Atrioventricular Valve Regurgitation in Single Ventricle Heart Disease: A Common Problem Associated With Progressive Deterioration and Mortality

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ABSTRACT: The Fontan procedure has provided patients with single ventricle physiology extended survival into adulthood and in many cases has improved their quality of life. Atrioventricular valve regurgitation (AVVR) is common in single ventricle patients and is associated with increased risk of mortality. AVVR is more common in patients with a systemic tricuspid or common atrioventricular valve but is generally progressive irrespective of underlying valve morphology. AVVR can be attributable to diverse structural and functional abnormalities at multiple levels of the valvar apparatus, as well as ventricular dysfunction and dilation. Multiple imaging modalities including recent advances in 3-dimensional echocardiography and cross-sectional imaging have been used to further understand AVVR. Surgery to address AVVR must be tailored to the underlying mechanism and the timing of surgical repair should be chosen carefully. In this review, we discuss the etiologies, treatment options, surgical timing, and outcomes of valve repair or replacement for AVVR in patients with single ventricle congenital heart disease, with a focus on those with a Fontan circulation as AVVR is associated with increased risk for Fontan failure and mortality. In-depth understanding of the current literature will help guide clinicians in their approach and management of AVVR in this population.

Key Words: atrioventricular valve regurgitation ■ Fontan ■ single ventricle congenital heart disease

The Fontan procedure has transformed the lives of patients with single ventricle (SV) congenital heart disease, providing improved survival and quality of life into adulthood.1 Since it was first performed in 1968, surgical techniques have evolved along with improvements in cardiac intensive care and cardiac catheterization approaches. As a consequence, outcomes have progressively improved but the incidence of cardiovascular and associated adverse events remains high and life expectancy is decades less than the population average.2,3 The 5-year risk of death for a 40-year-old Fontan patient is similar to that of a 75-year-old without congenital heart disease.4

Atrioventricular valve regurgitation (AVVR) is associated with increased risk of Fontan circulation failure, morbidity and premature mortality.5–8 In this paper, we review the problem of AVVR in SV patients, with a focus on the Fontan circulation. Imaging and surgical repair options are discussed, along with an overview of outcomes after atrioventricular valve (AVV) repair. Lastly, we hope to provide a concise review of the literature to support a more uniform approach in the evaluation and management of patients with AVVR.
AVVR INCIDENCE AND ASSOCIATED RISK FOR FONTAN FAILURE

Up to 75% of Fontan patients have some degree of AVVR, with moderate or severe AVVR in a sizable minority (~20%).8 King et al recently analyzed the outcomes of almost 1200 Fontan patients from an Australia and New Zealand Fontan registry.5 With a median follow-up of 11.7 years, the cumulative incidence of AVV failure, defined as moderate or greater regurgitation or referral for AVV operation, was 56% among those with a common AVV and 46% with hypoplastic left heart syndrome (HLHS) (single tricuspid valve) at 25 years of age. Patients with tricuspid atresia and those with 2 AVVs had a substantially lower cumulative incidence of AVV failure at 25 years, 8% and 26%, respectively. The authors further reported AVV failure to be associated with a 2-fold higher incidence of Fontan failure (FF), in this case defined as either: death, heart transplantation, Fontan takedown or conversion, plastic bronchitis, protein losing enteropathy or New York Heart Association functional class III or IV symptoms.5 By 20 years post-Fontan, freedom from FF was 54% and 77% in those with and without AVV failure, respectively.5 Importantly, this study makes apparent that AVVR is a progressive disease with long-term, life-limiting implications.

Etiologies for Tricuspid Regurgitation in HLHS

In HLHS, a small septal leaflet and anterior leaflet prolapse are associated with the development of tricuspid valve regurgitation (Videos S1 and S2).17 Frequently encountered abnormalities are valve leaflet dysplasia and leaflet prolapse that alter AVV geometry resulting in malcoaptation.16,18,19

Leaflet tethering can result in restricted leaflet motion, deficient coaptation, and regurgitation. A higher tethering volume has been correlated with increased AVVR.20 Tethering can also occur as a consequence of lateral displacement of the anterior PM because of the abnormal geometry and dilation of a single right ventricle in HLHS.17,20–22 Abnormal chordae tendineae, including elongation, deficiency, or malattachment, are pathologic findings that result in AVVR.

HLHS is also associated with systolic distortion and flattening of the typically saddle-shaped tricuspid valve (TV) during systole, resulting in decreased annular bending and limited septal-lateral coaptation at the anterosetal commissure.23 This results in abnormal 3-dimensional deformation throughout the cardiac cycle and increased dynamic changes in annular septo-lateral dimensions, which is associated with worse tricuspid regurgitation.21

Etiologies for Common AVVR in Unbalanced Atrioventricular Septal Defects

The common AVV is particularly prone to AVVR, with a 10-year cumulative incidence of valve failure of 34%.9 These valves have variable anatomy and are poorly adapted to sustain systemic afterload.24 Valve dysplasia, leaflet prolapse, and tethering are common

likely also contributes to formation of venous collaterals and exacerbates systemic arterial hypoxemia. Furthermore, a high regurgitant volume increases SV preload and decreases effective cardiac output, leading to SV dilation, adverse remodeling, and systolic dysfunction.5,13 The resulting decreased cardiac output activates the sympathetic nervous system and increases systemic vascular resistance. Progressive atrial enlargement secondary to AVVR contributes to an increased risk of atrial arrhythmias, which is strongly associated with worse outcomes.6,14,15

AVVR MECHANISMS

AVVR can be caused by many distinct structural valvar abnormalities and functional ventricular etiologies (Figure 2). Structural abnormalities are the most common cause of AVVR and can occur at all levels of the valve apparatus, including the leaflets, chordae, papillary muscles (PM) and annulus.11,16

Nonstandard Abbreviations and Acronyms

| Abbreviation | Description |
|--------------|-------------|
| AVV          | atrioventricular valve |
| AVVR         | atrioventricular valve regurgitation |
| CMR          | cardiac magnetic resonance |
| FF           | Fontan failure |
| HLHS         | hypoplastic left heart syndrome |
| PM           | papillary muscle |
| SV           | single ventricle |
| TEE          | transesophageal echocardiography |
| TV           | tricuspid valve |
| 2D           | 2-dimensional |
| 3D           | 3-dimensional |
etiolos of poor valve coaptation in this population (Videos S3 through S5). In a study of SV patients with unbalanced atrioventricular septal defect, increased tenting height, which is a measure of leaflet tethering, was found to be a predictor of severe AVVR. Leaflet tenting is measured from leaflet coaptation to leaflet annulus; the more distant the coaptation is from the annulus, the worse the leaflet tethering and the AVVR. Moreover, those with progressive reduction in tenting height maintained valve competency. This suggests that leaflet tethering is an important factor to consider in this subset of patients.

**Functional AVVR**

Functional AVVR occurs in the absence of structural abnormalities of the valve apparatus secondary to ventricular and annular dilation. This results in a stretched annulus and deficient coaptation of valve leaflets. Causes of functional AVVR can occur at any time in staged palliation. The interstage period between Stage I and Stage II palliation exposes the SV to an increased volume load and AVVR can evolve over time as a consequence of the resulting remodeling. In addition, etiologies of functional AVVR that are more common post-Fontan include chronic volume overload secondary to aortopulmonary collaterals, aortic (or neo-aortic) valve regurgitation, patent fenestration, or ventricular systolic dysfunction.

**IMAGING OF AVVR**

Various imaging modalities can assess AVV anatomy and function (Table 1). Transthoracic echocardiography is universally available, non-invasive, and relatively inexpensive, and thus is most often used as the initial
assessment. It usually provides excellent visualization of valve morphology, clefts, and leaflet motion in multiple planes.27 The degree of regurgitation can be determined by color flow pattern or quantification of vena contracta and regurgitant area.28 Grading of severity remains largely qualitative because of heterogeneous valve morphology, eccentric flow jets, and the frequency of multiple regurgitant jets. Additional pathologies that could contribute to the volume of AVVR independent of AVV regurgitant orifice size, including neo-aortic outflow or aortic arch obstruction, can also be readily evaluated by echocardiography. The valve and subvalvular apparatus are important to examine closely by transthoracic echocardiography. Potential etiologies of AVVR including the presence of leaflet prolapse, clefts, or leaflet tethering should be described as this can help dictate surgical repair options. PM and chordae attachments should be looked at closely, as abnormalities in these structures can be addressed during repair. Annular dilation, ventricular dilation, and ventricular function are important to assess as well to provide guidance for surgeons on type and timing of repair.

In patients with poor acoustic windows, transesophageal echocardiography (TEE) can provide a more detailed visualization of valve structure and motion.28–30 Benefits of TEE include the ability to visualize the AVV in multiple planes to improve understanding of the location of leaflet abnormalities and origin of the regurgitant jet. Since sedation or even general anesthesia may be required, TEE is less commonly used in the outpatient setting.

Nevertheless, identifying the mechanism of AVVR pre-operatively can be challenging. One study reported the experience of a single-center, comparing the expected pathophysiology based on echocardiography and direct surgical inspection during repair.30 By 2-dimensional (2D) echocardiography, valve prolapse, and tethering were the most common mechanisms of AVVR while direct surgical visualization diagnosed annular dilation and leaflet dysplasia as most common.30 There was poor agreement between echocardiography and surgical assessment; echocardiography described leaflet motion abnormalities well but was insensitive to structural abnormalities and leaflet dysplasia.
The use of 3-dimensional (3D) echocardiography has emerged recently and addressed some of the limitations of 2D echocardiography; 3D echocardiography can describe surface and volumetric details of AVVs as well as clarify spatial relationships of the leaflets and sub-valvar apparatus, measure tethering volumes, and describe dynamic geometric changes of the annulus.20–23,31 Although 3D echocardiography is an excellent new technology, its use is limited in the pediatric population. Most pediatric echocardiography probes do not have 3D technology. Additionally, 3D TEE generally cannot be performed adequately in small children who weigh <20 kg.

Cross-sectional imaging can also provide information about AVVR. Cardiac magnetic resonance (CMR) is especially useful in adults or children with poor echocardiographic windows (Video S6). CMR is better suited to evaluate flow and quantify AVVR.32 Serial CMR can assess the progression of ventricular dilation or systolic dysfunction, each of which predisposes to mortality after AVV intervention post-Fontan.16 The presence of stainless steel coils, Fontan pathway stents, or fenestration occlusion devices may cause imaging artifacts and limit evaluation by CMR. Computed tomography is an alternative as it requires a short imaging time and has high spatial resolution to provide some detail of the AVV anatomy and annular size (Video S7). One of the side effects of computed tomography is exposure to ionizing radiation.32 Although this is not an ideal method of imaging compared with CMR, it can be useful in patients with metallic stents or pacemakers that preclude CMR evaluation.

Because of the limitations and constraints of each available imaging modality, multimodality imaging is often useful to inform decision making. Initial evaluation should include precise transthoracic echocardiography. If the mechanism of AVVR is unclear or if there are poor acoustic windows, then we would recommend additional evaluation with TEE or CMR to quantify the regurgitation, ventricular size, and function, and assess valve anatomy. We also recommend that TEE be used pre- and intraoperatively to guide surgical repair.

### SURGICAL TECHNIQUES TO ADDRESS AVVR IN SV PATIENTS

There are many surgical techniques that address AVVR (Table 2). Surgical planning should include careful imaging of the valve as detailed above to determine mechanisms of AVVR and thus guide repair. In addition, intraoperative assessment with TEE is imperative to verify the mechanism of AVVR and can also provide information that may affect the surgeon’s approach to valve repair.

The most common surgical techniques are partial annuloplasty and commissuroplasty (Figure 3A and 3B).18,19,23 Annuloplasties can be performed using extended polytetrafluoroethylene strips, pericardial...
Ring annuloplasties decrease annular size and improve coaptation. A partial annuloplasty addresses leaflet restriction and/or annular dilation that results in deficient coaptation and central regurgitation. Two examples of partial annuloplasties to address tricuspid regurgitation include the DeVega and Kay annuloplasty. A DeVega suture annuloplasty involves placing parallel semicircular sutures along the annulus to decrease annular size typically from the septal-posterior commissure to the fibrous trigone (Figure 3C). With the Kay annuloplasty, sutures are placed at the annulus from the antero-posterior commissure to the posteroseptal commissure and tied down to exclude the posterior leaflet, creating a functional bicuspid valve and improving regurgitation (Figure 3D). Clefts or fenestrations can be successfully repaired by primary closure or lateral leaflet plication.

Valvuloplasty is another common method of repair. Edge-to-edge repair has been used successfully in both TV and common AVV repairs (Figure 3E). For a TV, the free edge of the septal and anterior leaflets are sutured together to close the anteroseptal commissure or a suture is placed where the regurgitant jet arises, creating a double orifice. In a common AVV, the superior and inferior bridging leaflets are sutured together to create a double orifice, commonly referred to as an “Alfieri stitch”. If coaptation is particularly poor, the free edges can be completely sutured together to form a single orifice.

In common AVVs, another repair strategy involves approximation of the leaflets with a polytetrafluoroethylene bridge or glutaraldehyde-treated autologous strips, or rings. Valvuloplasty is another common method of repair. Edge-to-edge repair has been used successfully in both TV and common AVV repairs (Figure 3E). For a TV, the free edge of the septal and anterior leaflets are sutured together to close the anteroseptal commissure or a suture is placed where the regurgitant jet arises, creating a double orifice. In a common AVV, the superior and inferior bridging leaflets are sutured together to create a double orifice, commonly referred to as an “Alfieri stitch”. If coaptation is particularly poor, the free edges can be completely sutured together to form a single orifice.

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| Table 2. Surgical Repairs of the Atrioventricular Valve |
|-----------------|------------------|
| Type of repair   | Indication       |
| Annuloplasty    | Annular dilation |
|                 | Leaflet restriction |
| Commissuroplasty| Atrioventricular valve clefts |
| Valvuloplasty   | Coaptation defects |
| Chordal procedure (shortening, elongation, repositioning, artificial chords) | Chordal absence, Chordal rupture, Elongated chordae, Leaflet prolapse |

Types of surgical techniques to address specific structural abnormalities causing atrioventricular valve regurgitation.

Figure 3. Surgical repair techniques for atrioventricular valve regurgitation.
A. Tricuspid valve (TV), partial annuloplasty; B. TV, commissuroplasty; C. TV, DeVega annuloplasty; D. TV, Kay annuloplasty; E. TV, edge-to-edge repair; F. Common atrioventricular valve, polytetrafluoroethylene bridge repair.
after valve replacement is also high at 20% to 40%. A 5-year mortality rate of nearly 40%. Heart block postoperative in-hospital mortality of almost 30% and from regurgitation. AVV replacement is associated with plastic AVV where repair is unlikely to be adequate. Repositioning of the anterior PM can alter ventricular geometry by increasing its spherical shape and improve valve tethering in HLHS. Leaflet size can be increased by incising and patching the restricted or deficient leaflet, thereby increasing the area of coaptation. Multiple techniques can be used simultaneously to address AVVR. Ultimately, the repair must be individualized to the patient’s anatomy and the mechanism of regurgitation.

Surgical valve repair is preferred to valve replacement, as it preserves native valve structure and has demonstrated good early results. However, AVV replacement may be necessary in severely dysplastic AVV where repair is unlikely to be adequate. Replacement is also more appealing in older patients or adults to improve the likelihood of long-term freedom from regurgitation. AVV replacement is associated with postoperative in-hospital mortality of almost 30% and 5-year mortality rate of nearly 40%. Heart block after valve replacement is also high at 20% to 40%.

Lastly, AVV replacements have been shown to be associated with higher mortality in those aged <2 years compared with those >2 years. Poor outcomes may be partly because of patient selection since AVV replacement is often considered after multiple attempts to repair the valve.

Finally, the recent revolution in transcatheter AVV interventions for mitral and TV in adults with structurally normal hearts raises the possibility that these techniques or modifications thereof may be useful in some SV patients. Case reports of transcatheter valve interventions in Fontan patients, such as the use of the Mitraclip device, valve-in-valve or heterotopic valve implantation, have emerged.

Further studies are needed to define appropriate candidates and percutaneous techniques in this population.

TIMING OF SURGICAL REPAIR OR REPLACEMENT

Significant AVVR and valve repair itself are known risk factors for ventricular dysfunction, FF, transplantation, or death after Fontan palliation. Questions remain about which patients benefit from valve repair or replacement and also about the optimal timing of surgery. Without intervention, chronic AVVR can cause pulmonary vascular disease, arrhythmias, and heart failure. Few data exist to aid in this decision. Much of the literature on surgical timing and outcomes has included AVV interventions across all stages of palliation, with most interventions performed before or at the time of Fontan. We will discuss the considerations on timing of AVV repair from infancy to the Fontan procedure, and end with the adult Fontan population.

Young SV patients with AVVR pose a particularly difficult conundrum. Early AVV repair between initial palliation and Stage II is independently associated with increased mortality. Some argue that with moderate AVVR, valve intervention is not required, based on the expectation that AVVR usually improves with the volume unloading intrinsic to completing Stage II. To further support delaying intervention, repair at Stage II or earlier predicts recurrent AVVR and reintervention, and some have seen a reduction in regurgitation after the Fontan operation even without an accompanying AVV repair. Younger age and smaller size are associated with re-intervention and mortality, suggesting potential deleterious consequences if repair is needed early in the surgical palliative course.

Of particular interest are patients with severe AVVR before the Fontan procedure. AVV repair can be performed in isolation, before staged palliation, or at the time of the Fontan procedure. Isolated AVV repair before Fontan is beneficial in that it simplifies Fontan surgery and reduces cardiopulmonary bypass time. Early AVV intervention may ameliorate the postoperative risks at the time of Fontan and turn a patient who is a high-risk Fontan candidate into a good Fontan candidate. Earlier repair at a separate stage before Fontan may be associated with fewer postoperative complications, such as decreased intensive care unit stay, chylothorax, and ascites, though data are inconclusive. In the short-term, patients who underwent a prior initial AVV repair had improved AVVR at discharge from Fontan completion and were less likely to undergo AVV reoperations. This approach also allows the surgeon to evaluate and re-repair the valve at the time of the Fontan as needed. However, it has also been shown that valve operation between Stage II and Fontan completion predicts late repair failure which is likely because of recurrence of AVVR after the Fontan.

AVV repair at the time of Fontan may be a reasonable option in selected patients. One single center retrospective study demonstrated that patients undergoing concomitant AVV repair at time of Fontan did
Table 3. Atrioventricular Valve Interventions and Outcomes

| First Author       | Y  | Number of AVV Interventions | Age, Y (IQR or Range) or Mean±SD | Failed AVV Interventions                                                                 | Timing of Repair Failure From Original Intervention, Y (IQR) or Mean±SD | Risk Factors for Repair Failure or Re-intervention                                                                 |
|-------------------|----|-----------------------------|----------------------------------|----------------------------------------------------------------------------------------|------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|
| King et al⁵       | 2019 | 120 repairs 110 replacements | 3.4 (1.6–6.9)                   | 41% re-interventions or recurrent moderate or greater AVVR                              | 3.4 (1.6–4.8)                                                        | Common AVV and tricuspid valve Systemic right ventricle                                                         |
| Sughimoto et al⁴²  | 2018 | 56 replacements             | 2.1 (0.8–10.5)                  | 20% repeat AVV replacement                                                               | 0.25 (0.04–0.78)                                                     | Tricuspid valve Valve replacement between Stage II and Fontan                                                   |
| King et al⁷        | 2017 | 28 repairs 4 replacements   | 3.5 (2.0–7.0)                   | 67% re-interventions or recurrent moderate or greater AVVR                              | 2.9±0.75                                                             | NR                                                                                                              |
| Laux et al⁹⁹       | 2015 | 31                          | 3.6 (range 0.1–36.5)            | 19% reoperations                                                                        | 2 (range 0.2–7.6)                                                    | Failed first AVV repair Higher total number of surgeries Lower body mass index Male sex Need for early repair before Stage II |
| Kotani et al²⁶     | 2012 | 58                          | 0.62* (range 0.02–13.33)        | 81% recurrent AVVR 21% repeat interventions                                             | 1.75 (range 0.17–5.33)                                               | Recurrent moderate-severe AVVR repair at Stage II, CPB time Re-intervention: valvuloplasty repair technique, CPB time, aortic cross-clamp time, significant residual AVVR on intraoperative transesophageal echo, poor postoperative ventricular function |
| Sano et al²⁴       | 2012 | 32                          | 1.25 (range 0.07–36.92)         | 38% repeat interventions for recurrent AVVR                                             | NR                                                                   | Moderate or more pre-operative AVVR Early failure of initial repair (moderate or more AVVR within 1 mo after operation) Younger age at initial AVV repair |
| Wong et al³         | 2012 | 76                          | 1 (range 0.27–3.3)              | 26% reoperations                                                                        | 2.6 (1–5)                                                            | Moderate or severe postoperative regurgitation Timing between Stage II and Fontan completion                      |
| Honjo et al⁶       | 2011 | 57                          | 0.57 (range 0.025–17.4)         | 17% recurrent AVVR requiring repeat repair or replacement                              | 1.75 (range 0.17–5.17)                                               | Younger age at repair Small body surface area increased indexed AVV annular and ventricular dimensions Leaflet dysplasia Residual AVVR |
| Ando and Takahashi⁵⁷| 2011 | 103                         | 9.9±9.6                         | 24% repeat interventions                                                               | NR                                                                   | NR                                                                                                              |
| Menon et al⁷¹       | 2010 | 61                          | 14 (range 3–41)                 | 13% of repairs                                                                          | NR                                                                   | NR                                                                                                              |

(Continued)
not have differences in postoperative complications and mortality compared with those who did not require AVV intervention. Comparing the approach of isolated AVV repair versus repair at time of Fontan has not been well studied because of possible selection bias, as symptomatic patients with more severe AVVR are likely to get an isolated repair rather than a repair during the Fontan operation.

Repair can also be performed after Fontan completion or during Fontan revision with postoperative improvement in the degree of regurgitation. However, those requiring late AVV repair have worse survival of 57% at 10 years and a higher risk of transplantation compared with Fontan patients who do not require AVV repair. AVV repair in the adult Fontan population carries a high risk, with mortality up to 13% in the postoperative period and 33% at 5 years. Development of protein-losing enteropathy has also been described to be a risk factor for mortality in valve repair in Fontan patients. On long-term follow-up, patients who underwent AVV repair after Fontan completion commonly developed arrhythmias (72%), protein-losing enteropathy (20%), and required pacemaker placement (26%). Adult congenital heart disease patients have higher complication rates and mortality after cardiac surgery in general and AVV surgery in the adult Fontan is a particularly high-risk surgery.

Lastly, patients with common AVVs, especially those with heterotaxy, are more likely to require AVV reintervention and are challenging to manage. There are limited data on the optimal timing of repair in this subset of single ventricle patients. Sano et al describes their 18-year experience with patients with heterotaxy syndrome who underwent AVV repair. The majority (87.5%) had a common AVV, which has been shown to be a risk factor for mortality. The 4-year freedom of AVV failure was 50% with an early mortality of 18% and estimated survival after repair of 54% at 10 years. This emphasizes the difficulty in repairing common AVV in this population and the persistent risk of recurrent AVVR and mortality.

The timing of AVV replacements is equally controversial and there is even less literature on this topic. Most are commonly performed between Stage II and Fontan or after the Fontan procedure. Patients who require AVV replacement before the Fontan often require a second valve replacement. The risks of early AVV replacement include thrombosis and patient prosthesis mismatch because of rapid somatic growth that leads to valve failure, especially in smaller children. AVV replacement at the time of Fontan completion has been also associated with increased mortality.

Identifying patients with risk factors for recurrent AVVR and mortality after initial repair is essential to improve patient selection and outcomes, and
the timing of repair can affect the recurrence rate of AVVR. Although the literature has provided some evidence, there have been variable results which are limited by the retrospective nature of most studies. AVVR intervention at a younger age and lower body weight, and in the older Fontan population have been shown on multiple occasions to be a risk factor for morbidity and mortality. Additionally, ventricular dysfunction, even in the setting of a successful valve repair, is associated with worse outcomes.8,19,51 One study found that 75% of patients with moderate to severely diminished ventricular function on post repair imaging required a heart transplantation or had the outcome of death.16 Earlier AVV intervention, especially in setting of progressive ventricular dilation, could prevent further irreversible changes in ventricular geometry, systolic dysfunction, or need for repeat interventions.16 Valve and ventricular morphology are also important to consider; those with 2 separate AVVs and a dominant left ventricle have the highest freedom from repair failure.5,56,57 Optimal timing, precise identification of AVVR mechanism and appropriate repair are imperative, as early failed repair or recurrent moderate to severe postoperative regurgitation are predictors of late reoperations.10

It is important to mention that it remains unclear if there is a subcategory of patients who may benefit from transplant rather than AVV intervention. Given the challenge of successful TV or common AVV repair, some recommend cardiac transplantation for patients with systolic ventricular dysfunction and moderate or worse tricuspid regurgitation or common AVV post Fontan.52 Transplantation may also be preferable to high-risk surgical intervention among adults with significant Fontan-related comorbidities.

Thus, management of AVVR in this population remains challenging. Our institutional practice is to repair the AV during a planned palliative staged surgery, ie, during Stage I, Stage II, or Fontan surgeries, if there is moderate or greater AVVR in asymptomatic patients. In symptomatic patients, repair is typically performed in between staged palliations or after Fontan completion. For those patients with unfavorable hemodynamics before the Fontan, we will repair the AVV first and re-evaluate candidacy for Fontan at a later stage. Table 3 summarizes the available data on timing of surgery across all stages of palliation.

CONCLUSIONS

AVVR is common in SV patients with Fontan circulation and is associated with worse outcomes including FF, arrhythmia, heart failure, and death. Mechanisms of AVVR are diverse, relating to both structural and functional abnormalities. These mechanisms are best assessed by a combination of imaging modalities. Optimal timing for AVVR intervention remains controversial and should be individualized; both early and late surgical repair have associated risk. In adult Fontan patients, AVV interventions are often performed in conjunction with other procedures and AVV replacement may be reasonable. Patients with significant AVVR who have already developed ventricular systolic dysfunction are at particularly high risk for adverse outcomes after AVV intervention and cardiac transplantation should be considered.

ARTICLE INFORMATION

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Disclosures
None.

Supplementary Materials
Video S1–S7

REFERENCES

1. Gersony WM. Fontan operation after 3 decades: what we have learned. Circulation. 2008;117:13–15.
2. Pundt KN, Johnson JN, Dearani JA, Pundi KN, Li Z, Hinck CA, Dahl SH, Cannon BC, O’Leary PW, Driscoll DJ, et al. 40-year follow-up after the Fontan operation: long-term outcomes of 1,052 patients. J Am Coll Cardiol. 2015;66:1700–1710.
3. Iyengar AJ, Winlaw DS, Galati JC, Wheaton GR, Gentles TL, Grigg LE, Justo RN, Radford DJ, Weintraub RG, Bullock A, et al. The extracardiac conduit Fontan procedure in Australia and New Zealand: hypoplastic left heart syndrome predicts worse early and late outcomes. Eur J Cardiothorac Surg. 2014;46:465–473.
4. Diller GP, Kempny A, Alonso-Gonzalez R, Swan L, Uebing A, Li W, Babu-Narayan S, Wort SJ, Dimopoulos K, Gatzoulis MA. Survival prospects and circumstances of death in contemporary adult congenital heart disease patients under follow-up at a large tertiary centre. Circulation. 2015;132:2118–2125.
5. King G, Ayer J, Celermajer D, Zentner D, Justo R, Disney P, Zannino D, d’Udekem Y. Atrioventricular valve failure in Fontan palliation. J Am Coll Cardiol. 2019;73:810–822.
6. Alsaaed T, Bokma JP, Engel ME, Kuipers JM, Hanke SP, Zuhike L, Zhang B, Veldtman GR, Factors associated with long-term mortality after Fontan procedures: a systematic review. Heart. 2017;103:104–110.
7. d’Udekem Y, Xu MY, Galati JC, Lu S, Iyengar AJ, Konstantinov IE, Wheaton GR, Ramsay JM, Grigg LE, Millar J, et al. Predictors of survival after single-ventricle palliation: the impact of right ventricular dominance. J Am Coll Cardiol. 2012;59:1178–1185.
8. Anderson PA, Steeper LA, Mahony L, Colin SD, Atz AM, Breitbart RE, Gersony WM, Gallagher D, Geva T, Margossian R, et al. Contemporary outcomes after the Fontan procedure: a Pediatric Heart Network multicenter study. J Am Coll Cardiol. 2008;52:85–98.
24. Sano S, Fujii Y, Arai S, Kasahara S, Tateishi A. Atrioventricular valve failure during single ventricle palliation. Eur J Cardiothorac Surg. 2017;51:1037–1043.

25. Vijarnsorn C, Khoo NS, Tham EB, Colen T, Rebeyka IM, Smallhorn JF. Functional unbalanced atrioventricular valve regurgitation in patients with hypoplastic left heart syndrome: a case-matched echocardiographic-surgical comparison study. Eur Heart J Cardiovasc Imaging. 2013;14:135–141.

26. Gewillig M, Brown SC. The Fontan circulation after 45 years: update in physiology. Heart. 2016;102:1081–1086.

27. Shah S, Jenkins T, Markowitz A, Gilkeson R, Rajap J. Multimodal imaging of the tricuspid valve: normal appearance and pathological entities. Insights Imaging. 2016;7:649–667.

28. Buber J, Schwagerl RG, Mazor Dray E. Echocardiographic evaluation of univentricular physiology and cavopulmonary shunts. Echocardiography. 2019;36:1381–1390.

29. Hahn RT. State-of-the-art review of echocardiographic imaging in the evaluation and treatment of functional tricuspid regurgitation. Circ Cardiovasc Imaging. 2016;9:e005332.

30. Bhuayut T, Horjo O, Seller N, Atlin CR, Redington A, Caldarone CA. Improved results of tricuspid valve repair in patients with Fontan circulation. Circ Cardiovasc Imaging. 2017;10:e004273.

31. Boyd JH, Edelman JBB, Scoville DH, Woo YJ. Tricuspid leaflet repair: innovative solutions. Ann Cardiothorac Surg. 2017;6:248–254.

32. Belluschi I, Del Forno B, Lapenna E, Nisi T, Iaci G, Ferrara D, Castiglioni A, Alferri D, De Bonis M. Surgical techniques for tricuspid valve disease. Front Cardiovasc Med. 2018;5:118.

33. Rychik J. The relentless effects of the Fontan paradox. Semin Thorac Cardiovasc Surg Pediatr Card Surg Ann. 2016;19:37–43.

34. Gewillig M. The Fontan circulation: past, present, and future. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu. 2018;21:232–241.

35. Gewillig M. The Fontan circulation: past, present, and future. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu. 2018;21:232–241.

36. Gewillig M. The Fontan circulation: past, present, and future. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu. 2018;21:232–241.

37. Gewillig M. The Fontan circulation: past, present, and future. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu. 2018;21:232–241.

38. Gewillig M. The Fontan circulation: past, present, and future. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu. 2018;21:232–241.

39. Gewillig M. The Fontan circulation: past, present, and future. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu. 2018;21:232–241.

40. Gewillig M. The Fontan circulation: past, present, and future. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu. 2018;21:232–241.
52. Mavroudis C, Deal BJ, Backer CL, Stewart RD, Franklin WH, Tsao S, Ward KM, DeFreitas RA. J. Maxwell Chamberlain Memorial Paper for congenital heart surgery. 111 fontan conversions with arrhythmia surgery: surgical lessons and outcomes. Ann Thorac Surg. 2007;84:1457–1465; discussion 1465-1466
53. Mavroudis C, Stewart RD, Backer CL, Deal BJ, Young L, Franklin WH. Atrioventricular valve procedures with repeat Fontan operations: influence of valve pathology, ventricular function, and arrhythmias on outcome. Ann Thorac Surg. 2005;80:29–36.
54. Setton M, He W, Benavidez OJ. Morbidity during adult congenital heart surgery admissions. Pediatr Cardiol. 2019;40:987–993.
55. d’Udekem Y, Iyengar AJ, Cochrane AD, Grigg LE, Ramsay JM, Wheaton GR, Penny DJ, Brizard CP. The Fontan procedure: contemporary techniques have improved long-term outcomes. Circulation. 2007;116:1157–1164.
56. Buratto E, Ye XT, King G, Shi WY, Weintraub RG, d’Udekem Y, Brizard CP, Konstantinov IE. Long-term outcomes of single-ventricle palliation for unbalanced atrioventricular septal defects: Fontan survivors do better than previously thought. J Thorac Cardiovasc Surg. 2017;153:430–438.
57. Ando M, Takahashi Y. Long-term functional analysis of the atrioventricular valve in patients undergoing single ventricle palliation. Ann Thorac Surg. 2011;92:1767–1773; discussion 1773