

Long-term outcomes of atrioventricular septal defect and single ventricle: A multicenter study



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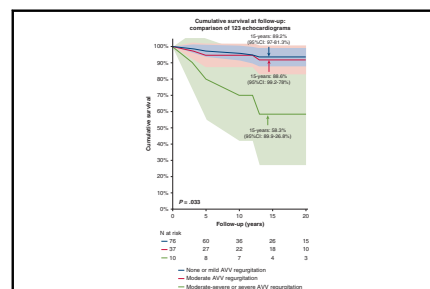
ABSTRACT

Objective: The study objective was to analyze survival and incidence of Fontan completion of patients with single-ventricle and concomitant unbalanced atrioventricular septal defect.

Methods: Data from 4 Dutch and 3 Belgian institutional databases were retrospectively collected. A total of 151 patients with single-ventricle atrioventricular septal defect were selected; 36 patients underwent an atrioventricular valve procedure (valve surgery group). End points were survival, incidence of Fontan completion, and freedom from atrioventricular valve reoperation.

Results: Median follow-up was 13.4 years. Cumulative survival was 71.2%, 70%, and 68.5% at 10, 15, and 20 years, respectively. An atrioventricular valve procedure was not a risk factor for mortality. Patients with moderate-severe or severe atrioventricular valve regurgitation at echocardiographic follow-up had a significantly worse 15-year survival (58.3%) compared with patients with no or mild regurgitation (89.2%) and patients with moderate regurgitation (88.6%) ($P = .033$). Cumulative incidence of Fontan completion was 56.5%, 71%, and 77.6% at 5, 10, and 15 years, respectively. An atrioventricular valve procedure was not associated with the incidence of Fontan completion. In the valve surgery group, freedom from atrioventricular valve reoperation was 85.7% at 1 year and 52.6% at 5 years.

Conclusions: The long-term survival and incidence of Fontan completion in our study were better than previously described for patients with single-ventricle atrioventricular septal defect. A concomitant atrioventricular valve procedure did not increase the mortality rate or decrease the incidence of Fontan completion, whereas patients with moderate-severe or severe valve regurgitation at follow-up had a worse survival. Therefore, in patients with single-ventricle atrioventricular septal defect when atrioventricular valve regurgitation exceeds a moderate degree, the atrioventricular valve should be repaired. (*J Thorac Cardiovasc Surg* 2022;163:1166-75)



In single-ventricle AVSD, severe AVV regurgitation affected survival.

CENTRAL MESSAGE

In patients with single-ventricle AVSD, AVV surgery did not increase mortality, whereas severe valve regurgitation decreased survival at follow-up and therefore should be treated.

PERSPECTIVE

Our bi-national study of 151 patients with single-ventricle AVSD showed long-term survival and Fontan completion better than previously reported. AVV surgery did not reduce survival or incidence of Fontan completion, whereas severe AVV regurgitation affected survival. Therefore, severe AVV regurgitation should be treated.

See Commentaries on pages 1176 and 1178.

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Abbreviations and Acronyms
AVSD = atrioventricular septal defect
AVV = atrioventricular valve
CI = confidence interval
PCPS = partial cavopulmonary shunt
TCPC = total cavopulmonary connection

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Newborns treated with single-ventricle palliation for unbalanced atrioventricular septal defect (AVSD) represent approximately 10% of patients with single-ventricle physiology and have limited long-term survival.¹ Significant atrioventricular valve (AVV) regurgitation has been shown to be associated with a lower incidence of Fontan completion and overall survival.^{1,2} The need for AVV surgery is reported to be associated with substantial mortality.² Up to 60% of the reported patients underwent an AVV operation in the course of single-ventricle palliation.¹⁻⁴ Many surgical techniques have been described to repair the AVV in the setting of a single ventricle, and the probability of reoperation varies between 30% and 50%, independent from the technique used at first valve repair intervention.^{2,3} Our multicenter retrospective study analyzed the survival and incidence of Fontan completion of patients with single-ventricle physiology and unbalanced AVSD and freedom from AVV reoperation after the first valve surgery.

MATERIAL AND METHODS

Study Design

This study was multicenter, retrospective, and bi-national (the “BeNe” experience means the scientific cooperation of Belgium and The Netherlands). University Medical Centers of Groningen, Leiden, Rotterdam, and Utrecht were the participating Dutch Centers. University Hospitals of Gent, Leuven, and Louvain were the participating Belgian Centers. Centers are reported in anonymized fashion. All patients with unbalanced AVSD who underwent single-ventricle palliation were selected from each institutional database and follow-up until 2019 was recorded. Unbalanced AVSD was defined as any AVSD with hypoplasia of 1 ventricle that was assessed to be unfeasible for biventricular repair. Preoperative, operative, and postoperative data from all patients were collected retrospectively. Echocardiographic studies at follow-up of 123 patients were collected. The last echocardiogram at follow-up for patients who were alive and the last echocardiogram before death for patients who died were collected. One patient who underwent a cardiac transplant was included in the study, and transplant was classified as death. Patients who crossed over to a biventricular repair after an initial palliation were excluded. Patients who underwent AVV surgery during their palliation (n = 36) were in the valve surgery group.

End Points

- Overall survival at follow-up.
- Fontan completion at follow-up.
- Freedom from AVV reoperation after the first AVV surgery.

The Institutional Review Board of the participating centers agreed to waive the need for an informed consent because data were collected as part of routine medical care and patients were not individually identifiable.

TABLE 1. Patients’ preoperative characteristics and surgical steps

Preoperative characteristics and surgical steps	N = 151 (%)
Centers	Center A: 18 (11.9) Center B: 12 (7.9) Center C: 29 (19.2) Center D: 23 (15.2) Center E: 26 (17.2) Center F: 15 (9.9) Center G: 28 (18.5)
Birth era	1966-1999: 49 (32.5) 2000-2009: 57 (37.7) 2010-2018: 45 (29.8)
Gender	Female: 59 (39.1) Male: 92 (60.9)
Coexisting syndrome	48 (31.8)
Isomerism	None 82 (54.3) Left: 23 (15.2) Right: 46 (30.5)
Hypoplastic left ventricle	61 (40.4)
Total anomalous pulmonary vein connection	25 (16.6)
AVV procedure	36 (23.8)
Palliative operation(s) before cavopulmonary shunt	
None	31 (20.5)
Pulmonary artery banding	32 (21.2)
Aortopulmonary shunt	56 (37.1)
Norwood stage I	10 (6.6)
Others	22 (14.6)
Cavopulmonary shunt	
None	39 (25.8)
Unilateral bidirectional	71 (47.1)
Bilateral bidirectional	37 (24.5)
Unilateral (classic Glenn)	4 (2.6)
Total cavopulmonary connection	
None	42 (27.8)
Extracardiac fenestrated	49 (32.5)
Extracardiac nonfenestrated	17 (11.3)
Lateral tunnel fenestrated	13 (8.6)
Lateral tunnel nonfenestrated	22 (14.6)
Atriopulmonary connection	3 (1.9)
Hepato-azygos shunt	5 (3.3)

AVV, Atrioventricular valve.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics 23 (IBM Corporation, New York, NY) and R version 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria). Values are reported as mean $\pm$ standard deviation or as number with percentages.

Survival curves for overall survival and freedom from AVV reoperation with associated point-wise linear 95% confidence intervals (CIs) were estimated using the Kaplan–Meier estimator and compared across groups using the log-rank test. The cumulative incidence curve of Fontan completion with the associated point-wise linear 95% CIs was estimated using the Aalen-Johansen estimator with death before Fontan completion included as a competing risk. Hazard ratios with 95% CIs of potential risk factors were estimated using a Cox proportional hazards regression model for the overall survival end point and a Fine and Gray regression model for the Fontan completion end point. In both models, time zero corresponded to the first surgical procedure performed per patient. Potential risk factors were first tested in an univariable analysis, and all risk factors with a *P* value .20 or less were entered in a multivariable analysis. In all analyses, study center was included as a stratification variable to account for possible differences in the patient populations across the 7 centers. Because AVV surgery was performed at different timings of the palliative treatment, a sensitivity analysis in which AVV surgery was included as a time-dependent covariate was also performed.

RESULTS

A total of 151 patients who underwent operation between 1966 and 2018 were included. Follow-up was complete in all patients. The median follow-up time was 13.4 years (95% CI, 9.7–17.11).

Table 1 shows the relevant preoperative characteristics and the surgical steps for all patients. Approximately one-third of the patients had a coexistent syndrome: heterotaxy in 30 patients, Down syndrome in 7 patients, and other chromosomal disorders in 11 patients. Figure 1 shows the flow diagram of all 151 patients, giving an overview of the surgical steps, interstage mortality, and outcome at follow-up. There was a significant difference in the prevalence of AVV surgery among centers: AVV surgery was performed

in only 1 patient at centers E and F, and in approximately half of the patients at center A (chi-square test, *P* = .03).

Overall Survival

The cumulative survival is shown in Figure 2, A: 71.2% at 10 years, 70% at 15 years, and 68.5% at 20 years. Postoperative mortality (defined as in-hospital or 30-day mortality) was 13.9% (21/151 patients); 12 patients died after the first palliation, 1 patient died after a partial cavopulmonary shunt (PCPS) procedure, and 8 patients died after a total cavopulmonary connection (TCPC) operation. Twenty-five patients died during follow-up, due to cardiac arrest (*n* = 4), failing Fontan circulation (*n* = 5), untreatable pulmonary hypertension (*n* = 1), miscellaneous causes (*n* = 15), including lung bleeding, sepsis, and shunt thrombosis. There was a trend of decrease in postoperative mortality in the last decade: 11.1% (2010–2018) versus 14.3% (1966–1999) and 15.8% (2000–2009), although not significant (chi-square test, *P* = .755).

In 123 echocardiographic studies at follow-up, 30 patients had undergone an AVV surgery. Median follow-up of last echocardiography was 11.6 years. AVV regurgitation was none or mild in 76 patients, moderate in 37 patients, and moderate-severe or severe in 10 patients. There was a significant difference in overall survival at follow-up comparing patients with increasing degree of AVV regurgitation: 89.2% by none or mild, 88.6% by moderate regurgitation, and 58.3% by moderate-severe or severe regurgitation at 15 years (*P* = .033), as shown in Figure 2, B.

Univariable and multivariable analyses of mortality are shown in Table 2. In univariable analysis, severe AVV regurgitation at follow-up was associated with worse survival, and a concomitant syndrome was associated with better survival. AVV surgery was not a risk factor for mortality (*P* = .65). When the time to AVV surgery was taken into

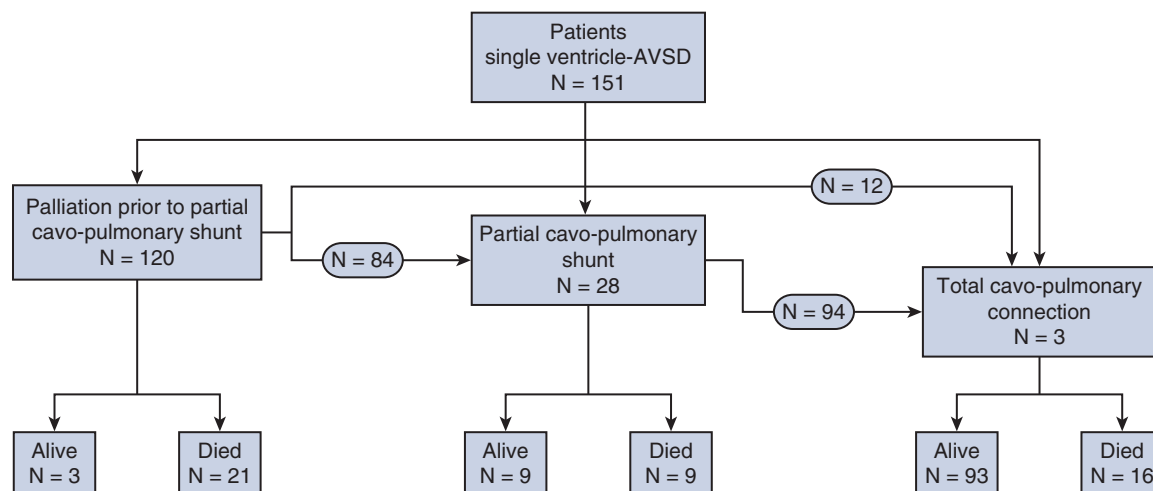


FIGURE 1. Flow-chart of 151 patients with single-ventricle AVSD. The flow-chart shows the main surgical steps of univentricular palliation: palliation before partial cavopulmonary shunt, partial cavopulmonary shunt, and total cavopulmonary connection. The interstage mortality and survival at follow-up are shown. AVSD, Atrioventricular septal defect.

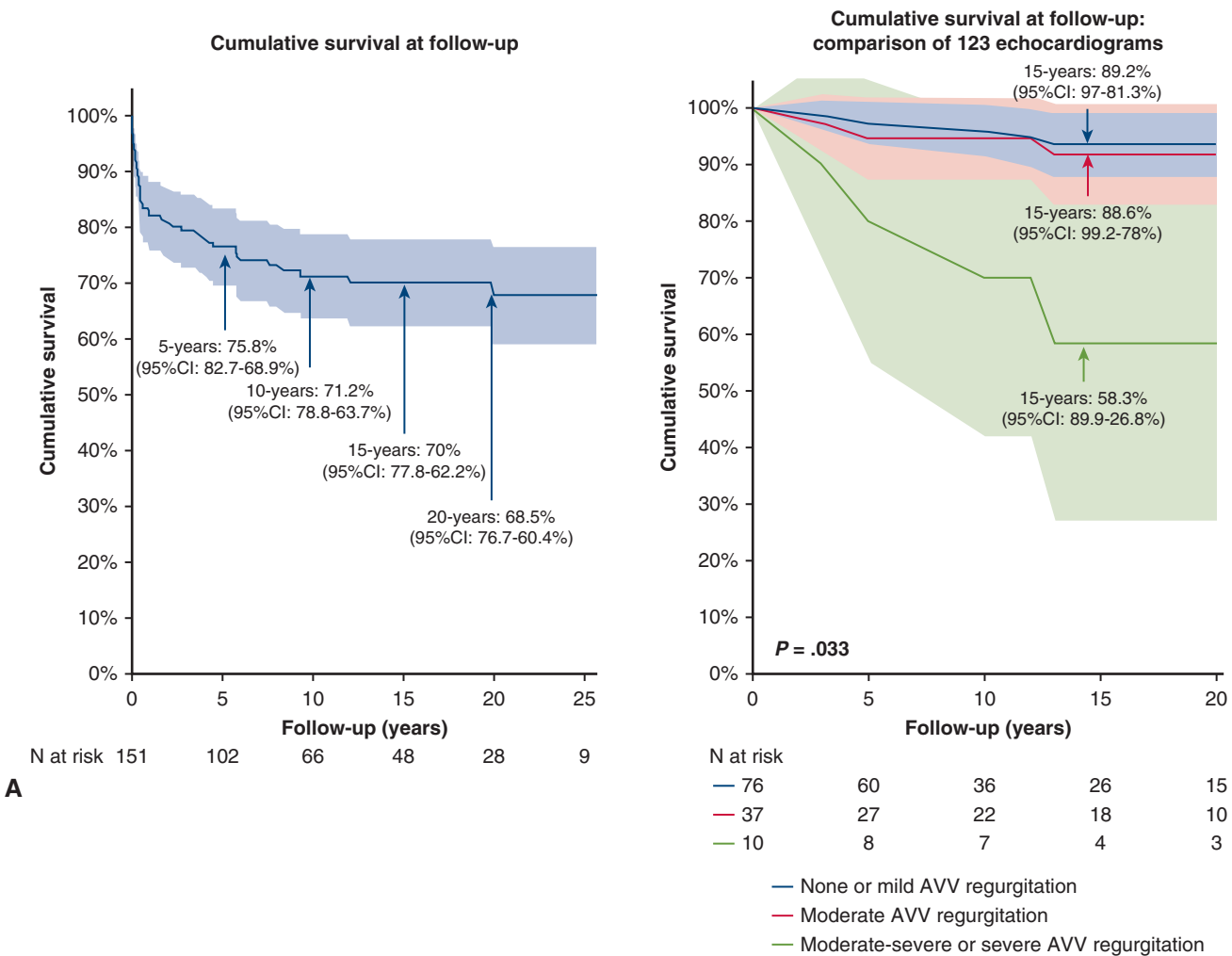


FIGURE 2. A, Overall cumulative survival at follow-up. B, Cumulative survival of 123 patients with available echocardiography at last follow-up comparing 3 categories: patients with no or mild AVV regurgitation (N = 76), patients with moderate AVV regurgitation (N = 37), and patients with moderate-severe or severe AVV regurgitation (N = 10). Shaded areas represent 95% CI. Time zero corresponds to the first surgical procedure performed per patient. AVV, Atrioventricular valve; CI, confidence interval.

account in a sensitivity analysis including AVV surgery as time-dependent covariate, AVV surgery was not a risk factor for mortality (hazard ratio, 1.35; 95% CI, 0.42-4.37, $P = .612$). Multivariable analysis identified a severe AVV regurgitation at follow-up as an independent risk factor for mortality (hazard ratio, 5.74, 95% CI, 1.54-21.43, $P = .009$).

Fontan Completion

The cumulative incidence of Fontan completion is shown in Figure 3: 56.5% at 5 years, 71% at 10 years, and 77.6% at 15 years. In 7 patients, the interval between PCPS and TCPC was longer than 10 years: Three patients had a previous Kawashima operation and then had their Fontan completion through an off-pump hepato-azygos shunt; the reason for delay for the other 4 patients is unknown.

Univariable and multivariable analyses of Fontan completion are shown in Table 3. In univariable analysis isomerism, decades of birth era and a concomitant syndrome were associated with the incidence of Fontan completion: Patients born in the last decade had a higher rate of Fontan completion, and patients with a concomitant syndrome and patients with left isomerism had a lower rate. AVV surgery was not associated with the incidence of Fontan completion ($P = .36$). In multivariable analysis, none of the factors were associated with incidence of Fontan completion.

Valve Surgery Group Analysis

Table 4 shows patients’ characteristics in the valve surgery group (36 patients). Among the surgical techniques for repair, annuloplasty and edge-to-edge were the most

TABLE 2. Univariable and multivariable analyses of mortality

Risk factors	Univariable analysis		Multivariable analysis	
	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
AVV surgery performed	1.18 (0.58-2.38)	.65		
Birth era				
1966-1999	1	.76*		
2000-2009	1.03 (0.46-2.30)	.95		
2010-2018	0.77 (0.30-1.97)	.59		
Female gender	1.34 (0.72-2.49)	.36		
Total anomalous pulmonary vein connection	1.54 (0.77-3.06)	.22		
Hypoplastic left ventricle	1.33 (0.72-2.45)	.37		
Isomerism				
No	1	.69*		
Left	0.70 (0.25-1.96)	.50		
Right	1.11 (0.57-2.17)	.75		
Concomitant syndrome	0.60 (0.27-1.33)	.20	0.27 (0.07-1.11)	.069
Severe AVVR at follow-up	4.55 (1.30-15.99)	.01	5.74 (1.54-21.43)	.009

Values in bold are statistically significant. *CI*, Confidence interval; *AVV*, atrioventricular valve; *AVVR*, atrioventricular valve regurgitation. *Wald test.

frequently performed. Mechanical valve replacement was performed in 2 patients.

The degree of valve insufficiency at postoperative echocardiography was none or mild in 26 patients, moderate in 4 patients, and moderate-severe or severe in 2 patients after the first repair. Freedom from AVV reoperation at follow-up was 85.7% at 1 year, 77.9% at 2 years, 52.6% at 5 years, and 47.3% at 10 years (Figure 4). An AVV reoperation was performed in 13 of 36 patients at a mean interval of 2.5 ± 1.8 months after the first operation.

Figure 5 shows the flow diagram of the patients in the valve surgery group. In 24 patients with no or mild postoperative AVV regurgitation after the first AVV operation, an AVV reoperation was performed in 5 patients. One patient had a moderate-severe AVV regurgitation after the AVV reoperation and died at follow-up because of Fontan failure. Fontan circulation was completed in 19 of 24 patients. In 4 patients with moderate AVV regurgitation after the first AVV operation, an AVV reoperation was performed in 2 patients. All 4 patients completed the Fontan circulation; 1

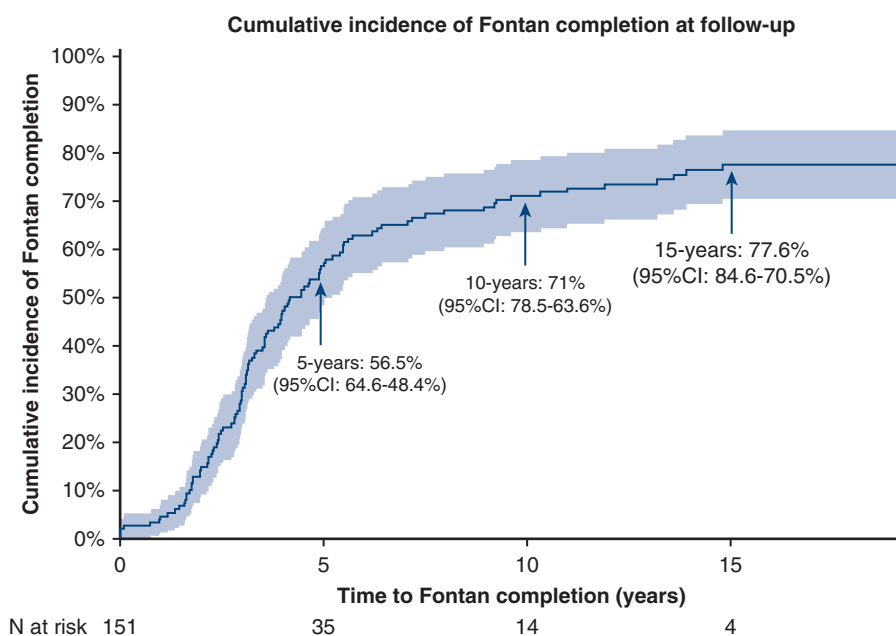


FIGURE 3. Overall cumulative incidence of Fontan completion at follow-up. Shaded area represents 95% CI. Time zero corresponds to the first surgical procedure performed per patient. *CI*, Confidence interval.

TABLE 3. Univariable and multivariable analyses of Fontan completion

Risk factors	Univariable analysis		Multivariable analysis	
	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
AVV surgery performed	1.26 (0.77-2.05)	.36		
Birth era				
1966-1999	1	.14*	1	.14*
2000-2009	1.18 (0.75-1.85)	.48	1.15 (0.72-1.86)	.55
2010-2018	1.66 (0.99-2.79)	.052	1.71 (0.99-2.95)	.0534
Female gender	1.18 (0.80-1.74)	.4		
Total anomalous pulmonary vein connection	1.10 (0.64-1.88)	.74		
Hypoplastic left ventricle	0.74 (0.50-1.09)	.13		
Isomerism				
No	1	.04*	1	.07*
Left	0.56 (0.33-0.93)	.026	0.69 (0.39-1.22)	.20
Right	1.02 (0.63-1.64)	.95	1.28 (0.76-2.14)	.35
Concomitant syndrome	0.69 (0.41-1.14)	.144	0.74 (0.42-1.31)	.30

Values in bold are statistically significant. CI, Confidence interval; AVV, atrioventricular valve. *Wald test.

patient who underwent an AVV replacement as reoperation died at follow-up, and 1 patient underwent a heart transplant after Fontan completion. All 4 patients with a moderate-severe or severe AVV regurgitation after the first AVV operation underwent an AVV reoperation. Only 1 patient could complete the Fontan circulation, 1 patient died before the completion and after AVV replacement, 1 patient was considered not eligible because of residual AVV regurgitation, and 1 patient was too young for the completion. Both patients who underwent a valve replacement as first valve surgery died at follow-up. In 2 patients, the degree of AVV regurgitation after the first valve repair was unknown. Freedom from AVV reoperation at 15 years in patients with no or mild AVV regurgitation after the first surgery was 76.5% compared with 33.3% in patients with moderate regurgitation ($P = .054$) and compared with 0% in patients with moderate-severe or severe regurgitation ($P < .001$). There was no significant difference in 15-year freedom from AVV reoperation between patients with moderate AVV regurgitation and patients with moderate-severe or severe regurgitation after the first AVV surgery ($P = .378$). The degree of AVV regurgitation after the first AVV surgery did not influence survival ($P = .981$) and incidence of Fontan completion ($P = .265$).

A valve replacement was performed in 3 patients by AVV reoperation: Two of the patients died during the hospitalization for valve replacement, which was performed together with TCPC. The degree of AVV regurgitation at postoperative echocardiography after the AVV reoperation was none or mild in 7 patients, moderate in 2 patients, and moderate-severe in 1 patient. In 3 patients, a third AVV reoperation was performed.

AVV surgery was performed before Fontan completion in 22 patients, at the time of TCPC in 14 patients, and after

TCPC in 1 patient. There was no difference in survival between patients who underwent an AVV surgery before Fontan completion and patients who underwent AVV surgery at the time of TCPC (at 15 years 59.3% vs 72.2%, respectively, $P = .34$). The same comparison showed a significant difference in terms of freedom from AVV reoperation: at 15 years 31.5% when AVV surgery was performed before Fontan completion compared with 87.5% when performed at the time of TCPC ($P = .03$). One patient who underwent AVV surgery after Fontan completion did not undergo an AVV reoperation.

DISCUSSION

Unbalanced AVSD in patients who require single-ventricle palliation is associated with poor survival; 60% at 25 years² and 50% at 2 years have been reported, although in smaller series.⁵ Our study including 151 patients with unbalanced AVSD who underwent single-ventricle palliation showed more favorable outcomes: 68.5% survival at 20 years.

Nevertheless, the 20-year survival of all categories of univentricular heart remains remarkably higher, approximately 80%.⁶⁻¹⁰ In addition, in our cohort of patients an associated syndrome did not increase the mortality and the survival of our cohort of patients with heterotaxy did not differ from that published in a recent meta-analysis.¹¹ Our study suggests that the presence of a genetic syndrome in association with single-ventricle AVSD does not preclude an excellent outcome for Fontan palliation.

Severe AVV regurgitation in single-ventricle physiology is known to be a risk factor for mortality, whereas a successful repair of the AVV could improve survival.¹²⁻¹⁵ Our study confirmed this finding because patients with no, mild, or moderate AVV regurgitation at follow-up had a significant

TABLE 4. Patient characteristics in valve surgery group

Valve surgery group (36 patients)				
Timing first AVV surgery	Pre-PCPS	7		
	At PCPS	12		
	Post-PCPS	17		
			Inter-stage	2
			At TCPC	14
			After TCPC	1
Degree of AVV regurgitation before surgery	Mild	1		
	Moderate	14		
	Moderate-severe	11		
	Severe	10		
Surgical technique	Annuloplasty	7		
	Edge-to-edge	7		
	Cleft closure	5		
	Commissuroplasty	3		
	Other or combined	12		
	Replacement	2		
Degree of AVV regurgitation after surgery (excluding valve replacement)	None	8		
	Mild	18		
	Moderate	4		
	Moderate-severe	2		
	Severe	2		
AVV reoperation in 13/36 patients				
Mean interval first operation up to reoperation (mo)	2.51 ± 1.8			
Surgical technique	Re-repair	10		
	Replacement	3		
Degree of AVV regurgitation after reoperation (excluding valve replacement)	None	2		
	Mild	5		
	Moderate	2		
	Moderate-severe	1		
	Severe	0		

AVV, Atrioventricular valve; PCPS, partial cavopulmonary shunt; TCPC, total cavopulmonary connection.

better survival than patients with moderate-severe or severe regurgitation, as clearly shown in Figure 6.

Our results merit interpretation in that at the end of Fontan completion the AVV should function satisfactorily and severe AVV regurgitation should be repaired adequately, even if it is at the cost of AVV surgery. Our study showed that AVV regurgitation that exceeds a moderate degree represents a risk factor for mortality in patients with single-ventricle AVSD and therefore should be repaired.

Our results in terms of cumulative incidence of Fontan completion (71% at 10 years) compare favorably to the literature, which varied between 40% and 60%.^{2,4,5} Multi-variable analysis did not identify independent risk factors for incidence of Fontan completion. Freedom from AVV reoperation in our cohort is not different from the range

previously reported, which varied between 45% and 56% at 15-year follow-up.^{4,12}

As expected, all patients with a moderate-severe or severe AVV regurgitation after the first AVV operation required an AVV reoperation and there was a significant difference in freedom from AVV reoperation compared with patients with no or mild AVV regurgitation (5/24 patients required AVV reoperation). However, a moderate-severe or severe degree of AVV regurgitation after the first AVV surgery did not significantly decrease survival or incidence of Fontan completion.

Valve replacement in patients with single ventricle does not have a favorable prognosis, although it could be the last option.¹⁶⁻¹⁹ In our study, a valve replacement was performed in only 2 patients as a first procedure, and both

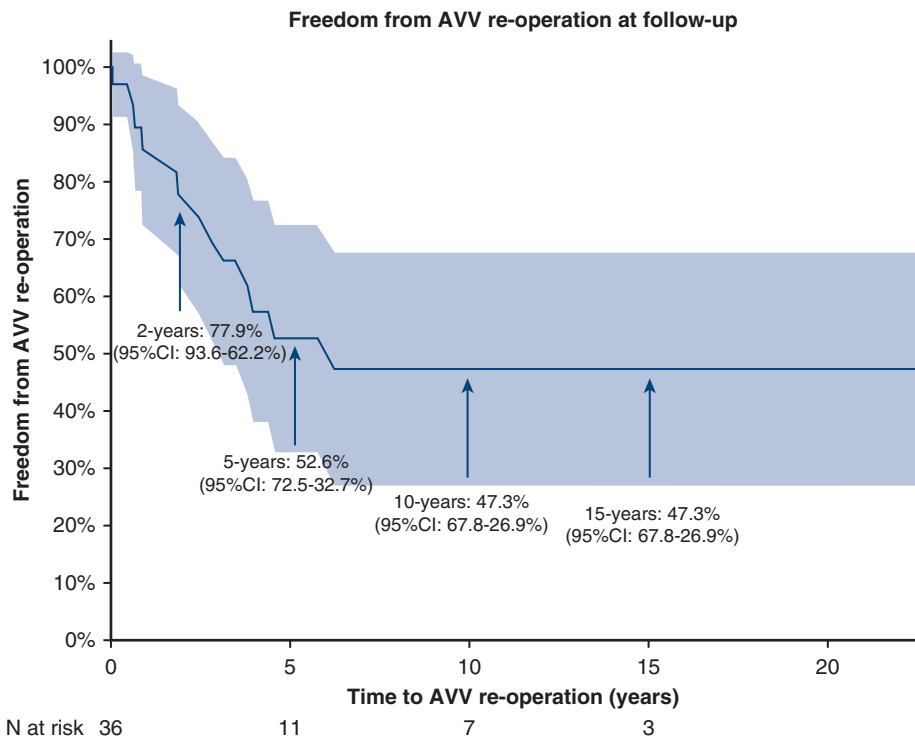


FIGURE 4. Freedom from AVV reoperation at follow-up in the valve surgery group. Time zero corresponds to the first AVV operation per patient. Shaded area represents 95% CI. AVV, Atrioventricular valve; CI, confidence interval.

patients died at follow-up. A valve replacement was performed in 3 patients as AVV reoperation. Two of the patients died during the hospitalization for valve replacement performed together with TCPC.

In regard to the timing of first AVV surgery, one-third of the operations were performed during PCPS, approximately half after PCPS and the majority during TCPC. The anticipated favorable effect of unloading the ventricle on AVV regurgitation may be a reason why the repair was delayed until TCPC in the majority of the patients. In fact, it could

be considered that the decrease in ventricular volume described after PCPS operation could result in reduction of atrioventricular annulus dimension, thereby improving the AVV regurgitation.^{20,21} Furthermore, in our study freedom from AVV reoperation was significantly lower in patients who underwent AVV surgery at the time of TCPC (87.5% at 15 years) compared with patients who underwent AVV surgery before Fontan completion (31.5% at 15 years, $P = .03$). However, the degree of AVV regurgitation, the deterioration of ventricular function, or the

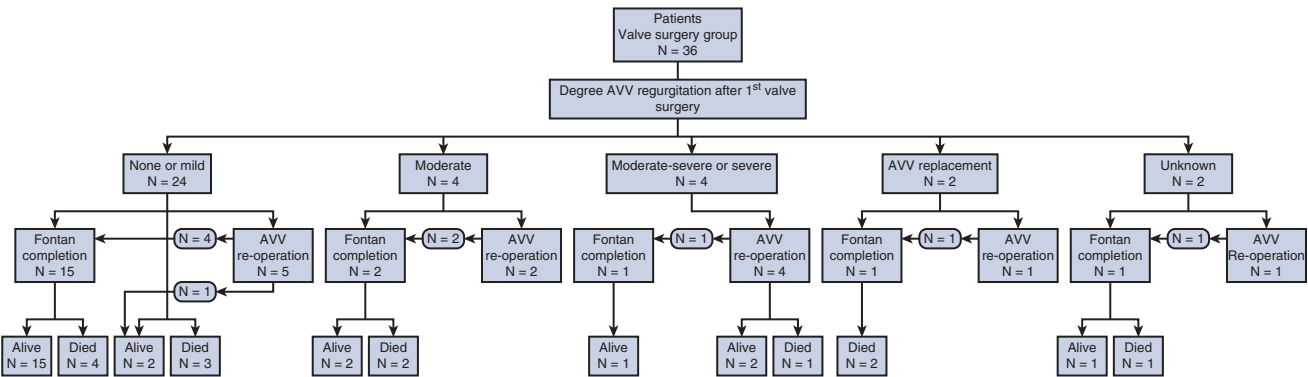


FIGURE 5. Flow-chart of 36 patients in valve surgery group. On the basis of the degree of AVV regurgitation after the first valve surgery, the patients were divided in 5 categories: none or mild, moderate, moderate-severe or severe, not estimable because of valve replacement, and unknown. Per category, the rates of Fontan completion and AVV reoperation are shown. Per category outcome (alive or died) at follow-up is reported. AVV, Atrioventricular valve.

Long-term outcomes of unbalanced atrioventricular septal defect and single ventricle: retrospective multi-center study of the Netherlands and Belgium

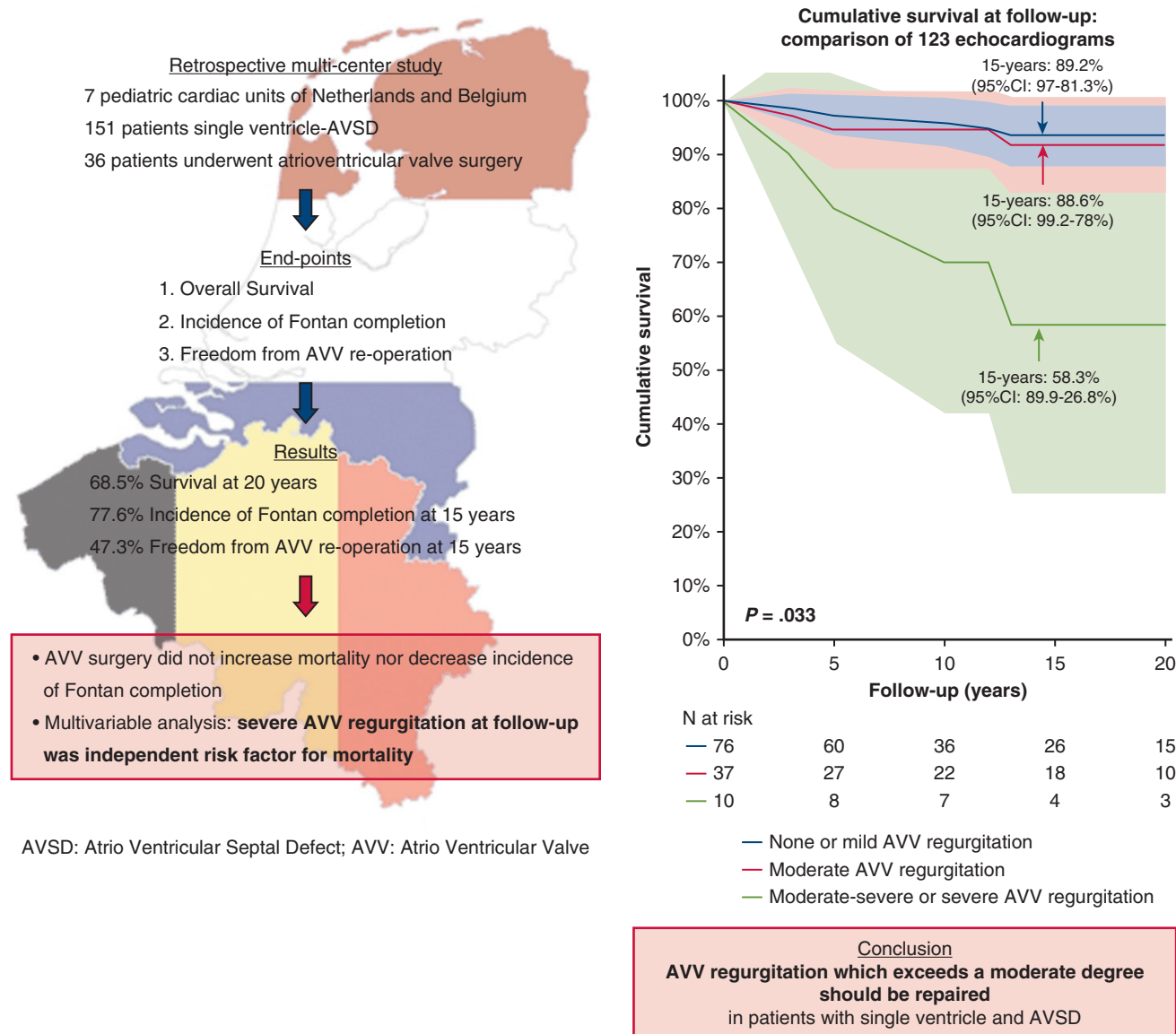
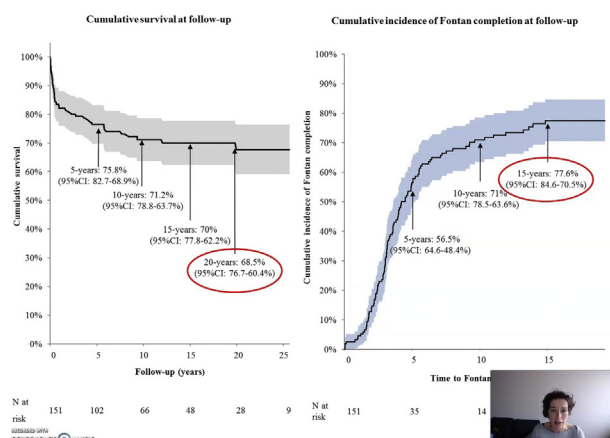


FIGURE 6. Our retrospective multicenter experience showed the results of 151 patients with single-ventricle AVSD of all 7 Dutch and Belgian congenital cardiac centers. AVV surgery was performed in 36 of the patients. Cumulative survival, incidence of Fontan completion, and freedom from AVV reoperation were the end points of the study. AVV surgery did not decrease survival or Fontan completion rate. The results of 123 echocardiographic studies at follow-up (shown in survival graph on the right side) found that patients with moderate-severe or severe AVV regurgitation had a worse survival compared with patients with no/mild or moderate AVV regurgitation. Our results showed that an AVV regurgitation exceeding a moderate degree should be repaired before finalizing Fontan circulation. AVSD, Atrioventricular septal defect; AVV, atrioventricular valve; CI, confidence interval.

patient's clinical picture did not allow us to wait until Fontan completion. AVV surgery performed before PCPS is unusual. In our study, only 7 patients underwent an AVV repair before PCPS, yielding disappointing results in 3 patients who still showed severe regurgitation postoperatively and required a take-down of the repair in 1 patient because the

regurgitation was even worse after the AVV repair. However, addressing severe AVV regurgitation at the initial palliative stage is advisable based on the favorable effect of a competent AVV on survival and Fontan completion, bearing in mind that its result might be imperfect and the likelihood of reoperation is high.



VIDEO 1. The highlights of our study describing the long-term outcome of 151 patients with single-ventricle AVSD as result of a joint scientific cooperation of all Belgian and Dutch pediatric cardiac units. Video available at: [https://www.jtcvs.org/article/S0022-5223\(21\)00800-X/fulltext](https://www.jtcvs.org/article/S0022-5223(21)00800-X/fulltext).

Study Limitations

The main limitation of this study is its retrospective and multicenter nature. There was a significant difference in the prevalence of AVV surgery among centers. This difference could be explained by the heterogeneous criteria for concomitant AVV surgery that could have varied over the decades, influencing patient selection among the participating centers. Moreover, the criteria for eligibility for Fontan completion may have varied among centers because of different clinical judgment and patient selection. We did not collect all echocardiograms performed per patient at follow-up to identify the first echocardiography where severe or moderate AVV regurgitation appeared; therefore, we could not analyze the degree of AVV regurgitation as a time-dependent covariate.

CONCLUSIONS

The “BeNe” experience of patients with AVSD Fontan showed 20-year survival of 68.5% and 10-year cumulative incidence of Fontan completion of 71%, both better than previously described (Video 1). A concomitant AVV surgery did not increase the mortality rate or decrease the incidence of Fontan completion, whereas patients with moderate-severe or severe AVV regurgitation at follow-up had a worse survival, reflecting the need for adequate AVV function. Therefore, in patients with single-ventricle AVSD, AVV regurgitation that exceeds a moderate degree should be repaired.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or

reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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