A review of the management of patients with advanced heart failure in the intensive care unit

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Contributions: (I) Conception and design: All authors; (II) Administrative support: All authors; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Abstract: Despite progress in the medical and device therapy for heart failure (HF), the prognosis for those with advanced HF remains poor. Acute heart failure (AcHF) is the rapid development of, or worsening of symptoms and signs of HF typically leading to hospitalization. Whilst many HF decompensations are managed at a ward-based level, a proportion of patients require higher acuity care in the intensive care unit (ICU). Admission to ICU is associated with a higher risk of in-hospital mortality, and in those who fail to respond to standard supportive and medical therapy, a proportion maybe suitable for mechanical circulatory support (MCS). The optimal pre-operative management of advanced HF patients awaiting durable MCS or cardiac transplantation (CTx) is vital in improving both short and longer-term outcomes. This review will summarize the clinical assessment, hemodynamic profiling and management of the patient with AcHF in the ICU. The general principles of pre-surgical optimization encompassing individual systems (the kidneys, the liver, blood and glycemic control) will be discussed. Other factors impacting upon post-operative outcomes including nutrition and sarcopenia and pre-surgical skin decolonization have been included. Issues specific to durable MCS including the assessment of the right ventricle and strategies for optimization will also be discussed.

Keywords: Heart failure (HF); heart transplantation; intensive care unit (ICU); mechanical circulatory support (MCS); pre-operative optimization; ventricular assist device

Submitted Jan 28, 2020. Accepted for publication Jun 01, 2020.
doi: 10.21037/atm-20-1048
View this article at: http://dx.doi.org/10.21037/atm-20-1048

Introduction

The definition of advanced heart failure (AHF) has evolved over the years. In 1998, Adams and Zannad limited the description to those patients with resting left ventricular ejection fraction (LVEF) <30%, and the presence of New York Heart Association (NYHA) class 3 or class 4 symptoms, or peak oxygen consumption <14 mLs/kg/min, on symptom limited exercise testing (1). With time, the definition has evolved (2-5); the contemporary statement is that from the Heart Failure Association of the European Society of Cardiology (ESC) (6). In addition to the aforementioned criteria this ESC definition recognizes patients in whom isolated right ventricular (RV) failure, inoperable valvular disease, congenital heart disease or heart failure with either preserved ejection fraction (HFpEF), or mid-range ejection fraction (HFmrEF) represents the underlying structural abnormality. These patients must also have had more than one unplanned hospital attendance or admission within the preceding 12 months for the treatment of congestion, low output state or malignant arrhythmia (6).

Despite the advances in medical and device therapy for heart failure (HF), the prognosis for patients with AHF

Table 1 Precipitating factors for acute heart failure

Acute coronary syndrome
Arrhythmia (tachyarrhythmia or bradyarrhythmia)
Infection
Pulmonary embolus
Drugs—cardiotoxic chemotherapy, non-steroidal anti-inflammatory drugs, steroids
Non-compliance with medical therapy and/or fluid restriction
Surgery (cardiac or non-cardiac)
Acute mechanical insult—acute regurgitation, myocardial rupture
Hypertension
Pregnancy
Endocrine disease—thyroid or adrenal dysfunction, diabetic ketoacidosis

remains poor. The Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management (ROADMAP) study enrolled 200 patients with non-inotrope dependent AHF across 41 centers in the United States and showed that survival was inferior at 12 months (80%±4% *vs.* 63%±5%; P=0.022), and 24 months (70%±5% *vs.* 41%±5%; P<0.001) in those managed in the medical therapy arm (7,8). Similarly, just over half of the patients with ambulatory AHF in the Medical Arm of Mechanically Assisted Circulatory Support (MedaMACS) Registry were alive on medical therapy alone at 2 years of follow-up, 24% died over the study period and 11% underwent left ventricular assist device (LVAD) implantation; 12% received CTx (9).

An episode of decompensation in the patient with AHF invariably results in hospitalization. Whilst many HF decompensations are managed at a ward-based level, a proportion of patients may require admission to the intensive care unit (ICU) for higher acuity care. The aims of this article are to discuss the management of patients with AHF in the ICU. The pre-operative optimization for those patients requiring mechanical circulatory support (MCS) or CTx are also discussed.

Acute heart failure (AcHF)

AcHF is the rapid development of, or worsening of symptoms and signs of HF typically leading to hospitalization (10). This may present in a patient with known HF or as a de-novo event. In the United Kingdom, the National Heart Failure Audit for 2016-17 reported that for England and Wales alone 73,616 patients were admitted to hospital with a primary diagnosis of HF (11). The median age of patients was 80.6 years, and the in-hospital mortality 9.4% after a 9-day median length of stay (11). For several reasons, there is wide center specific, and international variation in the admission rates to ICU for HF patients. The UK National Heart Failure audit does not detail the percentage of patients who are admitted to ICU. Across Europe alone admission to ICU varies from 5% to 45.4% (12). The prospective Romanian Acute Heart Failure Syndromes (RO-AHFS) registry found that 10.7% of 3,224 patients required care within the ICU, and that admission to ICU was associated with a higher risk of in-hospital mortality (17.3% *vs.* 6.5%, P=0.002) (13).

There are many potential precipitants to an episode of decompensated HF. The most commonly encountered triggers in clinical practice are listed in *Table 1*.

Clinical assessment of patients with AcHF

Hemodynamic profiles and prognosis

Advanced HF patients admitted to the ICU are usually in AcHF. Irrespective of whether the presentation is a decompensation of chronic HF or first presentation, this is a life-threatening scenario with very high mortality. Thirty-day mortality ranges from 12.9% to 27.4% and 1 year mortality from 39.7–46.5% (14,15). In hospital worsening of HF requiring advanced therapies (including inotropic or intravenous vasodilator therapy, MCS, mechanical ventilation or hemodialysis) is associated with an even higher mortality rate; 12.7% in hospital, 19% 30 days and 50% 1 year mortality (15).

Classification for this group of patients can be performed in several ways. The Interagency Registry of Mechanically Assisted Circulatory Support (INTERMACS) classification (*Table 2*) stratifies inpatients and outpatients with AHF who are awaiting durable MCS into one of seven profiles (3). A simple and alternative classification based on the assessment of congestion and peripheral perfusion can be used for inpatients with AcHF. This defines four different hemodynamic profiles; warm and wet, cold and wet, warm and dry, and cold and dry (16). Ninety five percent of AcHF patients are congested (17). Recognizing that hypo perfusion does not automatically equate to hypotension is

Table 2 INTERMACS stages for classifying patients with advanced heart failure (3)

INTERMACS level	Description	Time frame for intervention
1. Critical cardiogenic shock "Crash and burn"	Hemodynamic instability in spite of increasing doses of catecholamines and/or mechanical circulatory support with critical organ hypoperfusion	Definitive intervention needed within hours
2. Progressive decline despite inotropic support "Sliding on inotropes"	Intravenous inotropic support with acceptable blood pressure but rapid deterioration of renal function, nutritional state, or signs of congestion. Also describes declining status in patients unable to tolerate inotropic therapy	Definitive intervention needed within a few days
3. Stable but inotrope dependent "Dependent stability"	Hemodynamic stability with low or intermediate doses of inotropes, but necessary due to hypotension, worsening of symptoms, or progressive renal failure	Definitive intervention elective over a period of weeks to few months
4. Resting symptoms "Frequent flyer"	Temporary cessation of inotropic treatment is possible but patient presents with frequent symptom recurrences and typically with fluid overload. Doses of diuretics generally fluctuate at very high levels	Definitive intervention elective over a period of weeks to few months
5. Exertion intolerant "Housebound"	Complete cessation of physical activity, stable at rest, but frequently with moderate fluid retention and some level of renal dysfunction	Variable urgency, depends upon maintenance of nutrition, organ function, and activity
6. Exertion limited "Walking wounded"	Minor limitation on physical activity and absence of congestion while at rest. Easily fatigued by light activity	Variable urgency, depends upon maintenance of nutrition, organ function, and activity
7. Advanced NYHA III "Placeholder"	Patient in NYHA Class II with no current or recent unstable fluid balance	Transplantation or circulatory support may not currently be indicated

Table adapted from Stevenson LW, Pagani FD, Young JB, *et al*. INTERMACS profiles of advanced heart failure: the current picture. J Heart Lung Transplant 2009;28:535-41, with permission from Elsevier. INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support.

important. Cold extremities, oliguria, confusion, narrow pulse pressure, metabolic acidosis and elevated serum lactate can be signs of impaired peripheral perfusion even with preserved blood pressure. Therefore, identifying the correct clinical profile helps guide therapy and prognosis (16).

Monitoring of hemodynamics on ICU

There is no universal agreement on the optimal method of hemodynamic monitoring for patients admitted to ICU with AcHF. The current American College of Cardiology/American Heart Association (ACC/AHA) guidelines give a class I recommendation for monitoring with a pulmonary artery catheter (PAC) in AcHF patients with respiratory distress or impaired systemic perfusion, when clinical assessment is inadequate (4). The current ESC guidelines recommend consideration of an intra-arterial line and PAC in patients with hypotension and hypo perfusion despite treatment (17).

PAC monitoring is used in approximately a third of cardiogenic shock patients in European tertiary level hospitals (18). There are no randomized trials evaluating the use of PAC in the MCS population. In the ICU setting, randomized clinical trials have failed to demonstrate an improvement in clinical outcomes with the use of PACs. The sickest AcHF patients are under-represented in these studies however (19,20). The Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) trial studied the use of PAC specifically in an AcHF population and showed no mortality benefit with PAC use. These results should be interpreted with caution however as the study excluded those with previous inotrope use and significant renal impairment (21). In a propensity matched analysis of the Acute Decompensated Heart Failure Syndromes (ATTEND) registry (a cohort of 4,842 patients with acute decompensated heart failure in Japan), the appropriate use of PAC (502 patients matched to controls) reduced in-

hospital mortality in AcHF (4.4% controls *vs.* 1.4% in the PAC groups, P=0.006), particularly in patients with lower systolic blood pressure, or receiving inotropic support (22).

PACs provide an accurate assessment of filling pressures and pulmonary hemodynamics which are essential when optimizing patients prior to LVAD surgery and CTx. Cardiac Index and its derived parameters cardiac power index and stroke volume index are strong predictors of 30-day mortality in patients with cardiogenic shock (18). Obtaining and interpreting these data help when assessing the deteriorating patient, and identifying those who may be suitable for MCS or transplantation.

Treatment in the ICU

Management goals

Decongestion, maintenance of adequate systemic perfusion and preservation of end organ function are the primary goals of treatment of AcHF patients. The combination of pharmacological and non-pharmacological interventions is often required to achieve these. These strategies may be a temporizing measure, a bridge to recovery or a definitive treatment option such as durable MCS or CTx. Optimizing clinical status prior to surgery is imperative, as critically ill patients have poorer outcomes following CTx and LVAD surgery (23-26).

Supplemental oxygen and ventilation

Oxygen therapy is recommended only in patients with SpO_2 <90% or PaO_2 <60 mmHg (9.0 kPa). Noninvasive ventilation should be considered in patients with acute pulmonary edema to relieve symptoms and reduce the need for intubation. In a small number of studies, it has been shown to reduce mortality (27-29). Noninvasive ventilation can exacerbate hypotension and should be used with caution in patients with low or borderline blood pressure. Intubation may be required for patients with persistent hypoxemia, hypercapnia or acidosis.

Management of congestion

Elevated central venous pressure (CVP) is the most important hemodynamic factor in the development of worsening renal function and unfavourable outcomes in AcHF patients (30). Decongestion and the maintenance of normovolemia can be challenging, and often requires a progressive escalation of therapy.

Diuretics

Intravenous loop diuretics should be administered to all patients with congestion. Diuretics can be given as a continuous infusion or intermittent boluses with the initial dose at least equal to the pre-existing oral dose (31). Data from a meta-analysis has shown that a continuous infusion of loop diuretics is superior to intermittent boluses with regards to diuretic effect, with no impact on mortality (32). For diuretic resistance, the addition of metolazone, intravenous chlorothiazide or tolvaptan have all been shown to improve urine output without significant difference between the agents (33). Electrolytes and renal function must be closely monitored, particularly with the addition of sequential nephron blockade.

Ultrafiltration and renal replacement therapy

The development of diuretic resistance portends poorer long-term outcomes in hospitalized patients with AcHF (34). The major clinical trials evaluating ultrafiltration versus intravenous diuretics have reported inconsistent results (35-37); however, ultrafiltration does appear to have a role for management of refractory congestion not responding to medical therapy. Its use in this situation is supported by both ESC (17) and ACC/AHA guidelines (4). Ultrafiltration has the benefit of being able to remove large volumes of fluid in a relatively short period of time and can be particularly beneficial in optimizing patients prior to definitive surgery. Renal replacement therapy may also be required for patients with refractory congestion and acute kidney injury, particularly when accompanied by hyperkalemia or metabolic acidosis.

Vasodilators and inotropes

Vasodilators and inotropes have a similar impact on the reduction of left- and right-sided filling pressures in patients with AcHF and reduced LV function (38). Vasodilators reduce preload which relieves congestion and are also used to decrease afterload, which can help to increase cardiac output. They improve hemodynamics in the short-term. There is no evidence of a mortality benefit from vasodilator use (38-42) and their utility is limited to patients with adequate blood pressure (generally systolic blood pressure >90 mmHg). Nitrates are the most common

Table 3 Properties and doses of commonly available intravenous vasodilators

Agent	Class	Dose	Preload	Afterload	Elimination t1/2	Precautions
Nitroglycerine	Nitrate	Start 10–20 μg/min. Increase up to 200 μg/min	↓↓	↓ or –	1–4 minutes	Tachyphylaxis
Isosorbide Dinitrate	Nitrate	Start 1 mg/hr. Increase up to 10 mg/hr	↓↓	↓ or –	1–4 minutes	Tachyphylaxis
Nitroprusside	Nitrous oxide donors	Start 0.3 μg/kg/min. Increase up to 5 μg/kg/min	↓↓	↓↓	10 minutes	Isocyanate toxicity
Hydralazine	K^+ channel agonist	Bolus: 5–10 mg then further 5–10 mg q20-30 min as required. Infusion: 0.5–10 mg/hr	↓	↓↓	2–8 hours	Long half life
Nesiritide limited availability	Natriuretic peptide	Bolus 2 μg/kg then infusion 0.01 μg/kg/min	↓↓	↓↓	20 minutes	

vasodilator used in AcHF. Serelaxin and Ularitide are newer vasodilators; however, these have also been shown to have no significant benefit on long term outcomes in recent randomized control trials (40,42). *Table 3* lists the properties of commonly used vasodilators.

Patients with low cardiac output and end-organ hypoperfusion may be treated with inotropes. Although the published evidence suggests that treatment with inotropes is associated with an increased short- and long-term mortality (43), they may be used to bridge patients with AcHF to recovery, or definitive treatment. Inotropic agents should be used at the lowest required dose, for the shortest duration possible. There is no evidence to support the superiority of one agent over another (44). There are three main classes of inotropes currently used in the management of AcHF, beta adrenergic receptor agonists, phosphodiesterase III (PDE III) inhibitors and calcium sensitizer. *Table 4* displays the properties of commonly used inotropes. Patients treated with beta blockers (BB) may respond better to levosimendan or PDE III inhibitors, as these drugs act independently of the beta-adrenergic receptor pathway (45,46).

Optimizing patients prior to MCS, or cardiac transplantation

Kidneys

Over half of the 118,465 patients hospitalized with AcHF in the Acute Decompensated Heart Failure National Registry (ADHERE) in the United States had renal dysfunction (eGFR ≤59 mL/min/1.73 m^2), with in hospital mortality increasing from 1.9% in those with normal renal function to 7.6% in those with severe renal dysfunction (eGFR 15–29 mL/min/1.73 m^2) (47). In a study of 599 patients admitted to 60 French ICUs or coronary care units for the management of AcHF, renal dysfunction was associated with a greater than three-fold increased risk of death at 4 weeks (14). The presence of renal dysfunction is also associated with adverse outcomes following LVAD implantation with an almost 20% reduction in 2-year survival going from low to severe dysfunction in an analysis from the INTERMACS registry (48).

The timing of hemodialysis in those undergoing LVAD implantation has an impact on short-term survival. Schmack et al. reported significantly worse 30-day survival after LVAD implantation in those requiring post implant hemodialysis (92.1% in non-hemodialysis group; 83.3% in pre-implant dialysis group; 58.3% in post implant hemodialysis group; P<0.004) (49). In a study of 389 patients undergoing implantation of continuous flow LVAD, eGFR <40 mL/min/1.73 m^2 and proteinuria (urine protein to creatinine ratio ≥0.55 mg/mg) were significant predictors of the requirement for renal replacement therapy during a median follow-up of 9.9 months (50). An eGFR <30 mL/min/1.73 m^2 is a relative contraindication for heart transplantation alone, according to the 2016 ISHLT listing criteria for heart transplantation (51).

In HF patients with renal dysfunction, a right heart catheter study (RHC) to assess filling pressures and hemodynamics, urine analysis for proteinuria, and assessment of the kidneys and urinary tract on ultrasound or CT should be performed. Longitudinal assessment of

Table 4 Properties and doses of commonly available inotropic agents

Agent	Class	Dose	Bolus	CO	SVR	PVR	HR	Elimination t1/2
Dopamine	Beta-agonist	<3 μg/kg/min: renal vasodilation; 3–5 μg/kg/min: inotropic; >5 μg/kg/min: vasoconstrictor	No	>3 μg/kg/min: ↑↑	3–5 μg/kg/min: ↑ or – >5 μg/kg/min: ↑↑	3–5 μg/kg/min: – >5 μg/kg/min: ↑	↑↑	2 minutes
Dobutamine	Beta-agonist	1–20 μg/kg/min	No	↑↑	↓	↓ or –	↑↑	2 minutes
Epinephrine	Beta-agonist	0.05–0.5 μg/kg/min	No	↑↑	↑↑	↑ or –	↑↑	2 minutes
Nor-epinephrine	Beta-agonist	0.02–10 μg/kg/min	No	↑ or –	↑↑↑	↑	↑↑	2–3 minutes
Milrinone	PDE III inhibitor	0.375–0.75 μg/kg/min	25–75 μg/kg	↑	↓↓	↓↓	↑↑	2.5 hours**
Enoximone	PDE III inhibitor	1.25–7.5 μg/kg/min	0.25–0.75 mg/kg	↑	↓↓	↓↓	↑↑	6–7 hours**
Levosimendan	Calcium sensitizer	0.05–0.2 μg/kg/min	12–24 μg/kg	↑	↓↓	↓↓	↑	70–80 hours

**, longer with renal impairment. CO, cardiac output; SVR, systemic vascular resistance; PVR, pulmonary vascular resistance; HR, heart rate; PDE III, phosphodiesterase III.

the trajectory of renal function is intuitively attractive when considering the potential for improvement in renal function following optimization of hemodynamics. In those with significant renal impairment being considered for LVAD or cardiac transplantation, our institution would recommend the cessation of nephrotoxic drugs, minimization of exposure to iodinated contrast and optimization of adverse hemodynamics, with judicious use of diuretics, escalation of inotropes and consideration of temporary MCS.

Liver

Congestive hepatopathy is more common than reduced cardiac output as a cause of liver dysfunction in patients with HF (52). In the analysis of the 2679 North American patients enrolled in the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity Program (CHARM); low albumin (18.3%), raised total bilirubin (13%) and increased alkaline phosphatase (14%) were the most common liver function abnormalities (53). Elevated bilirubin was the strongest independent predictor of poor prognosis in this cohort. More than 40% of the 4,228 patients hospitalized with HF in the Acute Study of Clinical Effectiveness of Neseretide in Decompensated Heart Failure (ASCEND-HF) trial had abnormal liver function (54). This study also showed that elevated serum bilirubin was associated with an increased risk (HR 1.17 per 1 mg/dL increase, 95% CI, 1.04–1.32, P=0.13) of 30-day all cause death, or HF re-hospitalization. No relationship was found between aminotransferases and outcomes. Hypoxic or ischemic hepatitis is due to a combination of low cardiac output and passive hepatic venous congestion (55). There tends to a rapid rise in serum aminotransferases peaking at 1–3 days (up to 250 times the upper limit of normal) after a hemodynamic insult (52). Bilirubin levels rarely rise more than 4 times above the upper limit of normal, and alkaline phosphatase is usually within 2 times the upper limit of normal. Levels generally return to baseline within 7–10 days with supportive treatment (52).

Coagulation disorders, vasoplegia, immune dysfunction and poor nutritional status are associated with advanced liver disease (56). The Model for End-Stage Liver Disease (MELD) score is an objective score based on bilirubin, creatinine and INR. The MELD-XI (MELD eXcluding INR) score excludes INR and is an alternative to MELD in those receiving oral coumadins. A single center study of 264 patients undergoing LVAD implantation (60% pulsatile HeartMate and 40% continuous flow HeartMate II)

reported improved on-VAD and overall survival in patients with a MELD score or MELD-XI <17 (57). A more recent study of 524 patients implanted with continuous flow LVADs (403 Heart Mate II, 123 HeartWare) demonstrated lower survival at 1, 3, 6, 12 and 24 months (P<0.001 for all) and increased risk of early right heart failure and infections in those with MELD-XI score of 14 or more, compared to patients with a MELD-XI score of less than 14 (58).

Elevated MELD scores are also associated with poor survival following heart transplantation. In a study of 617 adults undergoing heart transplantation, patients with MELD score <14 had 1- and 5-year survival of 91.4% and 83.2% respectively. One- and five-year survival rates were 85.5% and 70.1% respectively in those with MELD score >20 (59). These scores are dynamic and can change with progressive HF, or improve with therapy. In patients with imaging features suggestive of fibrosis or cirrhosis of the liver, the addition of liver biopsy to MELD-XI improves risk stratification in patients with advanced HF being considered for heart transplantation (60).

In patients with AHF being considered for MCS or heart transplantation serial liver function tests (LFTs) should be performed. Patients with persistently deranged LFTs despite restoration of normovolemia and improvement in cardiac output following treatment should undergo further assessment with dedicated liver imaging. The specialist opinion of a hepatologist should be sought to exclude irreversible liver disease, or an alternative cause for deranged liver function.

Anemia and coagulation

The prevalence of anemia in patients with HF is reported between 6–70% reflecting the heterogeneity in screening, clinical setting and socio-economic status of the population (61). Pre-operative anemia is a known risk factor for adverse outcomes following cardiac surgery (62-64). Pre-transplant anemia is also an independent predictor of 1-year survival. In a single center study of 267 patients, one year survival was 70% among anemic patients (serum hemoglobin <12 g/dL regardless of sex) compared with 81% for those with a normal hemoglobin (P=0.027) (65). The Society of Thoracic Surgeons (STS) guidelines recommend transfusion when hemoglobin is less than 7 g/dL but acknowledge the lack of high level evidence to support this recommendation (66).

Iron deficiency (defined as serum ferritin <100 μg/L or ferritin <300 μg/L and transferrin saturation level of <20%) is seen in up to 50% of patients with HF and is an independent predictor of poor exercise capacity and worse survival (67,68). There is strong evidence to recommend the use of intravenous iron in iron deficient HF patients to improve exercise capacity and symptoms (10,69). Its recommendation (with or without erythropoietin) in anemic patients undergoing cardiac surgery is largely unproven (70,71).

HF is a hypercoagulable state (72). Patients with co-morbidities such as ischemic heart disease, atrial fibrillation, previous thromboembolic events, pulmonary emboli or deep vein thrombosis are likely to be on anti-platelets and/or anticoagulated. The STS guidelines recommend cessation of platelet P2Y12 receptor blockers at least 3 days before cardiac surgery (66). It also recommends consideration of discontinuation of most antithrombotic agents before surgery to reduce minor and major bleeding events, with the timing of discontinuation based on drug half-life and availability of reversal agents. Unfractionated heparin may not require discontinuation (66).

In our center, patients being considered for durable LVAD or listing for CTx intravenous iron is administered to those with iron deficiency. Platelet P2Y12 receptor antagonists are stopped, if possible, 3–5 days prior to elective LVAD implantation. Patients on direct oral anticoagulants (DOACs) are switched to warfarin prior to transplant listing. DOACs are stopped in those awaiting elective LVAD, with heparin bridging if required. In patients with liver dysfunction and deranged clotting, vitamin K is administered.

Glycemic control

Patients with HF and diabetes mellitus (DM) have a greater risk of recurrent hospitalization and death compared to non-diabetics (73). In patients undergoing cardiac surgery diabetes is an independent predictor for post-operative sternal instability with or without infection, perioperative stroke, post-operative delirium, prolonged ICU stay and renal dysfunction (74). In patients with DM undergoing LVAD implantation, there is insufficient data to determine whether short term glycemic control prior to LVAD implantation is related to the risks of device complications and mortality (75). The STS guidelines recommend cessation of oral hypoglycemic drugs 24 hours prior to scheduled cardiac surgery (76). The guidelines also recommend stopping insulin after dinner the evening before surgery and using either an insulin infusion protocol or

combination of long and short acting subcutaneous insulin.

Nutrition and sarcopenia

Malnutrition and sarcopenia is common in patients with HF. Up to 15% are overtly cachectic, 50% malnourished using broader definitions (77) and 20% sarcopenic compared with age matched controls (78). Patients at extremes of body mass index (<20 kg/m^2; >35 kg/m^2) have worse outcomes after LVAD implantation (79). The 2013 ISHLT guidelines recommend measuring serum albumin and pre-albumin prior to surgery (80). Those with indices of malnutrition should be evaluated by nutritional services. Resistance training is the main intervention used to improve sarcopenia and in combination with aerobic work is recommended both before and after transplantation (81). The use of testosterone supplementation is controversial (82).

Cardiac drugs

Patients with AcHF or cardiogenic shock in ICU are usually treated with inotropes for hemodynamic support. Levosimendan is a calcium channel sensitizer and an inotrope with vasodilatory effects. It provides a sustained hemodynamic response (for days after discontinuation of infusion) in patients with left ventricular impairment, without an increase in myocardial oxygen demand or ischemia (83). Meta-analyses comparing levosimendan and conventional treatment in cardiac surgical patients with left ventricular impairment report a reduction in perioperative mortality and need for renal replacement therapy (84,85). There remains insufficient high-quality evidence however to support or contraindicate its use (85). There may be a role for levosimendan as a pre-treatment for LVAD patients however the evidence to support this is not conclusive (86-88). A single center study of 21 patients reported an improvement in hemodynamics following levosimendan but no impact on reduction in post-operative RV failure (89).

Patients with chronic HF are usually on a combination of medical therapy including angiotensin converting enzyme inhibitor (ACEi) or angiotensin 2 receptor blockers (ARB), BB, mineralocorticoid receptor antagonists (MRA) and diuretic. Sacubitril/valsartan may be substituted in place of ACEi or ARB (10). In those with decompensated HF on ICU some of these drugs may have been stopped on admission because of hypotension, hypoperfusion and/or renal impairment. The use of an ACEi/ARB pre LVAD implant has been shown to have a negative correlation with improvement in glomerular filtration rate at one month post implant (90). Similarly, ACEI/ARB use has been reported to be a predictor of the requirement for early post-transplant renal replacement therapy (91). Profound vasoplegia in the post-transplant period has been described in a patient taking sacubitril/valsartan (92), and this drug should be discontinued on admission to ICU.

There is lack of data on the impact of pre-implant BB on post LVAD or post-transplant outcomes. In our institution, BB may be continued if the patient was pretreated and tolerating these. We do not recommend the initiation of BB in those with AcHF or cardiogenic shock prior to the restoration of normovolemia and adequate perfusion.

Decolonization

The prevention of post-surgical site infection (SSI) begins pre-operatively. Decolonization with topical chlorhexidine, and nares with mupirocin may reduce the risk of SSI (93,94). There is insufficient data at present to recommend its routine use in patients undergoing MCS, and practice varies by individual surgical center.

Specific issues

Patients undergoing implantation of temporary circulatory support

The placement of temporary MCS is often performed on an emergent basis. The device strategy and necessary work-up and are discussed separately within this issue of the journal. An assessment of the peripheral vasculature (femoral, lilac and thoraco-abdominal aorta) on CT provides additional information to inform device strategy, should this be a semi-planned procedure.

Patients undergoing durable LVAD implantation

An LVAD is dependent upon a functional RV for adequate filling. The RV functions to maintain a low systemic venous pressure, provide pulmonary circulation and fill the left ventricle (LV). All walls of the RV contribute to its function and the septum is a significant contributor in the situation of increased RV afterload (95). The implantation of an LVAD reduces RV afterload by reducing pulmonary pressure however this also increases RV pre-load. The septal contribution to RV contractility is impacted by leftward deviation of the interventricular septum, and the

Table 5 Hemodynamic formulas to assess right ventricle and predict right ventricular failure post LVAD insertion

Method of assessment	Formula	Values associated with increased incidence of post LVAD RV failure
Filling pressures	RAP/PCWP	>0.63 (98)
PA pulsatility index	(sPA-dPA)/RAP	<1.85 (99)
RV stroke work	(mPA-RAP) × SV ×0.0136	<15 (100)
RV stroke work index	(mPA-RAP)/SV index	<0.3–0.6 (98,99)

RAP, right atrial pressure; PCWP, pulmonary capillary wedge pressure; RVF, right ventricular failure; LVAD, left ventricular assist device; PA, pulmonary artery; sPA, pulmonary artery systolic pressure; dPA, pulmonary artery diastolic pressure; mPA, pulmonary artery mean pressure; SV, stroke volume.

surgical disruption of the pericardium leads to weakening of the LV/RV interplay.

The evaluation of RV function in the ICU is performed through a combination of imaging and hemodynamic assessment. Several studies have examined the utility of RV assessment on echocardiography in predicting post LVAD RV failure however these series are small and limited due to the complex RV geometry, adequate RV visualization and the impact of loading conditions. Semi quantitative assessment of RV function has poor reproducibility. Tricuspid annular plane systolic excursion (TAPSE) <7.5 mm is specific in predicting post LVAD RV failure, with poor sensitivity (96). Severe tricuspid regurgitation (grade 3/4) is also predictive of post LVAD RV failure (97).

Multiple hemodynamic abnormalities (*Table 5*) have been shown to be predictive of post implant RV failure (98-101); however, these cannot account for intra-operative events which may insult a previously adequate RV. Pre-operative RV optimization includes strategies which aim to lower CVP, and decrease pulmonary artery pressures (PAP). A pre-operative CVP >15 mmHg is associated with RV failure (98). We generally aim for a CVP <10 mmHg through a combination of diuresis or filtration. PDE III inhibitors provide inotropic support and vasodilatation, and may be more useful than catecholaminergic agents (102).

Cardiac transplantation

Cardiac transplantation is a treatment option for a few carefully selected patients with AHF (103). In the ICU, patients waiting for CTx are those requiring multiple inotropes or patients on short term MCS. Multiple transfusions can increase the risk of allosensitization and impact upon the ability to match an organ (104). Minimizing blood transfusion in patients waiting for CTx is essential. Those requiring blood should receive leucodepleted blood, but do not require cytomegalovirus negative blood (105). Higher rates of primary graft dysfunction have been reported in recipients with right atrial pressure >10 mmHg and in those with elevated pulmonary vascular resistance (106). We recommend measuring CVP and PA pressures in inotrope dependent patients awaiting CTx aiming for CVP <10 mmHg and PVR <5 Wood units.

Conclusions

The prognosis for patients with AcHF requiring admission to ICU is poor and hemodynamic profiling is important in guiding management. These critically ill patients benefit from the care of a multi-disciplinary team comprising the cardiac intensivist/anesthetist, HF cardiologist, cardiac surgeon and allied health professionals. Treatment goals are agreed upon by this team, and the ICU care includes optimization of volume status, vasodilatation and use of inotropes as a bridge to recovery of end organ function. In those suitable for MCS or CTx, a PAC is essential in hemodynamic tailoring prior to surgery. Finally, the timing of surgery, if required, is planned once these objectives are met in order to maximize the possibility of a successful outcome.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editor (Kamen Valchanov) for the series "Perioperative Management of Patients with undergoing

Mechanical Circulatory Support" published in *Annals of Translational Medicine*. The article was sent for external peer review organized by the Guest Editor and the editorial office.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm-20-1048). The series "Perioperative Management of Patients with undergoing Mechanical Circulatory Support" was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Cheshire C, Bhagra CJ, Bhagra SK. A review of the management of patients with advanced heart failure in the intensive care unit. Ann Transl Med 2020;8(13):828. doi: 10.21037/atm-20-1048

