13 Transplantation and Mechanical Circulatory Support in Adult Congenital Heart Disease-Related Advanced Heart Failure

Jonathan N. Menachem and Luke J. Burchill

13.1 Introduction

As transplant centers become more familiar with heart transplantation (HTx) in adult congenital heart disease (ACHD) patients, short- and long-term outcomes have improved. Long-term survival conditional on 1-year survival is now better for ACHD patients undergoing HTX than for non-ACHD patients [1]. Despite the perception that the risks associated with HTx are often too high, many ACHD patients have acceptable risk profiles, and all can benefit from review in an advanced heart failure (HF) program. This chapter is dedicated to breaking down barriers to advanced HF care for patients with ACHD-related HF. This chapter has six sections:

- Timing of referral for HTx assessment
- Risks and contraindications to HTx
- Wait-list outcomes and opportunities for decreasing wait-list mortality
- HTx outcomes
- Alternatives to transplantation
- Peri-/postoperative management

J. N. Menachem, M.D.
Heart Failure and Transplantation Program, Vanderbilt University Medical Center, Nashville, TN, USA

L. J. Burchill, M.B.B.S., Ph.D. (✉)
Adult Congenital Heart Disease Program, UHN 62, Knight Cardiovascular Institute, Oregon Health & Science University, Portland, OR, USA
e-mail: burchilu@ohsu.edu

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13.2 Timing of Referral for HTx Assessment

Predicting progression from stable to advanced and/or decompensated HF in ACHD-related HF is challenging, even more so than in acquired HF. Declining NYHA class, progressive ventricular dysfunction, elevated serum BNP [2, 3], reduced peak oxygen uptake (VO_2 max), low BMI [4], hyponatremia [5], anemia [6], renal dysfunction [7], elevated troponin [8], pulmonary hypertension (PH), and arrhythmias [9] have each been associated with increased ACHD mortality. More important than any single variable is the overall clinical picture. In particular, the emergence of clinical features of advanced HF portends adverse health outcomes (summarized in Table 13.1). Emphasized here is a history of repeated HF hospitalizations or emergency room visits, escalating diuretic dose, deteriorating kidney function, unexplained weight loss, and intolerance to ACE inhibitors or beta-blockers. Early referral to a is recommended for all ACHD patients with features of advanced HF. Advanced HF review is also recommended in those with idiosyncratic complications suggesting increased short-term mortality risk such as protein-losing enteropathy (PLE) in Fontan patients [10, 11].

An advanced HF service comprises an interdisciplinary team with expertise and formal training in advanced HF treatment strategies. Early referral does not equate to early listing for HTx. Nor does it imply transfer of care from the ACHD to the acquired HF team. Instead, the purpose of early assessment is to facilitate collaboration between the ACHD and HF programs and to afford the team sufficient time to understand each patient's anatomy, hemodynamics, and clinical course. The team should include clinicians with both traditional and advanced HF expertise but also ACHD clinicians. In addition to discussing advanced HF strategies, the team should assess each patient's understanding of mortality risk with and without treatment and advanced care preferences including resuscitation. Research into care preferences show most ACHD patients prefer to discuss life expectancy and advanced directives before their condition becomes life-threatening [12].

Table 13.1 Clinical features of advanced HF

Repeated (≥2) hospitalizations or emergency department for HF in the past year
Progressive deterioration in renal function (rising urea or creatinine)
Weight loss without other causes[a] (i.e., cardiac cachexia)
Intolerance to ACE inhibitors due to hypotension and/or worsening renal function
Intolerance to beta-blockers due to worsening HF or hypotension
Frequent hypotension with systolic BP <90 mmHg
Persistent dyspnea with dressing or bathing requiring rest
Inability to walk one block on the level ground due to dyspnea or fatigue
Escalating and/or high diuretic dose requirements (furosemide equivalent dose >160 mg/D and/or supplemental metolazone use)
Progressive hyponatremia with serum sodium <133 mEq/L
Frequent arrhythmia and/or ICD shocks
Fontan patients with diarrhea or coughing of casts leading to a diagnosis of protein-losing enteropathy or plastic bronchitis

Adapted from Russell et al. Congestive Heart Failure. 2008;14:316-21

[a]In Fontan patients consider also protein-losing enteropathy as an alternative cause of cachexia

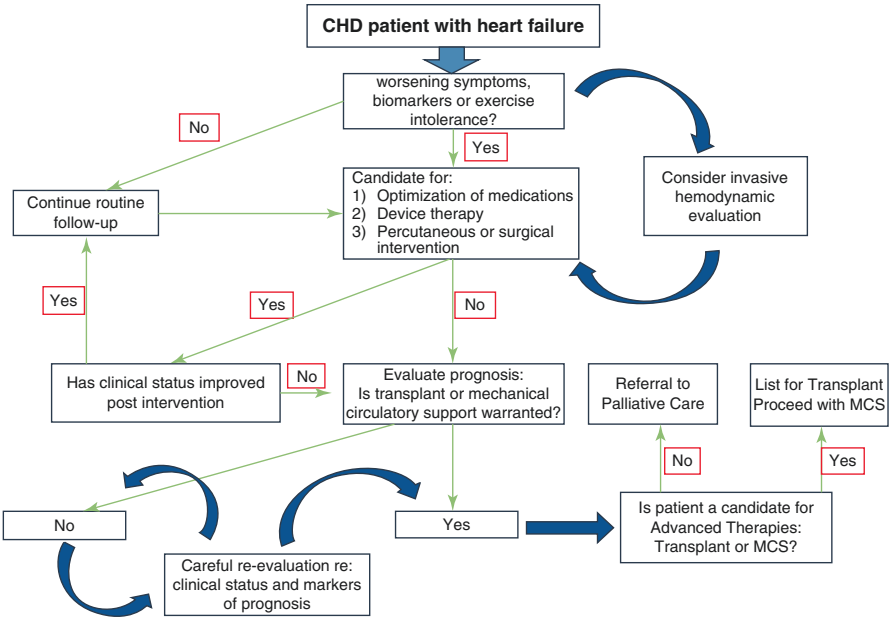

Fig. 13.1 Approach to advanced HF assessment in ACHD. MCS indicates mechanical circulatory support. Illustration used with permission and taken from Ross Circulation 2016

Figure 13.1 provides a stepwise approach to evaluation and treatment of ACHD patients with advanced HF [13]. Worsening symptoms, biomarkers, or exercise intolerance prompts review of medications and candidacy for percutaneous/surgical intervention and device therapies. Multimodality cardiac imaging (echocardiogram, cardiac MRI, cardiac CT, and/or vascular ultrasound) provides a detailed assessment of anatomy and hemodynamics. In addition to quantifying ventricular dimensions and function, attention is paid to the position of the heart and coronary vessels in relation to the sternum, arterial and venous connections, peripheral vascular access, and collateral vessels. Invasive hemodynamic evaluation by a CHD specialist is recommended for ACHD patients with newly diagnosed HF. In addition to guiding medical HF therapy, hemodynamic assessment identifies residual lesions contributing to HF pathophysiology. Advanced therapies (HTx and mechanical circulatory support) should be considered in any ACHD patient who is not responding to medical or device therapy or in whom repeat cardiac surgery is deemed too high risk or unlikely to reset the clinical course. Indications for HTx are summarized in Table 13.2.

13.3 Risks and Contraindications to HTx

Contraindications to HTx in ACHD patients are based on ISHLT guidelines [14] while also taking into account ACHD-related issues. ACHD-related factors such as complex anatomy, the presence of multiple congenital anomalies, or neurocognitive impairment

Table 13.2 Indications for heart transplantation in ACHD

Indications for heart transplantation in ACHD
Stage D HF refractory to medical therapy which will not benefit significantly from surgical, interventional, or electrophysiological intervention
ACHD patients with associated near sudden death or life-threatening arrhythmias refractory to all therapeutic modalities
Patients with stage C HF associated with reactive pulmonary hypertension and a potential risk of developing fixed, irreversible elevation of pulmonary vascular resistance that could preclude isolated orthotopic heart transplantation in the future
Fontan patients with protein-losing enteropathy ± plastic bronchitis refractory to medical therapy
Progressive cyanosis leading to functional decline not amenable to surgery- or catheter-based intervention

Table adapted from Ross et al. Circulation 2016

rarely serve as absolute contraindications in isolation. More frequently it is these issues in combination that lead to determination of excessive risk although risk thresholds vary significantly by transplant and ACHD center volume and expertise. Over time thresholds of risk in ACHD patients are being challenged. A good example is a history of multiple sternotomies which despite being associated with increased HTx risk can generally be managed with anticipatory measures (i.e., peripheral cannulation and bypass, careful dissection of adhesions) [15]. Absolute, relative, and ACHD-related contraindications are summarized in Table 13.3. For this review we have chosen to focus on three issues of major concern—liver disease, PH, and sensitization.

13.3.1 Liver Disease

Liver disease is common in ACHD patients due to the high prevalence of right heart disease, passive liver congestion and hepatitis C [16]. Fontan patients are at especially high risk due to systemic venous hypertension, hepatic congestion, and low cardiac output leading to cirrhosis and, in some patients, hepatocellular carcinoma [17]. Whether Fontan patients should undergo isolated heart versus combined heart-liver transplantation continues to be hotly debated with the current approach to assessment and treatment varying across transplant centers. The Hospital of the University of Pennsylvania reported outcomes in eight Fontan patients who underwent combined heart-liver transplantation for biopsy-proven advanced fibrosis or cirrhosis; 100% survival was achieved at 30 days and 1 year [18]. It has been postulated that the addition of liver transplant reduces bleeding risk in Fontan patients [19]. In addition, there is increasing evidence that cardiac cellular and antibody-mediated rejection are less frequent after combined heart-liver transplant [20] [21]. Despite these potential advantages, it remains unclear whether combined heart-liver transplant should be recommended in all Fontan patients. A recent UNOS study reported equivalent survival in CHD patients undergoing isolated heart versus combined heart-liver transplantation [15].

The model for end-stage liver disease excluding international normalized ratio (MELD-XI) score may be helpful for stratifying risk. A MELD-XI score

Table 13.3 Risk factors and contraindications to heart transplant in ACHD patients

Absolute contraindications
Systemic illness with life expectancy <2 years despite heart transplant including:
Active or recent solid organ or blood malignancy within 5 years
AIDS with frequent opportunistic infections
Active systemic lupus erythematosus, sarcoid, or amyloidosis with multisystem involvement
Irreversible renal or hepatic dysfunction in patients considered only for heart transplant
Significant obstructive pulmonary disease (FEV1 <1.0)
Fixed pulmonary hypertension
Pulmonary artery systolic pressure >60 mmHg
Mean transpulmonary gradient >15 mmHg
Pulmonary vascular resistance >6 Wood units
Relative contraindications
Age >70 years[a]
Active infection
Active peptic ulcer disease
Severe diabetes with poor glycemic control (HBA1c >7.5%) and/or end-organ damage (neuropathy, nephropathy, retinopathy)
Severe peripheral vascular or cerebrovascular disease not amenable to surgical or percutaneous therapy
Morbid obesity (body mass index >35 g/m^2) or cachexia (BMI <18 g/m^2)
Estimated glomerular filtration rate <40 mL/min/1.73 m^2
Bilirubin >2.5 mg/dL, serum transaminases >3×, INR >1.5 off warfarin
Irreversible neurological or neuromuscular disorder
Psychosocial instability limiting adherence after transplant
Active smoker or drug use within 6 months
Heparin-induced thrombocytopenia within 100 days
ACHD related
Complex anatomy combined with additional contraindication as listed above[b]
Multiple severe congenital anomalies (rare)
Severe metabolic disease (rare)
Neurocognitive impairment limiting adherence after transplant

[a]Carefully selected patients > 70 years of age may be considered for transplantation
[b]Complex anatomy alone is not a contraindication to heart transplantation. However, the combination of complex anatomy with additional risk factors is associated with increased mortality after heart transplantation. Adapted from Mancini D, Lietz K. Selection of cardiac transplantation candidates in 2010. Circulation 2010; 122:174

>18 has been associated with increased ACHD recipient mortality after HTx [22]. A second study reported significantly lower survival after HTx in Fontan patients when more than one of the following findings was identified: elevated MELD-XI, MELD-XI >19, EF <20%, moderate or severe AV valve regurgitation, Fontan pressure >16.5 mmHg, and need for dialysis and ECMO support [23]. Validation of these risk scores in larger patient populations will be important before these criteria, and cutoffs for liver disease can be integrated into transplant selection criteria.

Based on the existing data, a case-by-case approach is recommended with combined heart-liver transplant being an important consideration in those with high-risk features as described but particularly once cirrhosis is confirmed on liver biopsy.

13.3.2 Pulmonary Hypertension

Assessment of PH in ACHD patients is made more challenging by the presence of complex anatomy, passive pulmonary blood flow, imbalanced flow to the right and left lung, and alternative sources of pulmonary blood flow in the form of collateral vessels. Based upon current ISHLT HTx guidelines, a transpulmonary gradient (TPG) <15 mmHg and pulmonary vascular resistance (PVR) <3 Wood units are considered acceptable for HTx [14]. Vasodilator challenge should be undertaken if PH is confirmed at catheterization. Inotropes and diuretics are important in patients with pulmonary venous HT arising secondary to a failing systemic ventricle. Reversible PH has been associated with good outcomes after isolated HTx [24, 25] despite an increased risk of donor right HF during the first 30 days after HTx [26].

Although PVR and TPG are commonly used to differentiate HF patients with pulmonary vascular disease from those with passive PH, elevations in TPG and PVR do not always reflect precapillary PH. As such more sensitive measures of PH continue to be sought. An elevated diastolic pulmonary artery pressure-to-pulmonary capillary wedge pressure gradient (DPG) has been proposed as a better indicator of pulmonary vascular remodeling. However, in a study of over 5800 patients with PH, there was no difference in post-HTx survival in those with high versus low DPG indicating a limited prognostic role for this measure [27]. Others have shown the hemodynamic response to nitroprusside at the time of right heart catheterization to be useful for differentiating risk in PH patients with non-ACHD-related HF. Short-term mortality was significantly higher in patients with fixed PVR above 2.5 Wood units and those whose PVR could be reduced but only at the expense of systemic hypotension (SBP <85 mmHg) [28]. These findings are more applicable to patients with biventricular anatomy and are as yet unproven in ACHD.

Overall, these studies underscore the fact that reliance on one static measure to characterize PH type and severity prior to HTx is inadequate and that serial monitoring, provocative maneuvers, and integration of several indices are important at the time of ACHD HTx assessment.

13.3.3 Sensitization

Sensitization, the process by which preformed antibodies to human leukocyte antigens (HLA) are developed, remains an important barrier to HTx. Patients with panel reactive antibodies (PRA) greater than 10% are considered sensitized. Sensitization risk factors include prior blood transfusions, pregnancies, homografts, tissue allografts, and mechanical circulatory support [29]. HTx recipients with high degrees of sensitization have increased wait-list times and are at a higher risk of posttransplant rejection, cardiac transplant vasculopathy, graft failure, and mortality [30–33]. Treatment options for sensitization include plasmapheresis/intravenous immunoglobulin/rituximab (pre-/posttransplant) and thymoglobulin (posttransplant) (IVIg). By decreasing circulating antibodies, desensitization can

allow patients to undergo HTx with a negative prospective donor-specific crossmatch. Surprisingly, equivalent 5-year survival has been reported in sensitized patients undergoing HTx with and without prior desensitization [34]. These findings suggest desensitization increases the chance of sensitized patients proceeding to HTx with a negative crossmatch but without clear evidence for improved long-term survival.

13.4 Wait-List Outcomes and Opportunities for Decreasing Wait-List Mortality

The decision to proceed with listing for HTx is based on an estimated 1-year survival of less than 80%. Estimating survival in ACHD HF patients is challenging since patients are younger and often appear compensated despite significant circulatory dysfunction and end-organ disease. In a multicenter study of 45 ACHD patients undergoing HTx evaluation between 2000 and 2012, 13 were deemed too high risk, 6 because of liver cirrhosis, and 1 due to irreversible pulmonary HT. Five were considered too well [35]. As observed elsewhere [18], those declined were more likely to have single-ventricle physiology. No difference in survival was observed between those listed versus not listed for HTx. Among patients who underwent HTx, 1-year survival was 85% with four ACHD deaths occurring within 30 days of HTx. Of the 13 patients not listed due to high risk, 5 (38%) died secondary to progressive HF. Of the five patients considered too well for HTx, one died from a hemorrhagic stroke, and the other four continued to be managed medically without need for HTx. In reviewing these outcomes, it is clear that morbidity and mortality are high in ACHD HF patients, both with and without HTx.

Once listed, ACHD patients spend longer on the HTx wait list [36, 37]. Wait-list times in ACHD recipients are increased for several reasons including being listed at lower urgency, being more highly sensitized, and the need for non-lung donors to enable vascular reconstruction in some recipients [37]. Since 1996, the number of ACHD patients listed status 2 has remained constant, whereas for non-ACHD patients, this percentage has fallen likely due to a relative increase in the number of non-ACHD patients being upgraded to status 1 [38]. Changes in the organ allocation policies, including a provision that patients with a ventricular assist device (VAD) be listed as status 1B, have influenced this shift. VAD patients also receive 30 days of discriminatory 1A time as well as 1A status for VAD complications leaving ACHD patients, many of whom do not require or qualify for mechanical circulatory support, at a significant disadvantage.

Wait-list mortality of 10% in ACHD patients is comparable to others listed for HTx although ACHD patients are significantly more likely to die secondary to cardiac causes, most commonly sudden cardiac death [37]. Highlighting a need for improved arrhythmia risk stratification and treatment, ACHD patients are less likely to be protected with an implantable cardiac defibrillator while on the HTx wait list (44% of ACHD patients listed for transplantation have an ICD vs. 75% of non-ACHD patients; $p < 0.001$) [37].

13.5 HTx Outcomes

ACHD patients comprise approximately 3% of the total HTX population, although this number is growing rapidly with a 40% increase in ACHD HTx over the last two decades [36, 39]. Multicenter registries provide a broad overview of ACHD outcomes after HTx (Table 13.4). Single center studies report outcomes by congenital subtype and therefore enable comparison between ACHD subgroups and transplant center [18, 40–47].

ACHD is an independent predictor of increased mortality with a two- to threefold increase in the relative risk of 1-year posttransplant mortality [30, 36, 48]. Of the ACHD subgroups, evaluated mortality is highest in the Fontan population with posttransplant mortality of 25–30% [41, 44–46]. The main causes of increased mortality in Fontan recipients are primary graft failure (reflecting longer ischemic times), early rejection (due to sensitization), and the combined effect of comorbid disease (hypoalbuminemia, immune dysfunction, liver disease, coagulopathy, renal dysfunction, and occult PH).

Technical complications are important with death secondary to bleeding and other surgical factors accounting for 10% of ACHD HTx recipient deaths vs. 4% of others ($p < 0.0001$) [1]. Ischemic times are significantly longer due to the need for reconstructive surgery, required in up to 75% of CHD patients undergoing HTx [49]. Bleeding risks are especially high in patients with single-ventricle anatomy following reconstruction of the aortic arch, vena cavae, or pulmonary arteries and those with dense sternal adhesions from previous sternotomies [50]. For these reasons congenital surgical expertise at the time of HTx in CHD recipients is essential. Excellent outcomes have been reported with congenital heart and adult HTx surgeons working in collaboration, not only at the time of surgery but also in the assessment and planning stages [18, 40]. Current guidelines recommend all ACHD patients undergo transplantation in high-volume centers with combined expertise in congenital heart disease and HTx [14].

A survival paradox exists among ACHD recipients whose high early mortality is balanced by better long-term survival. Compared to other HF subgroups, ACHD patients who survive the early period after HTx have better long-term survival due to lower infection and malignancy-related mortality as well as decreased incidence of coronary allograft vasculopathy. Lower rates of infection and malignancy are likely due to ACHD patient's younger age and a more robust immune system but with a converse increased risk of graft failure and rejection. The clinical implication of this finding is that immunosuppression protocols need to be carefully adjusted in ACHD recipients to maintain the balance between the competing risks of rejection, infection, and malignancy.

With appropriate risk stratification, patient selection, planning, and team-based care, ACHD patients can successfully undergo transplantation in high-volume

Table 13.4 Multicenter studies evaluating heart transplant outcomes in patients with congenital heart disease

Author (year)	Registry and age group	Major findings
Shah (2016)	UNOS >18 years	Graft dysfunction, cardiovascular, and multiple organ failure are the top three causes of death in ACHD HTx recipients. The graft dysfunction rate is significantly higher in ACHD ($p = 0.03$). Postoperative hemorrhage as a cause of death was higher in ACHD HTx (2% vs. 0.5%, $p < 0.01$) A 30-day mortality has improved in the current era (2010–2014) to 6.8% from 14.3% in the early era (2000–2004), $p < 0.0001$)
Burchill (2014)	ISHLT >18 years	Early death due to technical reasons is higher among ACHD HTx recipients vs. controls (10% vs. 4%, $p < 0.0001$) ACHD HTx recipients who survive the first 30 days after HTx have superior long-term survival vs. controls ($p < 0.0001$) which is in part due to lower infection ($p < 0.0001$) and malignancy-related ($p < 0.01$) mortality
Davies (2011)	UNOS >18 years	Early HTx mortality higher in ACHD HTx recipients vs. others (18.9% vs. 9.6%, $p = XX$) MCS was not associated with improved survival in ACHD patients awaiting HTx
Karamlou (2010)	UNOS >18 years	HTx in ACHD patients increased by 41% between 1990 and 2008 ACHD is an independent risk factor for death and pre-transplantation
Patel (2009)	UNOS >17 years	Early HTx mortality higher in ACHD patients vs. others (16% vs. 6%, $p = XX$) ACHD HTx recipients are more likely to die from primary graft and MOF ($p=$) ACHD HTx recipients have longer wait-list time ($p=$) ACHD HTx recipients have higher PVR ($p=$)
Lamour (2009)	Pediatric Heart Transplant Study, Cardiac Transplant Registry Database; infants, children, and adults combined	Survival after HTx lower in Fontan vs. non-Fontan congenital heart disease patients ($p=$) Predictors of death in ACHD HTx recipients; older age, older donors, longer ischemic time, Fontan
Bernstein (2006)	Pediatric Heart Transplant Study; Fontan patients age <17 years	Survival in Fontan children after HTx 76% at 1 year and 68% at 5 years Protein-losing enteropathy resolved in all who survived >30 days after HTx Cause of death in Fontan children undergoing HTx: infection (30%), graft failure (17%), rejection (13%), sudden death (13%), and coronary allograft vasculopathy (9%)

(continued)

Table 13.4 (continued)

Author (year)	Registry and age group	Major findings
Doumouras (2016)[a]	Meta-analysis	Meta-analysis of 12 studies including 2007 patients with congenital heart disease A 30-day mortality significantly higher in CHD versus non-CHD patients (RR 2.33, 95% CI 1.80–3.03). A 30-day mortality risk was significantly higher in Fontan/Glenn CHD patients than others with congenital heart disease

ACHD adult congenital heart disease, *HTx* heart transplantation, *ISHLT* International Society of Heart and Lung Transplantation, *MCS* mechanical circulatory support, *MOF* multi-organ failure, *UNOS* United Network for Organ Sharing, *PVR* pulmonary vascular resistance
[a]In press, *Journal of Heart and Lung Transplantation* 2016

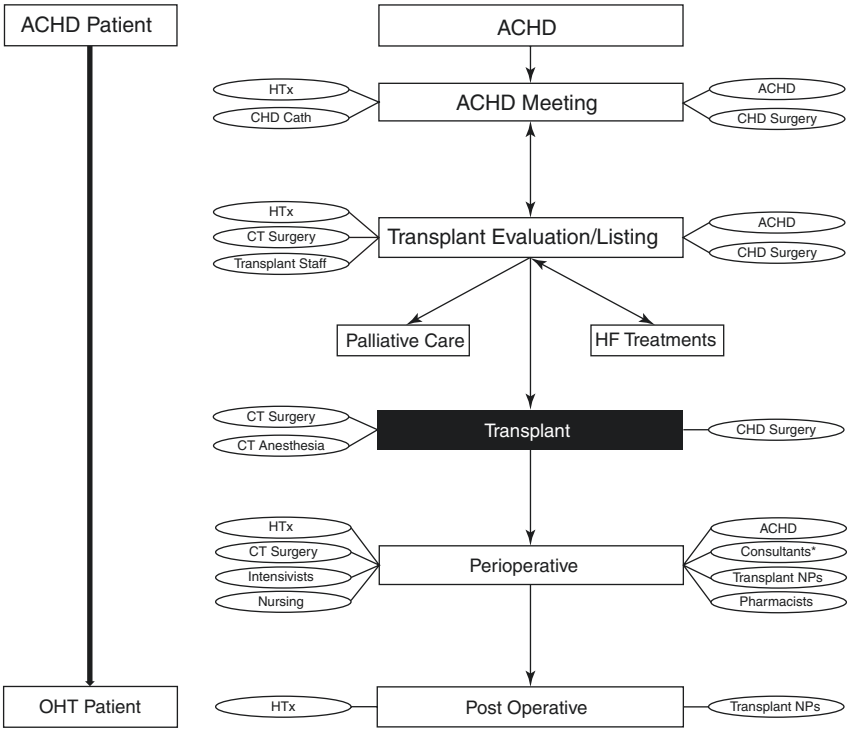

Fig. 13.2 An interdisciplinary team providing subspecialist expertise at the time of ACHD patient evaluation/listing, HTx, and perioperative and postoperative care is recommended

centers with combined expertise in congenital heart disease and HTx [14]. An interdisciplinary team providing subspecialist expertise at the time of ACHD patient evaluation/listing, HTx, and perioperative and postoperative care is recommended [18] (Fig. 13.2).

13.6 Alternatives to Transplantation

13.6.1 Mechanical Circulatory Support

A recent analysis of the INTERMACS data demonstrated that VAD use is limited overall in the ACHD population [51]. ACHD patients frequently require alternative positioning and surgical implantation techniques that vary by anatomy and device (Fig. 13.3) [52–56].

Outcomes in ACHD patients with biventricular anatomy supported by LVAD alone are equivalent to non-ACHD HF patients [51]. However, for those requiring biventricular assist device or total artificial heart, outcomes are poor with low short-term survival and a high incidence of stroke and thromboembolic complications [55]. For most ACHD patients, VAD is used as a bridge to HTx (rather than destination therapy) although little is known about outcomes after HTx in this population. For non-ACHD HF patients bridged to HTx with a VAD, 60-day survival is significantly lower [57]. Future research into outcomes in ACHD patients being bridged to HTx on VADs is important given the potential for higher early mortality related to complex anatomy, multiple sternal reentries, dense scarring, longer ischemic times, and higher sensitization [58].

Mechanical support has been used in patients with a systemic right ventricle (RV) [52, 59] to support the failing RV and to reverse pulmonary (venous) HT. Practical considerations in Mustard/Senning patients include the integrity of the

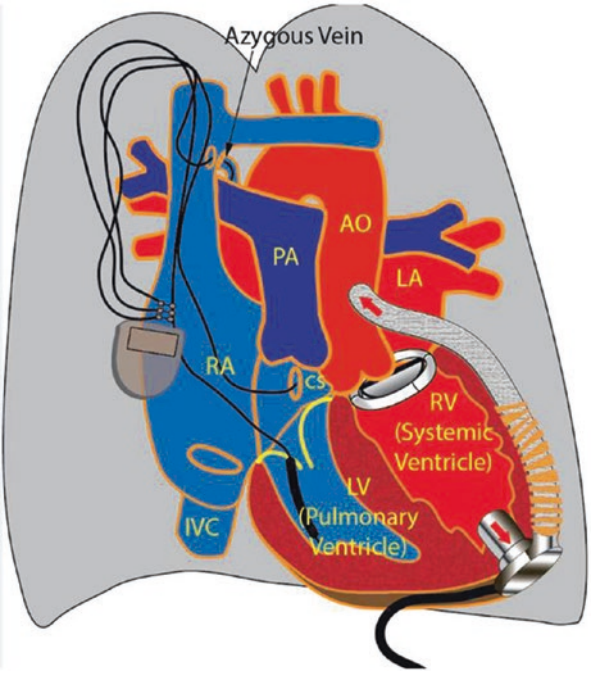

Fig. 13.3 Illustration detailing the orientation of VAD placement and the direction of blood flow in a patient with congenitally corrected transposition of the great arteries. *AO* aorta, *CS* coronary sinus, *IVC* inferior vena cava, *LA* left atrium, *LV* left ventricle, *PA* pulmonary artery, *RA* right atrium, *RV* right ventricle. Illustration used with permission and taken from Menachem Congenital Heart Disease 2015

atrial baffles which must be assessed prior to RVAD implant. Baffle stenosis interferes with VAD flow and may contribute to persistent PH in the case of pulmonary baffle stenosis. Baffle leaks increase the risk of thromboembolism, cyanosis, and ventricular volume overload. Preemptive treatment of arrhythmia substrate should also be considered prior to VAD implant given the impact of uncontrolled atrial and ventricular arrhythmias on VAD flows and ventricular function. There is a perception that the subpulmonic LV is less prone to failing after systemic RV implantation [52]. However, failure of the subpulmonic LV is not uncommon and requires preemptive planning at the time of RVAD implant. For those not responding to inotropes and volume removal with ultrafiltration/dialysis, temporary LVAD support may be needed.

13.6.2 Extracorporeal Membrane Oxygenation (ECMO)

Extracorporeal membrane oxygenation (ECMO) is arguably the most commonly used mechanical support platform for ACHD patients. Most commonly ECMO is used to support ACHD patients who develop acute HF in the postoperative period [60] witnessed as failure to wean from cardiopulmonary bypass. Among 77 CHD patients undergoing HTx between 1988 and 2014, postoperative ECMO was required in 14 patients [61]. Eleven of these patients were placed on ECMO in the operating room due to failure to wean from cardiopulmonary bypass. The remaining three were placed on ECMO within 48 h of surgery due to low cardiac output. Of these 14 patients, 7 died in the hospital. In addition to highlighting poor outcomes with ECMO support, these findings emphasize the importance of ACHD patient selection for cardiac surgeries. ACHD HF patients with significantly reduced ventricular systolic function are especially high risk for acute HF, and candidacy for "exit strategies" (i.e., ECMO transitioning to VAD as a bridge to HTx) is important to consider before surgery is undertaken.

13.6.3 Palliative Care

Palliative care improves quality of life, anxiety, depression, and spiritual well-being in patients with HF [62]. Increasingly, advanced HF teams incorporate palliative care specialists with expertise in symptom management and end-of-life therapies in the care of all patients with HF requiring advanced therapies. Palliative care can be offered in addition to advanced HF therapies or as the mainstay of treatment in those with contraindications to transplant and mechanical circulatory support.

13.7 Peri-/Postoperative Management

The perioperative period has been described as the "Achilles' heel" for transplantation in ACHD patients [48]. In an evaluation of UNOS from 2000 to 2014, graft and cardiovascular dysfunction were found to be the top two reasons for early mortality

and were most likely due to the elevated PVR, allosensitization, and longer donor ischemic times. The management of PH in the perioperative setting is paramount to a successful outcome. Following congenital heart surgery, the incidence of perioperative pulmonary hypertensive crisis is in the range of 2–5% [63]. Pulmonary vasoconstriction leads to right HF and systemic hypotension. Treatment options include inhaled nitric oxide, prostacyclins, endothelin receptor antagonists, phosphodiesterase inhibitors, inotropes, and pressors.

Conclusion

Both HF and ACHD are rapidly growing subspecialties of cardiology, but it is only relatively recently that ACHD HF is being recognized as complication requiring particular expertise. As the number of ACHD patients grows, there will be a shortage of appropriately trained providers to care for them. Over time, advanced fellowships will need to collaborate to adequately train both specialties to handle the vast number of patients with ACHD-related HF [64].

In conclusion, HTx is an effective treatment strategy for selected ACHD patients with end-stage cardiac disease. Diagnosis and treatment of ACHD-related HF rely heavily on the art rather than science of medical practice. A number of opportunities for improving outcomes in patients are identified including:

(1) Earlier collaboration with advanced HF teams
(2) Mitigation of risk through team-based evaluation
(3) Recognition that liver disease, PH, and sensitization play important roles in the risk profile of patients
(4) Assessment of sudden cardiac death risk while awaiting transplantation
(5) Multicenter studies to better define guidelines for transplant
(6) Expert surgical planning involving congenital and transplant surgeons to reduce ischemic time and bleeding risk
(7) Tailored immunosuppression protocols in the posttransplant period
(8) Identification of centers of excellence specializing in transplant ACHD patients
(9) The use of VAD as a bridge to HTX
(10) Palliative care as a vital component of care irrespective of the decision to proceed with HTx or not

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