Does leaving native antegrade pulmonary blood flow at the time of the superior cavopulmonary connection impact long-term outcomes after the Fontan?

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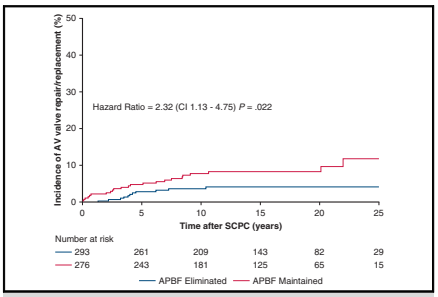
ABSTRACT

Objectives: Antegrade pulmonary blood flow (APBF) may be left or eliminated at the time of the superior cavopulmonary connection (SCPC). Our aim was to assess the impact of leaving native APBF at the SCPC on long-term Fontan outcomes.

Methods: In the Australia and New Zealand Fontan Registry (1985-2021), 587 patients had pre-existing native APBF at the SCPC. At the SCPC, 302 patients had APBF eliminated ($APBF^-$) and 285 patients had APBF maintained ($APBF^+$). The incidence of Fontan failure (composite end point of Fontan takedown, transplant, plastic bronchitis, protein losing enteropathy and death) and atrioventricular (AV) valve repair/replacement post SCPC was compared between the 2 groups.

Results: Sex, predominant-ventricle morphology, isomerism, primary diagnosis, and age/type of Fontan were similar between groups. $APBF^-$ versus $APBF^+$ had a higher incidence of arch obstruction/coarctation (17% vs 7%) and previous pulmonary artery band (54% vs 45%) and a lower rate of Fontan fenestration (27% vs 41%). The risk of Fontan failure was similar between the 2 groups (hazard ratio [HR], 1.01; 95% confidence interval [CI], 0.58-1.78; $P = .96$). The risk of AV-valve repair/replacement was greater in $APBF^+$ versus APBF– (HR, 2.32; CI, 1.13-4.75; $P = .022$). The risk of AV-valve repair/replacement remained after adjustment for arch obstruction/coarctation, previous pulmonary artery band and Fontan fenestration (HR, 2.27; CI, 1.07-4.81; $P = .033$).

Conclusions: Maintaining APBF at the time of the SCPC does not impact the risk of Fontan failure but may increase the incidence of AV-valve repair and/or replacement post-SCPC. (JTCVS Open 2023;16:825-35)



Cumulative incidence of AV-valve repair or replacement in both groups after SCPC.

CENTRAL MESSAGE

Maintaining native APBF at the SCPC is associated with a greater incidence of AV-valve failure after Fontan completion but does not seem to impact other long-term outcomes after the Fontan.

PERSPECTIVE

Maintaining native APBF at the time of the SCPC has potential advantages and disadvantages with diverse practice and conflicting evidence. We have demonstrated a greater incidence of AV-valve failure in those who have had APBF maintained, which is known to affect long-term outcomes after the Fontan. This has been demonstrated in a larger cohort and with longer follow-up time than previous studies.

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Abbreviations and Acronyms

ANZFR = Australia and New Zealand Fontan Registry
APBF = antegrade pulmonary blood flow
$APBF^{-}$ = antegrade pulmonary blood flow eliminated at the time of the SCPC
$APBF^{+}$ = antegrade pulmonary blood flow maintained at the time of the SCPC
AV = atrioventricular valve
AVVR = atrioventricular valve regurgitation
BDG = bidirectional Glenn shunt
CI = confidence interval
DKS = Damus-Kaye-Stansel
HR = hazard ratio
IQR = interquartile range
SCPC = superior cavopulmonary connection

The superior cavopulmonary connection (SCPC) is the standard interim procedure for surgical palliation of patients with single-ventricle physiology before Fontan completion. It is used to stabilize pulmonary blood flow while alleviating volume loading of the systemic ventricle.[1,2] There is a certain subgroup of patients with single-ventricle physiology in whom a clinical decision is made at the time of the SCPC as to whether to maintain or interrupt native antegrade pulmonary blood flow (APBF). Whether APBF should be preserved or eliminated at the time of the SCPC remains controversial. Preserving APBF has been shown to improve systemic arterial saturation and promote growth of the pulmonary arteries following the SCPC.[3-8] However, preserving APBF has been associated with increased interstage mortality and morbidity, including prolonged chest tube drainage[6,9-13] and longer hospital length of stay at the time of the SCPC.[6,14] Putative adverse effects of preserving APBF include elevation of systemic venous pressure and increased ventricular volume loading, which may negatively impact the single-ventricle circulation.[6,10-12] Long-term data on the impact of leaving APBF at the time of the SCPC is limited. We therefore reviewed data from the Australian and New Zealand Fontan Registry to investigate the impact of leaving native APBF at the time of the SCPC on long-term outcomes after the Fontan procedure.

METHODS

The Australian and New Zealand Fontan Registry (ANZFR) is a binational registry that was established in 2008 and includes patients who had their Fontan procedure from 1975 in either country, as well as patients who had their Fontan procedure overseas who are followed up within the region. When the ANZFR was created, all Fontan procedures were audited retrospectively, and this information was entered into a REDcap database (hosted by the Murdoch Children's Research Institute). Prospective follow-up information continues to be collected annually for patients who consented to participate in the ANZFR. Ethical approval for the ANZFR was obtained from the lead human research ethics committee (Royal Children's Hospital Melbourne HREC Project number 28121; approved July 18, 2008) and site-specific approval at all participating centers. Informed consent was obtained from parents and/or patients for access to health-related information from medical records from participating sites and for use of deidentified data in research publications. The design, structure, and protocol for the ANZFR has been previously described.[15] Data for this study were extracted from the ANZFR REDCap database on March 22, 2022.

Patient Selection/Data Collection

A total of 1589 Fontan operations were recorded for patients born from January 1985 to June 2019. Only patients with native antegrade pulmonary blood flow before the SCPC were included for analysis (Figure 1). A total of 783 patients were excluded who had an initial cardiac diagnosis of pulmonary atresia or where APBF was eliminated at the first palliation before the SCPC; for example, hypoplastic left heart syndrome postneonatal Damus–Kaye–Stansel (DKS) or initial Starnes procedure. For the remaining 806 patients, baseline characteristics, operative details, and follow-up data were extracted from the ANZFR including from clinical summaries, hospital discharge, and outpatient records. In total, 48 patients had inadequate pre-Fontan information to determine APBF status at the time of the SCPC operation. There were 171 patients who underwent single-stage Fontan completion who were excluded from the analysis; of these, 128 had a previous pulmonary artery band or systemic to pulmonary artery shunt as their initial palliation, and 43 had no previous procedures. The remaining 587 patients who had APBF before the SCPC (including bidirectional Glenn shunt [BDG; n = 506], bilateral BDG [n = 52], Kawashima [n = 11], BDG and Kawashima [n = 4], and hemi-Fontan [n = 14]) constituted the cohort of this study. Clinical data collated from the ANZFR included baseline characteristics, cardiac diagnoses, pre-Fontan procedures, pre-Fontan cardiac catheter data, Fontan surgical data, and follow-up data.

PRIMARY AND SECONDARY END POINTS

The primary end points of interest were Fontan failure and atrioventricular (AV)-valve failure. Fontan failure was defined as a composite end point of death, heart transplantation, Fontan takedown, plastic bronchitis, and/or protein-losing enteropathy, whichever occurred first. AV valve failure was defined as AV-valve repair, replacement, or patch closure for the indication of atrioventricular-valve regurgitation (AVVR) *after* the SCPC.

Secondary end points were (1) oxygen saturation, mean pulmonary artery pressure, aortopulmonary or venovenous collateral vessels (presence yes/no), pulmonary arteriovenous malformation (presence yes/no) documented at the

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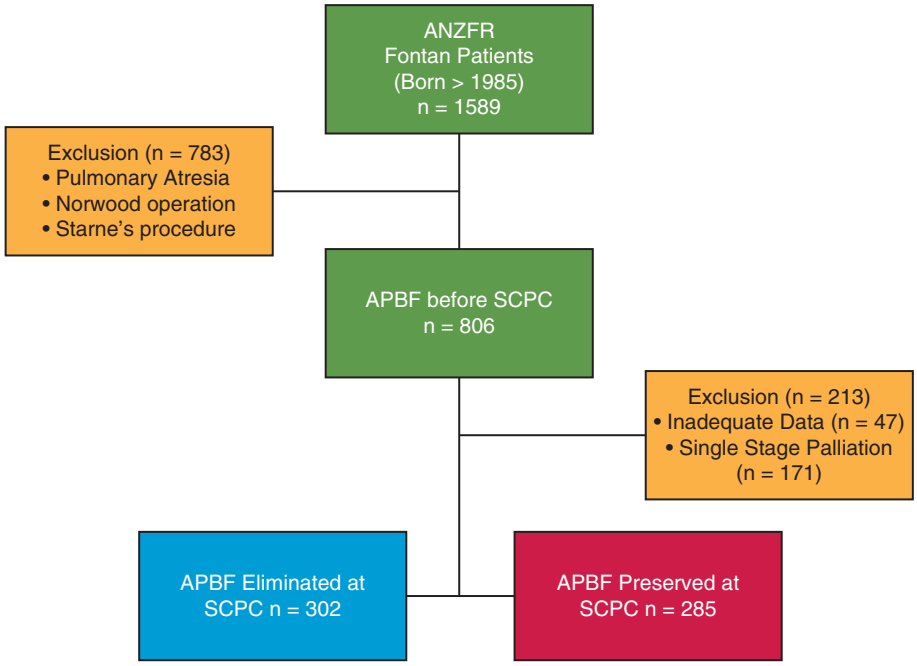

FIGURE 1. Flow diagram of study cohort in each group. Among the 1589 patients who underwent Fontan in the ANZFR, there were 806 who had pre-existing APBF before the SCPC. Patients with pulmonary atresia, previous Norwood, or Starne's procedure and those who underwent single-stage palliation or had inadequate data to determine APBF status were excluded. APBF was eliminated in 302 patients ($APBF^-$) and maintained in 285 patients ($APBF^+$). *ANZFR*, Australia and New Zealand Fontan Registry; *APBF*, antegrade pulmonary blood flow; *SCPC*, superior cavopulmonary connection.

pre-Fontan cardiac catheter; (2) hospital length of stay at the time of the Fontan procedure; and (3) ventricular function at last post-Fontan follow-up (qualitative echocardiogram assessment obtained from outpatient reports and categorized as normal, mild-to-moderate dysfunction, or moderate-to-severe dysfunction).

STATISTICAL ANALYSES

All statistical analyses were performed in R software (version 4.2.1; R Foundation for Statistical Computing). Patient baseline characteristics were summarized using median and interquartile range (IQR) or mean and standard deviation for continuous variables and counts and percentages for categorical variables. Unless stated otherwise, the calculation of percentages did not include the missing category. If applicable, the number of missing data points was reported in the manuscript and tables. Comparisons of baseline characteristics between $APBF^-$ and $APBF^+$ groups were based on either Student *t* test or the Wilcoxon rank sum test for continuous variables or Fisher exact test for categorical variables. Time to Fontan failure was measured from the Fontan procedure to the time of the first Fontan failure event or censored at the last time known alive and was depicted with Kaplan–Meier curves with corresponding 95% confidence intervals (CIs). Time to AV-valve failure was measured from the SCPC operation to the first instance of AV-valve failure and was censored at the time the patient was last known alive with death and heart transplantation as competing risks. Cumulative incidence curves were used to depict time to AV-valve failure with corresponding 95% CIs. Cause-specific Cox regression was used to obtain the hazard ratio (HR) (and corresponding 95% CI) for the risk of AV-valve failure in $APBF^-$ compared with $APBF^+$ groups. Adjustment for potential confounders (arch obstruction/coarctation, previous pulmonary artery band, and Fontan fenestration) was also performed using multivariable cause-specific Cox regression. An analysis strategy of matching using propensity scores as weights was explored but then not pursued, as the number of outcome events became prohibitively small.

RESULTS

Baseline Characteristics

There were 302 patients who had APBF eliminated (ie, $APBF^-$) and 285 patients who had it maintained (ie, $APBF^+$) at the time of SCPC. In those patients who were $APBF^+$ at the time of the SCPC, there were 6 patients who had APBF eliminated before Fontan completion for related complications including prolonged chylothorax. There were 8 patients who had antegrade flow maintained after the Fontan, and the remaining 271 patients who had it eliminated at the time of the Fontan.

The baseline characteristics of patients are displayed in Table 1. The median length of follow-up from the Fontan was 10.8 years (IQR, 5.1-16.4 years) or 14.9 years from the SCPC (IQR, 9.3-20.5 years). Age, sex, predominant

TABLE 1. Baseline characteristics of both groups

Characteristic	APBF^{-} n = 302 (%)	APBF^{+} n = 285 (%)	*P* value
Surgical site			
New South Wales	129 (43)	72 (25)	<.001
New Zealand	43 (14)	76 (27)	
Queensland	38 (13)	34 (12)	
Victoria	85 (28)	86 (30)	
Western Australia	7 (2)	17 (6)	
Sex			
Male	171 (57)	160 (56)	.934
Predominant ventricle			
Biventricular	26 (9)	23 (8)	.939
Indeterminate	12 (4)	12 (4)	
Left	186 (62)	179 (63)	
Right	76 (25)	65 (23)	
Missing	2 (1)	6 (2)	
Isomerism			
LAI	12 (4)	9 (3)	.520
RAI	24 (8)	16 (6)	
Missing	2	7	
Primary diagnosis			
Tricuspid atresia	84 (28)	99 (35)	.001
DILV	68 (23)	47 (16)	
uAVSD	46 (15)	35 (12)	
DORV	45 (15)	42 (15)	
Mitral atresia	27 (9)	13 (5)	
ccTGA	22 (7)	14 (5)	
Complex TGA	6 (2)	21 (7)	
Ebstein anomaly	0 (0)	3 (1)	
Other	4 (1)	11 (4)	
Secondary diagnosis			
Arch obstruction	52 (17)	21 (7)	<.001
TAPVR	14 (5)	14 (5)	>.999
Genetic diagnosis			
Yes	32 (11)	27 (9)	.682
Procedures before Fontan			
PA band	162 (54)	128 (45)	.039
Systemic to PA shunt	71 (24)	112 (39)	<.001
Arch repair	50 (17)	17 (6)	<.001
TAPVR repair	9 (3)	11 (4)	.651
Procedures before SCPC to pulmonary blood flow			
Native PBF (no previous palliation)	75 (25)	75 (26)	<.001
Systemic to PA shunt	65 (22)	107 (38)	
PA band	156 (52)	97 (34)	
PA band and shunt	6 (2)	6 (2)	
Fontan type			
ECC	270 (89)	249 (87)	.333
LT	30 (10)	34 (12)	
AP	2 (1)	0 (0)	
Missing	0 (0)	2 (1)	

(Continued)

TABLE 1. Continued

Characteristic	APBF$^-$ n = 302 (%)	APBF$^+$ n = 285 (%)	*P* value
Fontan era			
1990-1999	47 (16)	36 (13)	.455
2000-2009	126 (42)	137 (48)	
2010-2019	119 (39)	103 (36)	
2020-2021	10 (3)	9 (3)	
Fontan fenestration			
Yes	79 (26)	115 (40)	<.001
No	218 (72)	165 (58)	
Missing	5 (2)	5 (2)	
Age at Fontan, y			
Median age	4.64	4.81	.05
IQR	(3.88-5.55)	(3.94-6.17)	
Age at SCPC, y			
Median age	1.01	0.90	.69
IQR	(0.59-1.54)	(0.48-1.93)	
Interval SCPC to Fontan, y			
Median age	3.51	3.73	.07
IQR	(2.67-4.40)	(2.78-4.64)	

Percentages relate to proportion within a column. *APBF$^-$*, Antegrade pulmonary blood flow eliminated; *APBF$^+$*, antegrade pulmonary blood flow maintained; *LAI*, left atrial isomerism; *RAI*, right atrial isomerism; *DILV*, double-inlet left ventricle; *ıAVSD*, unbalanced atrioventricular septal defect; *DORV*, double-outlet right ventricle; *ccTGA*, congenitally corrected transposition of the great arteries; *TGA*, transposition of the great arteries; *TAPVR*, total anomalous pulmonary venous return; *PA band*, pulmonary artery band; *SCPC*, superior cavopulmonary connection; *PBF*, pulmonary blood flow; *ECC*, extra cardiac conduit; *LT*, lateral tunnel; *AP*, atriopulmonary connection; *IQR*, interquartile range.

ventricle, cardiac diagnosis, primary cardiac position, and genetic diagnosis were similar between the 2 groups. Patients in the APBF$^-$ group had a greater incidence of arch obstruction (17% vs 7%, $P < .001$) compared with the APBF$^+$ group. The proportion with total anomalous pulmonary venous return or isomerism was similar between the 2 groups. In the APBF$^+$ group, a greater proportion of patients had a systemic to pulmonary artery shunt before the SCPC than in the APBF$^-$ group (39% vs 24% $P < .001$). The type of Fontan and Fontan era were similar between the 2 groups. The median age at Fontan was also similar between the 2 groups (4.64 vs 4.81 years, $P = .05$). The APBF$^+$ group had a greater incidence of Fontan fenestration (41% vs 27%, $P < .001$).

Fontan Failure

The risk of Fontan failure was similar between the 2 groups (HR, 1.01; CI, 0.58-1.78; $P = .96$) (Figure 2).

AV-Valve Intervention

The risk of AV-valve failure was greater in the APBF$^+$ group compared with the APBF$^-$ group (HR, 2.32; CI, 1.13-4.75; $P = .022$) (Figures 3 and 4). When we adjusted for potential confounding variables (arch obstruction, pulmonary artery band, systemic-to-pulmonary artery shunt, and Fontan fenestration) the increased risk of AV-valve failure remained significantly greater (HR, 2.27; CI, 1.07-4.81; $P = .033$). When surgical center was included in the same model, the association remained significant (HR, 2.44; 95% CI, 1.11-5.35; $P = .027$). When adjusting for era, the risk of AV-valve intervention remained greater in the APBF$^+$ group (HR, 2.23; 95% CI, 1.13-4.76).

In our cohort, a total of 62 of 587 patients underwent at least 1 AV-valve operation either before or after the Fontan operation. Thirty patients were excluded from this part of the analysis: 28 patients who had AV-valve operation before or at the time of the SCPC (that is, before the decision to eliminate or maintain APBF) and 2 patients who had AV-valve operations for indications other than AV-valve regurgitation (1 patient had mitral valve closure as the mitral valve was causing systemic outlet obstruction, 1 patient had the tricuspid valve damaged intraoperatively). The characteristics of the remaining 32 patients with AV-valve failure are shown in Table 2. The median age at first AV-valve operation was 4.8 years (IQR, 3.75-8.2 years). The index AV-valve intervention was AV-valve repair in 23 patients, AV-valve replacement in 4 patients, and AV-valve patch closure in 5 patients. The most common valve morphology was unbalanced AV septal defect (n = 13, 40%), followed by a tricuspid valve (n = 10, 31%), and then a mitral valve (n = 9, 28%). Of the 32 patients who had AV-valve intervention, 10 patients (31%) also had Fontan failure.

Exclusion of Those Requiring a DKS Anastomosis at the Time of SCPC

In those subjects requiring a DKS at or soon after the SCPC, APBF cannot be maintained because the main

TABLE 2. Characteristics of patients who underwent AV-valve intervention

Characteristic	N = 32	%
APBF		
APBF^{+}	21	66%
APBF^{-}	11	34%
Location		
New South Wales	7	22%
New Zealand	9	28%
Queensland	3	9%
Victoria	12	38%
Western Australia	1	3%
Sex		
Male	15	47%
Isomerism		
LAI	4	13%
RAI	8	25%
None	20	63%
Primary diagnosis		
Unbalanced AVSD	13	41%
DORV	5	16%
DILV	5	16%
Tricuspid atresia	4	12%
Other	5	16%
Secondary diagnosis		
Arch obstruction	6	19%
TAPVR	7	22%
Previous procedures		
PA band	19	60%
Systemic to PA shunt	11	34%
Fontan fenestration		
Yes	14	44%
Predominant ventricle		
Right	6	19%
Left	22	69%
Biventricular	2	6%
Indeterminate	2	6%
AV-valve morphology		
Common AV valve	13	41%
Mitral valve	9	28%
Tricuspid valve	10	31%
Average age at Fontan		
Median, y	5.15	IQR (4.2-7.9)
Time from SCPC		
Median, y	4.02	IQR (2.3-7.1)
Type of intervention		
Repair	23	72%
Replacement	4	12%
Patch closure	5	16%
Outcomes		
Died	5	16%
Transplant	2	6%
PLE/PB	2	6%
Fontan takedown	1	3%

APBF^{-}, Antegrade pulmonary blood flow eliminated; *APBF^{+}*, antegrade pulmonary blood flow maintained; *LAI*, left atrial isomerism; *RAI*, right atrial isomerism; *AVSD*, atrioventricular septal defect; *DORV*, double-outlet right ventricle; *DILV*, double-inlet left ventricle; *TAPVR*, total anomalous pulmonary venous return; *PA*, pulmonary artery; *AV*, atrioventricular valve; *IQR*, interquartile range; *SCPC*, superior cavopulmonary connection; *PLE*, protein-losing enteropathy; *PB*, plastic bronchitis.

pulmonary artery is incorporated into the systemic outflow. In the APBF^{-} group after excluding patients who underwent a DKS at the time of the SCPC (n = 81), there remained a group of patients (n = 221) where a decision was made to eliminate APBF. When compared with this group, the APBF^{+} group still had an increased risk of AV-valve failure post-Fontan completion (HR, 2.13; 95% CI, 0.99-4.61; $P = .05$). The risk of Fontan failure was the same in both groups (HR, 0.91; 95% CI, 0.50-1.65; $P = .76$).

Secondary Outcomes

Oxygen saturations at the pre-Fontan cardiac catheter were similar between the 2 groups, 83.7% ± 6.2% in APBF^{+} versus 82.6% ± 6.6% in the APBF^{-} group ($P = .07$; APBF^{+} [n = 233, missing data n = 52], APBF^{-} [n = 243, missing data n = 59]). Mean pulmonary artery pressure before Fontan completion was slightly greater in the APBF^{+} group (n = 234, missing data n = 51) than the APBF^{-} group (n = 244, missing data n = 58) (11.7 ± 4.5 mm Hg vs 10.5 ± 2.4 mm Hg, $P < .001$). There was no difference between the 2 groups in presence of collateral vessels at the pre-Fontan cardiac catheter, 33% in APBF^{-} group (n = 256; missing data n = 46) versus 38% in the APBF^{+} group (n = 240; missing data n = 45) $\chi^2_{(3,\ 482)} = 1.353$ ($P = .72$). The presence of pulmonary arteriovenous malformations at the pre-Fontan cardiac catheter was similar between the 2 groups, 9% in ABPF^{+} group (n = 234, missing data n = 51) versus 7% in ABPF^{-} group (n = 249, missing data n = 53). Hospital length of stay at the time of the Fontan was marginally shorter in the APBF^{+} group (n = 227, missing data n = 58) than the APBF^{-} group (n = 259, missing data n = 43) (median of 13 days [IQR 10-19] vs 14 days [IQR 11-20] $P = .04$). There was no significant difference in ventricular function at last follow up between the 2 groups (Table E1).

DISCUSSION

Our principal findings in relation to maintaining or eliminating APBF at the time of SCPC were (1) equivalent freedom from Fontan failure and (2) greater AV failure in those with APBF maintained. The strengths of our study

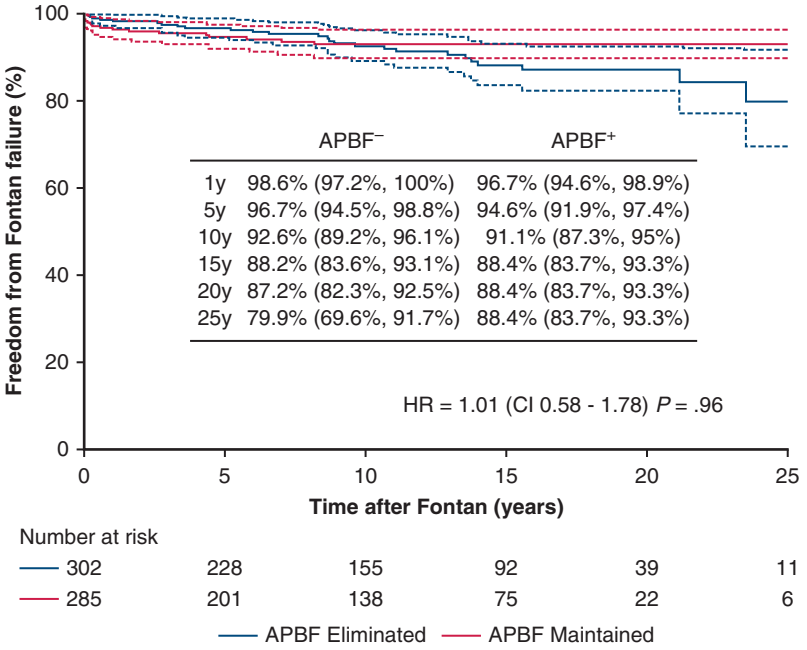

FIGURE 2. Cumulative incidence of freedom from Fontan failure after Fontan in both groups. The risk of Fontan failure was similar between the 2 groups, HR 1.01 (CI 0.58-1.78), $P = .96$. Confidence limits 95%. *APBF*$^{-}$, Antegrade pulmonary blood flow eliminated; *APBF*$^{+}$ antegrade pulmonary blood flow maintained; *HR*, hazard ratio; *CI*, confidence interval.

include the relatively large cohort size (n = 587) and long duration of follow-up (median 14.9 years from the time of SCPC or 10.8 years from Fontan). Furthermore, unlike some studies, which have included patients with pulmonary atresia or hypoplastic left heart syndrome with pulsatile and nonpulsatile pulmonary blood flow,[3-8,11,13,14,16,17] we have only included those patients with preexisting native APBF. This is a group of patients where a clinical decision is made to maintain or eliminate native antegrade pulmonary blood flow when performing the SCPC.

Impact of Leaving APBF on Pulmonary Artery Development

A putative reason for maintaining APBF is to stimulate pulmonary artery growth and pulmonary vascular development. Pulmonary endothelial dysfunction has been demonstrated in patients with a Fontan circulation, which is hypothesized to be related to the absence of pulsatile flow, which in turn may influence pulmonary vascular resistance.[18-20]

Some studies have demonstrated that maintaining APBF at the time of the SCPC improves pulmonary artery growth after the SCPC.[3,5,6,8,10,16] Ferns and colleagues[6] and Gray and colleagues[8] demonstrated maintenance of pulmonary artery growth more in line with somatic growth in patients who had APBF maintained at the time of the SCPC. Ferns and colleagues[16] also demonstrated that pulmonary artery growth in these patients continued after APBF was ligated at the time of the Fontan; however, these changes did not confer any additional clinical benefit. None of these studies demonstrated any benefit in survival in those with APBF maintained.[3,5,6,8,10,16] In contrast, Berdat and colleagues[21] did not demonstrate any difference in pulmonary artery growth in those with APBF preserved at the time of the SCPC.

Impact of Leaving APBF on Oxygen Saturations

Another putative reason for maintaining APBF is improvement in oxygen saturations. Maintenance of APBF has been associated with improved oxygen saturations pre-Fontan in some[6,8-10,17] but not all[5,7,21] studies. Some studies have demonstrated a benefit in maintaining APBF for the prevention of pulmonary arteriovenous malformations.[11,22] However, other studies have reported no significant difference in pulmonary arteriovenous malformations in those with APBF.[3,4,23] On the pre-Fontan cardiac catheter, we could not demonstrate any significant difference between the groups in oxygen saturation or presence of collaterals or pulmonary arteriovenous malformations.

Impact of Leaving or Eliminating APBF on Survival

Previous studies have provided conflicting results on the impact of maintaining APBF on survival with limited data on the long-term outcomes post-Fontan.[7,10,24] For example, in the study by Baek and colleagues (n = 110 APBF^{-} and n = 92 APBF^{+} with n = 104 and n = 81, respectively, achieving Fontan completion), the authors reported worse transplant-free survival after SCPC in the APBF^{+} group

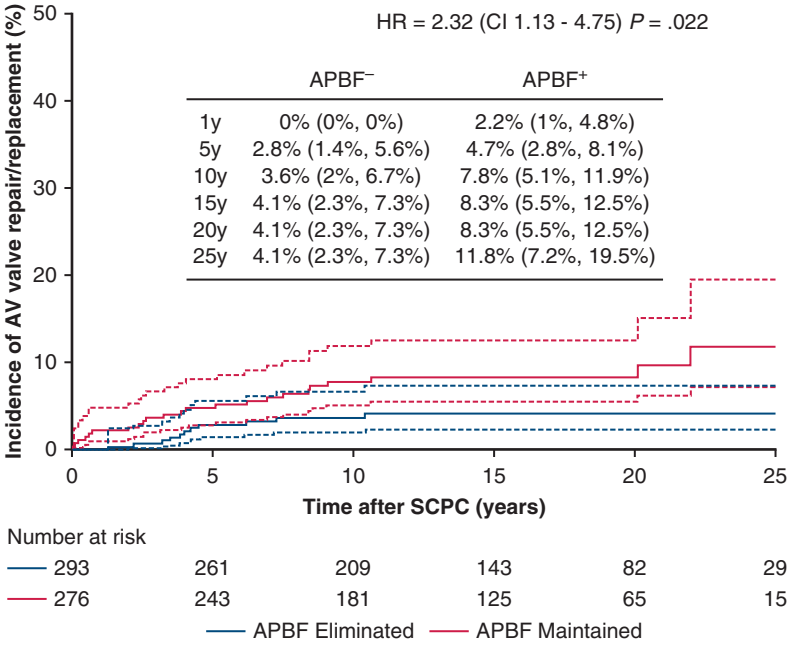

FIGURE 3. Cumulative incidence of AV-valve repair or replacement in both groups after SCPC. The risk of AV-valve repair or replacement was 2.32 times greater in the APBF+ group. Confidence limits 95%. *HR*, Hazard ratio; *CI*, confidence interval; *APBF*$^{-}$, antegrade pulmonary blood flow eliminated; *AV*, atrioventricular; *APBF*$^{+}$ antegrade pulmonary blood flow maintained; *SCPC*, superior cavopulmonary connection.

compared with the APBF^{-} group (HR, 2.37; CI, 1.089-5.152; $P = .03$). The cumulative incidence of death or transplant in both groups was steepest in the first 3 years after SCPC and plateaued after Fontan completion The mean duration of follow-up after Fontan was 8.4 ± 4.8 years.[10] By contrast, in the study by Chen and colleagues[7] (n = 54 APBF^{-} and n = 57 APBF^{+} with n = 35 and n = 30, respectively, achieving Fontan completion), the authors demonstrated a lower mortality in the APBF^{+} group compared with the APBF^{-} group (10-year survival of 96% [84%-98%] in APBF^{+} vs 82% [66%-91%] in APBF^{-}).[7] Once again, the majority of deaths in this study occurred in the interstage period between SCPC and Fontan completion. In our larger study, in which all patients have already achieved Fontan completion, we found no impact of leaving or eliminating APBF on the composite endpoint of Fontan failure which included death and transplantation.

Impact of Leaving or Eliminating APBF on AV-Valve Regurgitation

AVVR is a known risk factor for adverse outcome in patients undergoing Fontan palliation, associated with increased risk of Fontan circulation failure, morbidity, and premature mortality.[25,26] Although Baek and colleagues[10] found no significant difference in severity of AVVR before the Fontan or need for interstage AV-valve procedures, these authors noted that of 11 interstage events (death or transplant) 7 were related to heart failure secondary to progressive AVVR or ventricular dysfunction. Of the 2 early deaths and 11 events (late death, transplant or takedown) after the Fontan, 8 patients had common AV-valve morphology. Other studies have also not shown a difference in AV-valve regurgitation or ventricular dysfunction between the 2 groups.[3,5,6,10,16] By contrast, we have demonstrated an increased risk of AV-valve failure after Fontan completion where APBF is preserved at the time of the SCPC. In our cohort, 40% of subjects who developed AV-valve failure after Fontan had a common AV valve and 65% of those with AVV failure had APBF maintained at the time of the SCPC. Our data would support the notion that in those patients with single-ventricle physiology with a common AV valve, additional sources of pulmonary blood flow including APBF should be eliminated at the time of the SCPC.

Limitations

There are several potential limitations in our study. First, as subjects are enrolled into the ANZFR at the time of their Fontan operation, we are unable to include subjects who died before Fontan completion. Thus, our study was specifically designed to ascertain the impact of APBF only on post-Fontan rather than interstage outcomes. Second, data were not available before SCPC on the degree of AV-valve regurgitation. We are thus unable to ascertain whether both groups had comparable AV-valve regurgitation before SCPC. We did, however, exclude patients who underwent AV-valve intervention before or at the time of the SCPC; therefore, for this part of the analysis, we are likely to

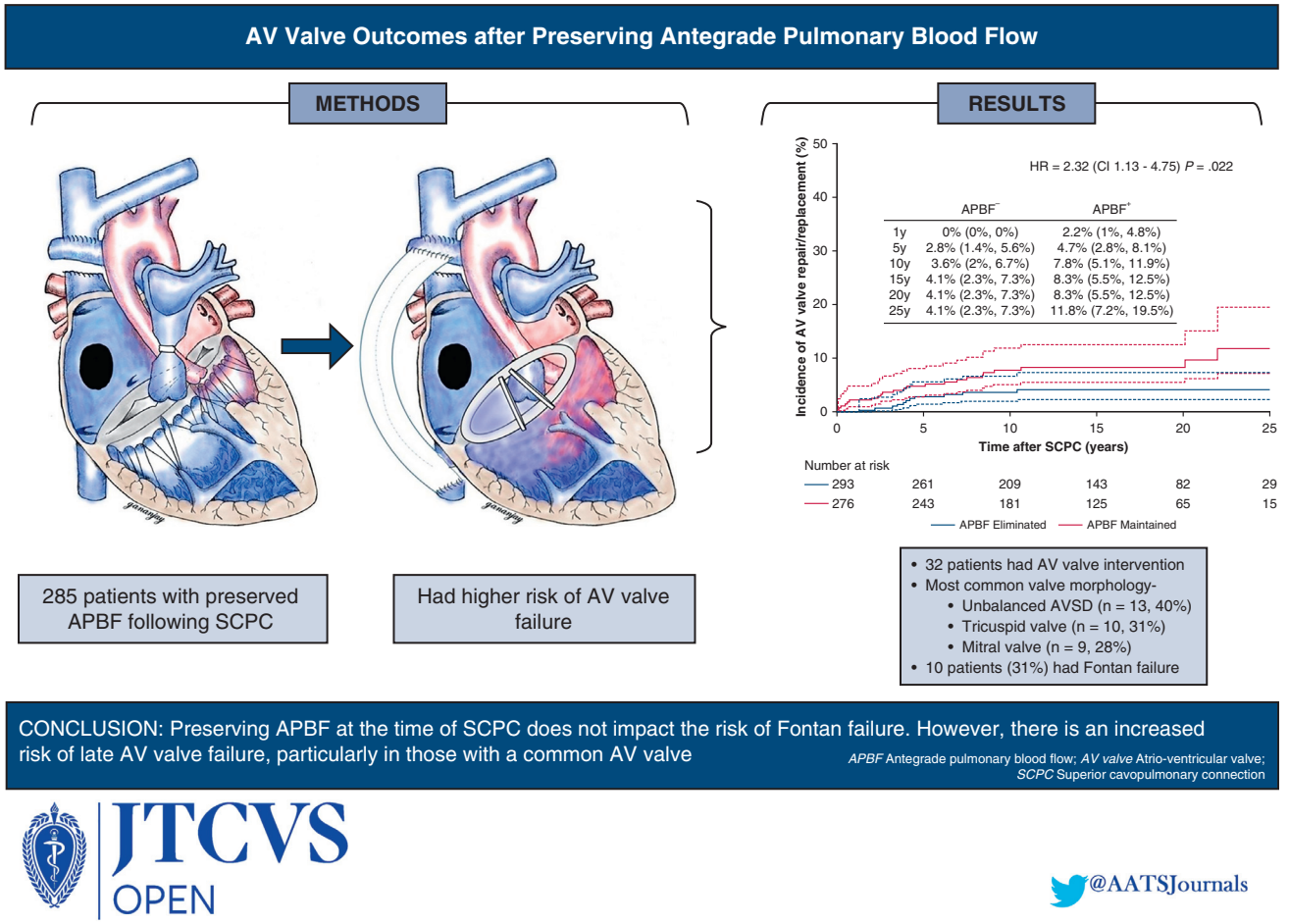

FIGURE 4. In the Australia and New Zealand Fontan Registry, there were 587 patients with pre-existing antegrade pulmonary blood flow (*APBF*) before the superior cavopulmonary connection (*SCPC*). There were 285 patients who had their APBF maintained at the time of the SCPC. These patients had high incidence of atrioventricular (*AV*)-valve repair/replacement, HR 2.32 (95% CI 1.15, 4.75; $P = .02$). Of those patients who had AV-valve repair/replacement the majority had common AV-valve morphology. *HR*, Hazard ratio; *CI*, confidence interval.

have included only those patients in whom AV-valve regurgitation was mild or less at the time of SCPC. Third, patient-level indications for leaving or eliminating APBF were not recorded. Data on pre-SCPC pulmonary artery size or the degree of pulmonary stenosis that could have been potential factors for leaving APBF were not available in our cohort. In contrast, elimination of APBF may have been favored in those with preexisting AV-valve regurgitation or ventricular dysfunction, which may have underestimated the impact of maintaining APBF on AV-valve failure. Fourth, the amount of APBF or aortopulmonary collateral flow could not be quantified. Pre-Fontan aortopulmonary collateral flow as measured by cardiac magnetic resonance imaging can be high.[27,28] In the ANZFR, only the presence or absence of collaterals at the time of the pre-Fontan catheter was available. Given the nature of the ANZFR, there was missing data for secondary outcomes; however, the missing data were equally represented in both groups. Finally, we decided to use AV-valve repair or replacement for AV-valve regurgitation rather than using echocardiography reports as a measure of AV-valve failure. In our retrospective study, echocardiography data were incompletely ascertained and subject to variable interpretation. We considered that the need for intervention was a more objective measure of AV-valve failure.

CONCLUSIONS

Maintaining APBF at the time of the SCPC does not seem to impact the risk of Fontan failure. However, there may be an increased risk of late AV-valve failure in those in whom APBF is maintained, particularly in those with a common AV valve.

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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Key Words: superior cavopulmonary connection, antegrade pulmonary blood flow, Fontan, atrioventricular valve regurgitation

TABLE E1. Ventricular function at last follow-up

Ventricular function/dysfunction	APBF^{-} n (%)	APBF^{+} n (%)
Normal	242 (91)	201 (86)
Mild to moderate	22 (8)	27 (12)
Moderate to severe	3 (1)	6 (3)
Timing of echo at last follow-up (years from Fontan) Mean ± SD	11.71 ± 6.6	11.33 ± 6.1

There was no significant difference between the 2 groups related to ventricular dysfunction at last follow up APBF^{-}, n = 267 (35 missing data); APBF^{+}, n = 234 (51 missing data).
APBF^{-}, Antegrade pulmonary blood flow eliminated; *APBF*$^{+}$, antegrade pulmonary blood flow maintained; *SD*, standard deviation.