	2010	Fibroelastosis, postop death (Norwood, day 1)	LV		Norwood procedure
8	25	96	1995	Cath complication (second procedure), mitral regurg		Mitral regurgitation	Mitral plasty (6 days postcath)
9	5	81	1999	Cath complication (second procedure), cerebral hemorrhage	LV	Streptokinase for femoral thrombosis	
10	41	392	1994	Postop death (valvuloplasty, day 1)			AO valvuloplasty air embolism
11	4	2564	2001	Fibroelastosis, postop death (transplant, ECMO, day 2)	LV		Transplant, ECMO, cerebral hemorrhage

**Fig. 3** Freedom from surgery after BAV at 5, 10, and 20 years of follow-up were, respectively, 82, 72, and 66 %

the Congenital Heart Surgeons' Society reported similar survival and outcomes following valvotomy, performed surgically or by transcatheter balloon dilatation [10]. Historical series demonstrate, as does our study, that balloon valvuloplasty achieves at least similar results to surgery in terms of survival and reoperation rates. For the pediatric population, even with the advent of new surgical techniques, aortic valve repair or replacement must be reserved for patients who failed to benefit from balloon valvuloplasty.

Ultimately, most patients will require a reintervention by surgery or balloon dilatation (Fig. 4). Balloon valvuloplasty is easy to repeat if necessary, as it was performed twice in 18 patients and three times in five. This procedure did not preclude a successful aortic surgical valvuloplasty in eight children.

Study Limitations

This was a retrospective, monocenter, and non-comparative study. Our cohort was not very large compared with other studies reported in the literature, and our results must thus be interpreted carefully. Furthermore, the data were collected over a long time period, and the

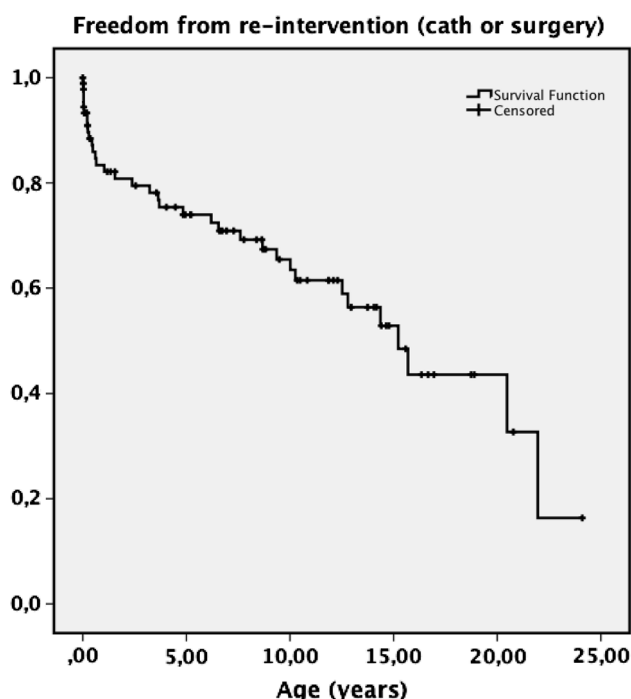


Fig. 4 Freedom from reintervention, 58 % of patients were free from any reintervention, surgery, or balloon dilatation at last follow-up

interventions were performed by different physicians, using different materials and techniques, which could have impacted the results [15]. It is important to note that during the study period, BAV was performed by six different cardiologists. While our results reflect a realistic picture of general BAV outcomes, this could have reinforced differences in patient selection and treatment strategy, partially explaining some of the neonatal deaths.

Echocardiographic data were collected by reviewing echo reports, although these were not standardized and had been performed by multiple cardiologists. Another limitation was the use of LV shortening fraction to assess LV systolic function, which does not precisely reflect myocardial contractility [9], as well as the use of LV end-diastolic dimension to assess LV dimensions. Our center uses BAV as standard management for congenital AS, and no primary surgical aortic valvuloplasty was performed during this time period. For this reason, it was not possible to compare the outcomes of primary BAV with those of primary surgical aortic valvuloplasty.

Conclusion

This study confirmed that BAV is an efficient and low-risk primary treatment for congenital AS in infants and children, resulting in a 98 % survival and over half the

population remaining free from any reintervention after a mean period of 11.4 ± 7 years. In neonates with critical aortic stenosis selected for biventricular repair, the 72.9 % survival at 10 years in our series was in line with the 72 % survival at 5 years reported by BW. Mc Crindle in the Congenital Heart Surgeons' Society prospective non-randomized study [10]. In neonates, the prognosis appears more severe, clearly related to "borderline LV" and the challenge of recognizing which is suitable or not for a biventricular management strategy [14].

Conflict of interest None to declare.

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