Cardiology in the Young (2015), **25(Suppl. 2)**, 67–73
doi:10.1017/S1047951115000852

Original Article

Clinical management of patients with acute heart failure*

Joseph W. Rossano

Cardiac Center, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States of America

Abstract Acute heart failure is a common and serious complication of congenital and acquired heart disease, and it is associated with significant morbidity, mortality, and costs. When a patient is admitted to the hospital with acute heart failure, there are several important goals for the hospital admission, including maintaining adequate perfusion, establishing the underlying aetiology for the heart failure, patient and family education, and discharge from the hospital in a stable condition. The pathway to home discharge is variable and may include inotropic therapy, mechanical circulatory support, and/or heart transplantation. This review will cover the epidemiology, presentation, and management of acute heart failure in children.

Keywords: Acute heart failure; paediatric heart failure; ventricular assist device

Received: 5 February 2015; Accepted: 1 May 2015

Heart failure is an important global public health concern.[1] In the United States, it is currently estimated that greater than five million adults have heart failure,[2] and worldwide it is estimated that over 23 million people are living with heart failure.[3,4] The costs associated with heart failure are staggering. The total annual cost of heart failure in the United States is estimated to be nearly $70 billion by 2030, with the majority of these costs arising from hospital care.[3–5] As a chronic condition, heart failure is characterised by acute exacerbations leading to hospitalisations. These acute events will be the focus of this review.

Epidemiology and outcomes of acute heart failure

Commonly accepted definitions of acute heart failure include acute symptoms that result from abnormalities of heart function.[6–8] The European Society of Cardiology defines acute decompensated heart failure as "the rapid onset of, or change in, symptoms or signs of heart failure. It is a life threatening condition that requires immediate medical attention and usually leads to urgent admission to the hospital".[9] For the purpose of this review, acute heart failure is essentially hospitalisations for the treatment of heart failure.

Acute heart failure is one of the most important pathophysiological syndromes in industrialised nations in terms of overall mortality, morbidity, and cost.

It is also a relatively common and serious condition in children. There were nearly 14,000 heart failure-related hospitalisations in 2006 in the United States, from all aetiologies, corresponding to a prevalence of 15–18 admissions/100,000 children.[10] To place this in context, severe sepsis has a reported prevalence in the order of ~50 admissions/100,000 children.[11] Thus, when one considers serious acute onset diseases of childhood, heart failure is among the more prevalent. Most of the admissions are of patients with CHD, although ~15% have a cardiomyopathy or myocarditis. The disease also carries substantial morbidity and mortality. Paediatric heart failure-related hospitalisations have an over 20-fold increase in the risk of death compared with admissions without heart failure.[10]

The incidence of acute heart failure among patients with newly diagnosed cardiomyopathies has been described as 0.87/100,000 children <16 years of age.[12] Acute heart failure in patients with cardiomyopathies appears to be a significantly more morbid condition in children as compared with adults. Children have greater mortality, length of hospital stay, and hospital charges

*Presented at Johns Hopkins All Children's Heart Institute, International Pediatric Heart Failure Summit, Saint Petersburg, Florida, United States of America, 4–5 February, 2015.

Correspondence to: J. W. Rossano, MD, Cardiac Center, The Children's Hospital of Philadelphia, 34th Street & Civic Center Boulevard, Philadelphia, PA 19104, United States of America. Tel: + 267 426 3063; E-mail: rossanoj@email.chop.edu

when hospitalised with heart failure.[13] It is striking that hospital length of stay and hospital charges are greater for every age group of children compared with every age group of adults. This trend is also true for hospital mortality, with the exception of children >10 years and adults >70 years of age (Fig 1).[13] In addition, the use of advanced heart failure therapies such as extracorporeal membrane oxygenation, heart transplantation, and ventricular assist devices are also significantly more common in paediatric versus adult hospitalisations.[13] Thus, acute heart failure in children is common, morbid, and associated with worse outcomes compared with adults with heat failure.

Categorisation of heart failure

Symptoms of acute heart failure generally result from a congestion and/or decreased perfusion. As such, one useful method for categorising acute heart failure was proposed by Grady et al[14], and it categorises patients based on the presence or absence of congestion (wet or dry) and based on poor versus adequate perfusion

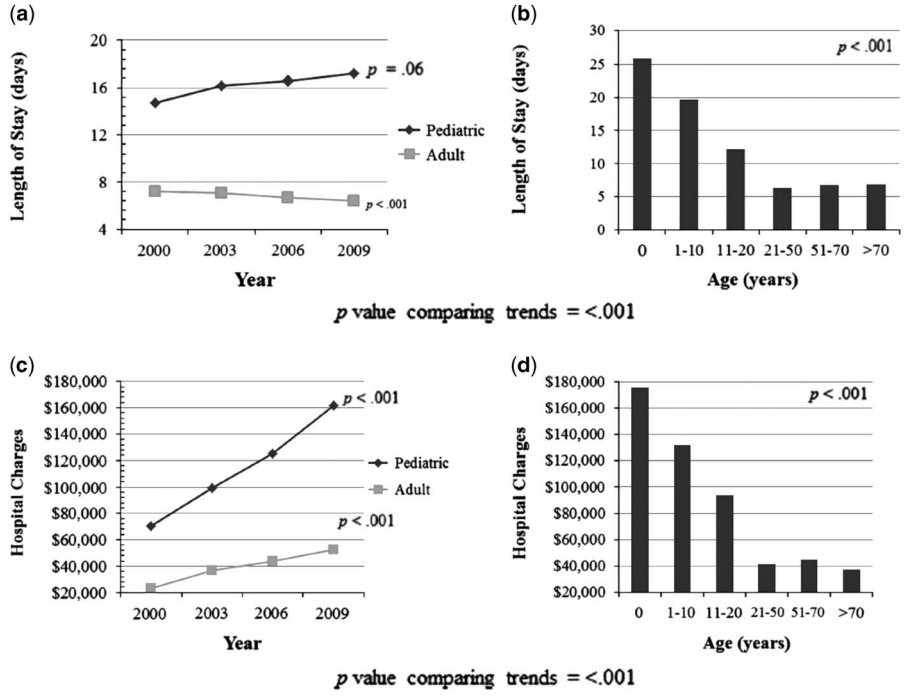

Figure 1.
*Comparison of paediatric and adult hospital length of stay (**a**) by year and (**b**) by age and hospital charges (**c**) by year and (**d**) by age. Reproduced with permission from Wittlieb-Weber et al.[13]*

	No Congestion	Congestion
	"Warm and Dry"	"Wet and Warm"
Adequate perfusion	A	B
	Optimal profile: focus on prevention of disease progression and decompensation	Diuresis with continuation of standard therapy
	"Cold and Dry"	"Wet and Cold"
Critical hypoperfusion	L	C
	Limited further options for therapy	Diuresis and redesign of regimen with other standard therapies

Figure 2.
Model for categorising patients with acute heart failure. The letter L represents the group with low output without congestion. Patients frequently progress from profile A to profile B. When that occurs, profile C commonly occurs after profile B. For the less-common profile of low output without congestion, the letter L was chosen rather than the letter D to avoid the implication that this profile necessarily follows profile C or is a less-desirable profile than C. Reproduced with permission from Grady et al.[14]

https://doi.org/10.1017/S1047951115000852 Published online by Cambridge University Press

(cold or warm) (Fig 2), with the ideal state of compensated heart failure being warm and dry. Categorising patients in this manner is not only a useful tool for medical management, but it also has prognostic information about adults with acute heart failure.[15] When a patient is admitted to the hospital with acute heart failure, there are several important goals for the hospital admission, including maintaining adequate perfusion, establishing the underlying aetiology for the heart failure, patient and family education, and discharge from the hospital is a stable condition.

Maintaining adequate perfusion

Patients with congestion but adequate perfusion: "warm and wet"

Many patients with acute heart failure are well-perfused on presentation, but have elevated atrial pressures contributing to pulmonary and systemic congestion.[7,12,16] For these patients, vasodilators and diuretics can lead to rapid symptomatic improvement, although these medications do not likely affect the long-term outcome.[16–19] It is important to note that diuretics and volume depletion can lead to increased activation of the renin–angiotensin–aldosterone system, which can be detrimental in heart failure.[20] In addition, aggressive diuresis can lead to decreased renal function, which is associated with increased mortality in heart failure patients.[8,21–26]

For these patients with maintained perfusion, inotropic agents may not be necessary, and indeed may be harmful. Among adults with chronic heart failure, a randomised controlled trial found milrinone use to be associated with increased mortality.[27] In addition, the short-term use of milrinone for acute heart failure in adults was found in a randomised trial to be associated with sustained hypotension and new atrial arrhythmias with no survival benefit compared with placebo.[28] There are also multiple other non-randomised studies that describe a strong association between inotrope use and worse outcomes in adult heart failure patients, although this association may be more prominent in ischaemic versus non-ischaemic cardiomyopathy.[29–31] There are limited data on the safety and efficacy of inotropic medications for children with acute heart failure, although they are frequently utilised medications.[32,33] In one multi-centre study, vasoactive medications were used in over 85% of heart failure admissions to the ICU. Importantly, the use of vasoactive medications was associated with increased hospital mortality.[32] In another single-centre study, the use of dopamine was independently associated with death or the need for mechanical circulatory support in paediatric heart failure patients.[21] Thus, for patients with adequate perfusion, inotropic mediations should be used with caution, and ideally withdrawn after a period of clinical stability. Chronic heart failure medications can be initiated or modified during these hospital admissions, generally after demonstration of adequate perfusion.

Understanding the aetiology of heart failure is important, as it may have important implications for prognosis and treatment. Overall, ~50% of patients with dilated cardiomyopathy will die or undergo heart transplantation within 5 years of their diagnosis.[34] Nevertheless, there are multiple aetiologies that can lead to a dilated and dysfunctional left ventricle, many of which have disease-specific therapy and superior outcomes with proper therapy – for example, in infants with coarctation of the aorta or anomalous left coronary artery from the pulmonary artery can lead to a phenotype similar to dilated cardiomyopathy. Careful attention to arch and coronary artery imaging is of paramount importance, as these diseases have excellent long-term survival with appropriate surgical therapy.[35,36] There are multiple other aetiologies of dilated cardiomyopathy, including myocarditis, metabolic/mitochondrial disorders, tachycardia-induced cardiomyopathy, and endocrinopathies that should be part of the diagnostic evaluation (Table 1).[37] An important part of the diagnostic evaluation is the consideration of cardiac catheterisation and endomyocardial biopsy. Although cardiac MRI in increasing utilised in heart failure patients and can be useful in assessing the presence of myocarditis, endomyocardial biopsy can be helpful in challenging cases.[38–45] The risk of this invasive procedure must be carefully considered; however, in experienced centres, it can be performed safely even in critically ill patients.[46–48] Importantly, these findings may lead to changes in management in a significant number of patients.[45]

Table 1. Aetiologies of dilated cardiomyopathy.

Aetiologies of dilated cardiomyopathy
Cytoskeletal–sarcomeric link disruption
Genetic mutation
Infections
Toxic (e.g. anthracyclines, alcohol)
Autoimmune disease
Metabolic storage diseases
Mitochondrial disease
Ion channelopathies
Peripartum
Infiltrative disease
Tachycardia-induced cardiomyopathy
Endomyocardial disease
Endocrine disorders (e.g. hypothyroidism)
Nutritional deficiencies
Electrolyte disturbances

Adapted from Jefferies et al[37]

https://doi.org/10.1017/S1047951115000852 Published online by Cambridge University Press

Patients with poor perfusion: "cold and wet" & "cold and dry"

Acute heart failure patients with poor perfusion constitute a significant proportion of children admitted to the hospital.[7,12,32] These patients are generally admitted to the ICU where the immediate priority is to improve the perfusion and stabilise the circulation. Inotropic medications are utilised in essentially all of the patients, with wide variability among centres as to the preferred vasoactive medications of choice. Commonly utilised inotropic medications for these patients include milrinone, dopamine, dobutamine, and epinephrine.[32] There are few data to guide clinical practice with regard to the optimal intotropic agent for acute heart failure. Our practice is to use milrinone as the first-line agent, for patients without hypotension. For patients with hypotension or an inadequate response to milrinone, catecholamines such as dopamine or epinephrine are added. In the setting of escalating medical therapy, intubation with mechanical ventilation and mechanical circulatory support may be needed.[32,49,50]

There are a variety of options available for short- and long-term mechanical circulatory support in children (Table 2).[49–52] Short-term mechanical circulatory support with either extracorporeal membrane oxygenation or a temporary ventricular assist device can be effective for patients in whom the ventricular function is expected to recover in a relatively short period of time – for example, acute rejection in a heart transplant recipient or fulminant myocarditis.[50,53,54] These devices can also be used as a bridge to a more durable ventricular assist device if the patient requires longer duration of mechanical support. Of note, extracorporeal membrane oxygenation is of limited utility for long-term mechanical circulatory support. In the Berlin Heart Trial, no one was alive on extracorporeal membrane oxygenation by 30 days of support, and the use of extracorporeal membrane oxygenation as a bridge to heart transplant remains one of the strongest risk factors of post-transplant mortality.[55–57]

Long-term mechanical circulatory support can be achieved with a high degree of success with the use of either pulsatile or continuous-flow ventricular assist devices.[52,55,58,59] The best outcomes of long-term ventricular assist device support are obtained in older children with dilated cardiomyopathy. Small children, especially those <5 kg, and those with complex circulations remain a challenging group to provide long-term support.[60–63] Among adult heart failure patients, continuous-flow ventricular assist devices have essentially replaced older-generation pulsatile pumps, although size limitations preclude their use in infants and small children. The use of these device has allowed some children to be discharged from the hospital while on support. For the vast majority of these patients, durable ventricular assist devices are used as a bridge to transplantation; however, some patients will be able to have the device explanted after myocardial recovery.[52,64–66] Rarely, these devices are utilised as destination therapy – ventricular assist device implantation without the expectation of transplant or myocardial recovery.[67]

Road to discharge

In the present era, there are many pathways to home for a child with acute heart failure. The patient may be stabilised with inotropic therapy, transitioned to an oral regimen, and be discharged home in a compensated state. The patient's condition may also deteriorate on medical therapy and can be placed on mechanical circulatory support. Although on support, the patient may have the device explanted after myocardial recovery, be transplanted during that hospital admission from a ventricular assist device, or

Table 2. Commonly used and approved ventricular assist devices by the United States Food and Drug Administration.

Device	Manufacturer	Type	Approved indication
HeartMate II	Thoratec	Continuous-flow	BTT, DT
Berlin Heart EXCOR Paediatric	Berlin Heart	Pulsatile paracorporeal	BTT
Thoratec pVAD	Thoratec	Pulsatile paracorporeal	BTT, PC
DeBakey VAD *Child*	Micromed	Continuous-flow	BTT
TandemHeart	CardiacAssist	Centrifugal	ECS < 6 hours
HeartWare Ventricular Assist System	HeartWare	Centrifugal	BTT
SynCardia Total Artificial Heart	SynCardia Systems	Artificial heart	BTT
Impella	Abiomed	Continuous-flow	ECS < 6 hours
Centrimag	Thoratec	Centrifugal	ECS < 6 hours
Rotaflow	Maquet	Centrifugal	ECS < 6 hours

BTT = bridge to transplant; DT = destination therapy; PC = post-cardiotomy support; ECS < 6 hours = extracorporeal support of <6 hours duration
Adapted with permission from O'Connor and Rossano[49]

https://doi.org/10.1017/S1047951115000852 Published online by Cambridge University Press

be discharged home on the ventricular assist device. Alternatively, the patient may be stable, but inotropic-dependent. These patients may be transplanted during that hospitalisation or discharged home on inotropic medications.[33,68]

Patient and family education are crucial during these hospitalisations. For many patients, the heart failure hospitalisation may be the initial presentation of heart disease, especially in young persons who were thought to be healthy. Not only are there significant risks of morbidity and mortality for heart failure hospitalisations, but there are also significant risks of morbidity and mortality after discharge. It is important that the family understands the risks associated with the disease, the medical regimen, concerning symptoms, follow-up plans, and who to call with questions or concerns. Most of the serious adverse events occur within the 1st year of the diagnosis.[34] A multi-disciplinary team able to provide comprehensive care and family support is a critical factor for success. It is important to note that a significant number of patients will have meaningful improvement and even normalisation of systolic function during the first 2 years after the diagnosis of dilated cardiomyopathy;[69–71] however, long-term follow-up is still needed as recurrent heart failure and death can occur, even among patients who have normalised ventricular function.[69]

Conclusion

Acute heart failure is a common and serious complication of congenital and acquired heart disease in children. It is associated with significant morbidity, mortality, and cost. Advanced therapies including mechanical circulatory support and ventricular assist devices are frequently needed, and a multidisciplinary comprehensive team approach to these complicated patients can help assure optimal outcomes.

References

1. Cook C, Cole G, Asaria P, et al. The annual global economic burden of heart failure. Int J Cardiol 2014; 171: 368–376.
2. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2014 update: a report from the American Heart Association. Circulation 2014; 129: e28–e292.
3. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics-2015 update: a report from the American Heart Association. Circulation 2015; 131: e29–e322.
4. Ambrosy AP, Fonarow GC, Butler J, et al. The global health and economic burden of hospitalizations for heart failure: lessons learned from hospitalized heart failure registries. J Am Coll Cardiol 2014; 63: 1123–1133.
5. Heidenreich PA, Albert NM, Allen LA, et al. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. Circ Heart Fail 2013; 6: 606–619.
6. Adams KF Jr, Fonarow GC, Emerman CL, et al. Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE). Am Heart J 2005; 149: 209–216.
7. Macicek SM, Macias CG, Jefferies JL, et al. Acute heart failure syndromes in the pediatric emergency department. Pediatrics 2009; 124: e898–e904.
8. Butler J, Forman DE, Abraham WT, et al. Relationship between heart failure treatment and development of worsening renal function among hospitalized patients. Am Heart J 2004; 147: 331–338.
9. McMurray JJ, Adamopoulos S, Anker SD, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J 2012; 33: 1787–1847.
10. Rossano JW, Kim JJ, Decker JA, et al. Prevalence, morbidity, and mortality of heart failure-related hospitalizations in children in the United States: a population-based study. J Card Fail 2012; 18: 459–470.
11. Watson RS, Carcillo JA, Linde-Zwirble WT, et al. The epidemiology of severe sepsis in children in the United States. Am J Respir Crit Care Med 2003; 167: 695–701.
12. Andrews RE, Fenton MJ, Ridout DA, et al. New-onset heart failure due to heart muscle disease in childhood: a prospective study in the United Kingdom and Ireland. Circulation 2008; 117: 79–84.
13. Wittlieb-Weber CA, Lin KY, Zaoutis TE, et al. Pediatric versus adult cardiomyopathy and heart failure-related hospitalizations: a value-based analysis. J Card Fail 2015; 21: 76–82.
14. Grady KL, Dracup K, Kennedy G, et al. Team management of patients with heart failure: a statement for healthcare professionals from The Cardiovascular Nursing Council of the American Heart Association. Circulation 2000; 102: 2443–2456.
15. Nohria A, Tsang SW, Fang JC, et al. Clinical assessment identifies hemodynamic profiles that predict outcomes in patients admitted with heart failure. J Am Coll Cardiol 2003; 41: 1797–1804.
16 Publication Committee for the Vmac Investigators. Intravenous nesiritide vs nitroglycerin for treatment of decompensated congestive heart failure: a randomized controlled trial. JAMA 2002; 287: 1531–1540.
17. McMurray JJ, Adamopoulos S, Anker SD, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail 2012; 14: 803–869.
18. O'Connor CM, Starling RC, Hernandez AF, et al. Effect of nesiritide in patients with acute decompensated heart failure. N Engl J Med 2011; 365: 32–43.
19. Felker GM, Lee KL, Bull DA, et al. Diuretic strategies in patients with acute decompensated heart failure. N Engl J Med 2011; 364: 797–805.
20. Mentz RJ, Stevens SR, DeVore AD, et al. Decongestion strategies and renin-angiotensin-aldosterone system activation in acute heart failure. JACC Heart Fail 2015; 3: 97–107.
21. Price JF, Mott AR, Dickerson HA, et al. Worsening renal function in children hospitalized with decompensated heart failure: evidence for a pediatric cardiorenal syndrome? Pediatr Crit Care Med 2008; 9: 279–284.
22. Dupont M, Wu Y, Hazen SL, et al. Cystatin C identifies patients with stable chronic heart failure at increased risk for adverse cardiovascular events. Circ Heart Fail 2012; 5: 602–609.
23. Pronschinske KB, Qiu S, Wu C, et al. Neutrophil gelatinase-associated lipocalin and cystatin C for the prediction of clinical events in patients with advanced heart failure and after ventricular assist device placement. J Heart Lung Transplant 2014; 33: 1215–1222.

24. Damman K, Valente MA, Voors AA, et al. Renal impairment, worsening renal function, and outcome in patients with heart failure: an updated meta-analysis. Eur Heart J 2014; 35: 455–469.
25. Shlipak MG, Massie BM. The clinical challenge of cardiorenal syndrome. Circulation 2004; 110: 1514–1517.
26. Klein L, Massie BM, Leimberger JD, et al. Admission or changes in renal function during hospitalization for worsening heart failure predict postdischarge survival: results from the Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIME-CHF). Circ Heart Fail 2008; 1: 25–33.
27. Packer M, Carver JR, Rodeheffer RJ, et al. Effect of oral milrinone on mortality in severe chronic heart failure. N Engl J Med 1991; 325: 1468–1475.
28. Cuffe MS, Califf RM, Adams KF Jr, et al. Short-term intravenous milrinone for acute exacerbation of chronic heart failure: a randomized controlled trial. JAMA 2002; 287: 1541–1547.
29. Costanzo MR, Johannes RS, Pine M, et al. The safety of intravenous diuretics alone versus diuretics plus parenteral vasoactive therapies in hospitalized patients with acutely decompensated heart failure: a propensity score and instrumental variable analysis using the Acutely Decompensated Heart Failure National Registry (ADHERE) database. Am Heart J 2007; 154: 267–277.
30. Abraham WT, Adams KF, Fonarow GC, et al. In-hospital mortality in patients with acute decompensated heart failure requiring intravenous vasoactive medications: an analysis from the Acute Decompensated Heart Failure National Registry (ADHERE). J Am Coll Cardiol 2005; 46: 57–64.
31. Felker GM, Benza RL, Chandler AB, et al. Heart failure etiology and response to milrinone in decompensated heart failure: results from the OPTIME-CHF study. J Am Coll Cardiol 2003; 41: 997–1003.
32. Shamszad P, Hall M, Rossano JW, et al. Characteristics and outcomes of heart failure-related intensive care unit admissions in children with cardiomyopathy. J Card Fail 2013; 19: 672–677.
33. Price JF, Towbin JA, Dreyer WJ, et al. Outpatient continuous parenteral inotropic therapy as bridge to transplantation in children with advanced heart failure. J Card Fail 2006; 12: 139–143.
34. Towbin JA, Lowe AM, Colan SD, et al. Incidence, causes, and outcomes of dilated cardiomyopathy in children. JAMA 2006; 296: 1867–1876.
35. Azakie A, Russell JL, McCrindle BW, et al. Anatomic repair of anomalous left coronary artery from the pulmonary artery by aortic reimplantation: early survival, patterns of ventricular recovery and late outcome. Ann Thorac Surg 2003; 75: 1535–1541.
36. Fesseha AK, Eidem BW, Dibardino DJ, et al. Neonates with aortic coarctation and cardiogenic shock: presentation and outcomes. Ann Thorac Surg 2005; 79: 1650–1655.
37. Jefferies JL, Towbin JA. Dilated cardiomyopathy. Lancet 2010; 375: 752–762.
38. Friedrich MG, Sechtem U, Schulz-Menger J, et al. Cardiovascular magnetic resonance in myocarditis: A JACC White Paper. J Am Coll Cardiol 2009; 53: 1475–1487.
39. Nugent AW, Davis AM, Kleinert S, et al. Clinical, electrocardiographic, and histologic correlations in children with dilated cardiomyopathy. J Heart Lung Transplant 2001; 20: 1152–1157.
40. Bowles NE, Ni J, Kearney DL, et al. Detection of viruses in myocardial tissues by polymerase chain reaction. Evidence of adenovirus as a common cause of myocarditis in children and adults. J Am Coll Cardiol 2003; 42: 466–472.
41. Neilan TG, Coelho-Filho OR, Danik SB, et al. CMR quantification of myocardial scar provides additive prognostic information in nonischemic cardiomyopathy. JACC Cardiovasc Imaging 2013; 6: 944–954.
42. Gulati A, Jabbour A, Ismail TF, et al. Association of fibrosis with mortality and sudden cardiac death in patients with nonischemic dilated cardiomyopathy. JAMA 2013; 309: 896–908.
43. Puntmann VO, Voigt T, Chen Z, et al. Native T1 mapping in differentiation of normal myocardium from diffuse disease in hypertrophic and dilated cardiomyopathy. JACC Cardiovasc Imaging 2013; 6: 475–484.
44. Yamada T, Hirashiki A, Cheng XW, et al. Relationship of myocardial fibrosis to left ventricular and mitochondrial function in nonischemic dilated cardiomyopathy—a comparison of focal and interstitial fibrosis. J Card Fail 2013; 19: 557–564.
45. Bennett MK, Gilotra NA, Harrington C, et al. Evaluation of the role of endomyocardial biopsy in 851 patients with unexplained heart failure from 2000-2009. Circ Heart Fail 2013; 6: 676–684.
46. Daly KP, Marshall AC, Vincent JA, et al. Endomyocardial biopsy and selective coronary angiography are low-risk procedures in pediatric heart transplant recipients: results of a multicenter experience. J Heart Lung Transplant 2012; 31: 398–409.
47. Yoshizato T, Edwards WD, Alboliras ET, et al. Safety and utility of endomyocardial biopsy in infants, children and adolescents: a review of 66 procedures in 53 patients. J Am Coll Cardiol 1990; 15: 436–442.
48. Zhorne D, Petit CJ, Ing FF, et al. A 25-year experience of endomyocardial biopsy safety in infants. Catheter Cardiovasc Interv 2013; 82: 797–801.
49. O'Connor MJ, Rossano JW. Ventricular assist devices in children. Curr Opin Cardiol 2014; 29: 113–121.
50. Wilmot I, Morales DL, Price JF, et al. Effectiveness of mechanical circulatory support in children with acute fulminant and persistent myocarditis. J Card Fail 2011; 17: 487–494.
51. Mossad EB, Motta P, Rossano J, et al. Perioperative management of pediatric patients on mechanical cardiac support. Paediatr Anaesth 2011; 21: 585–593.
52. Cabrera AG, Sundareswaran KS, Samayoa AX, et al. Outcomes of pediatric patients supported by the HeartMate II left ventricular assist device in the United States. J Heart Lung Transplant 2013; 32: 1107–1113.
53. Morales DL, Braud BE, Price JF, et al. Use of mechanical circulatory support in pediatric patients with acute cardiac graft rejection. ASAIO J 2007; 53: 701–705.
54. Teele SA, Allan CK, Laussen PC, et al. Management and outcomes in pediatric patients presenting with acute fulminant myocarditis. J Pediatr 2011; 158: 638–643.
55. Fraser CD Jr, Jaquiss RD, Rosenthal DN, et al. Prospective trial of a pediatric ventricular assist device. N Engl J Med 2012; 367: 532–541.
56. Singh TP, Almond CS, Semigran MJ, et al. Risk prediction for early in-hospital mortality following heart transplantation in the United States. Circ Heart Fail 2012; 5: 259–266.
57. Dipchand AI, Kirk R, Edwards LB, et al. The Registry of the International Society for Heart and Lung Transplantation: Sixteenth Official Pediatric Heart Transplantation Report–2013; focus theme: age. J Heart Lung Transplant 2013; 32: 979–988.
58. Almond CS, Morales DL, Blackstone EH, et al. Berlin Heart EXCOR pediatric ventricular assist device for bridge to heart transplantation in US children. Circulation 2013; 127: 1702–1711.
59. Morales DL, Almond CS, Jaquiss RD, et al. Bridging children of all sizes to cardiac transplantation: the initial multicenter North American experience with the Berlin Heart EXCOR ventricular assist device. J Heart Lung Transplant 2011; 30: 1–8.
60. Rossano JW, Woods RK, Berger S, et al. Mechanical support as failure intervention in patients with cavopulmonary shunts (MFICS): rationale and aims of a new registry of mechanical circulatory support in single ventricle patients. Congenit Heart Dis 2013; 8: 182–186.
61. Rossano JW, Goldberg DJ, Fuller S, et al. Successful use of the total artificial heart in the failing Fontan circulation. Ann Thorac Surg 2014; 97: 1438–1440.

62. Conway J, St. Louis J, Morales DL, et al. Delineating survival outcomes in children <10 kg bridged to transplant or recovery with the Berlin Heart EXCOR Ventricular Assist Device. JACC Heart Fail 2015; 3: 70–77.
63. Weinstein S, Bello R, Pizarro C, et al. The use of the Berlin Heart EXCOR in patients with functional single ventricle. J Thorac Cardiovasc Surg 2014; 147: 697–704.
64. Lowry AW, Adachi I, Gregoric ID, et al. The potential to avoid heart transplantation in children: outpatient bridge to recovery with an intracorporeal continuous-flow left ventricular assist device in a 14-year-old. Congenit Heart Dis 2012; 7: E91–E96.
65. Irving CA, Crossland DS, Haynes S, et al. Evolving experience with explantation from Berlin Heart EXCOR ventricular assist device support in children. J Heart Lung Transplant 2014; 33: 211–213.
66. Kirklin JK, Naftel DC, Pagani FD, et al. Sixth INTERMACS annual report: a 10,000-patient database. J Heart Lung Transplant 2014; 33: 555–564.
67. Amodeo A, Adorisio R. Left ventricular assist device in Duchenne cardiomyopathy: can we change the natural history of cardiac disease? Int J Cardiol 2012; 161: e43.
68. Birnbaum BF, Simpson KE, Boschert TA, et al. Intravenous home inotropic use is safe in pediatric patients awaiting transplantation. Circ Heart Fail 2015; 8: 64–70.
69. Everitt MD, Sleeper LA, Lu M, et al. Recovery of echocardiographic function in children with idiopathic dilated cardiomyopathy: results from the pediatric cardiomyopathy registry. J Am Coll Cardiol 2014; 63: 1405–1413.
70. Alexander PM, Daubeney PE, Nugent AW, et al. Long-term outcomes of dilated cardiomyopathy diagnosed during childhood: results from a national population-based study of childhood cardiomyopathy. Circulation 2013; 128: 2039–2046.
71. O'Sullivan JJ, Roche SL, Crossland DS, et al. Recovery of heart function in children with acute severe heart failure. Transplantation 2008; 85: 975–979.

https://doi.org/10.1017/S1047951115000852 Published online by Cambridge University Press