Post–Heart Transplantation Intensive Care Unit Recovery
A Phase-Based Approach

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KEYWORDS

• Heart transplantation • Primary graft dysfunction • Inotropes • Vasoplegic syndrome • Coagulopathy • Mechanical circulatory support • Diuresis • Rejection

KEY POINTS

- Primary graft dysfunction occurs in up to 30% of transplants. Treatment is pharmacologic, with early escalation to mechanical circulatory support if needed.
- Vasoplegia and right ventricular dysfunction require careful hemodynamic and pharmacologic management to prevent end-organ injury.
- As graft function stabilizes, consider early ventilator liberation and initiate diuresis to optimize preload, afterload, and end-organ perfusion.
- Immunosuppression should be balanced with infection risk. Routine rejection surveillance with endomyocardial biopsies should follow institutional protocols.
- Mechanical circulatory support may be required for single- or biventricular dysfunction.

INTRODUCTION
Background

Orthotopic heart transplantation (OHT) represents the definitive therapy for end-stage heart failure refractory to medical and device-based treatment.[1] Among centers reporting to the International Thoracic Organ Transplant Registry of the International Society of Heart and Lung Transplantation (ISHLT), an average of 2400 to 3000 heart transplants are performed annually, with a progressive increase over the past decade, particularly in North America.[2] The portion of recipients bridged with temporary mechanical circulatory support (MCS) immediately before transplant has steadily grown to 39.1% in 2024, increasing the level of acuity and impacting the postoperative course of transplant recipients.[1,2] Despite increasing complexity, short-term survival continues to improve, with the 1-year post-transplant survival among adult recipients reaching 92.1% during 2018 to 2023.[2] The postoperative management of heart transplant recipients requires careful attention to hemodynamic parameters and a proactive phase-based approach related to the anticipated course following transplantation (**Fig. 1**).

A Phase-Based Framework

The ICU recovery of a heart transplant recipient can typically be broken down into a 3-phase framework that parallels physiologic recovery and anchors multidisciplinary communication:

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Abbreviations

CI	cardiac index
CMV	cytomegalovirus
CO	cardiac output
CVP	central venous pressure
ECMO	extracorporeal membrane oxygenation
EMB	endomyocardial biopsy
ISHLT	International Society of Heart and Lung Transplantation
IV	intravenous
MCS	mechanical circulatory support
OHT	orthotopic heart transplantation
PEEP	positive end-expiratory pressure
PGD	primary graft dysfunction
PT	physical therapy
PVR	pulmonary vascular resistance
RRT	renal replacement therapy
SBT	spontaneous breathing trials
SvO_2	mixed venous oxygen saturation
VA-ECMO	venoarterial extracorporeal membrane oxygenation

1. *Resuscitation*—Hemodynamic stabilization, primary graft dysfunction (PGD) prevention, and lung protection.
2. *Diuresis*—Volume mobilization, ventilator liberation, and infection surveillance.
3. *Inotrope Wean & Rehabilitation*—Gradual withdrawal of pharmacologic support, early ambulation, and functional recovery.

Each phase defines distinct priorities in preload management, afterload modulation, inotropic support, and overall ICU care.

DISCUSSION

Phase 1: Resuscitation

Clinical presentation

The resuscitation phase is characterized by labile hemodynamics, metabolic acidosis, and variable oxygenation. The denervated heart typically exhibits a resting tachycardia (90–110 bpm) with blunted chronotropic response to hypotension. Maintaining a normal pH and adequate mixed venous oxygen saturation (SvO_2) are imperative in this phase, and they serve as important guides for resuscitation. Acidosis is particularly detrimental for heart grafts, as it exacerbates myocardial ischemia, disrupts cellular metabolism, and threatens graft viability.[3]

Inotropes There is limited guidance on the optimal pharmacologic support for low cardiac output (CO) following heart transplantation, but a detailed understanding of each agent's mechanism and side-effect profile helps tailor therapy to individual clinical scenarios.[4]

- Dobutamine: synthetic catecholamine that binds β_1 and β_2 adrenergic receptors in a 3:1 ratio. It is a potent inotrope with some chronotropic activity. Also has weak α_1 receptor agonism and antagonism, with a net effect of vasodilation. At high doses, vasoconstriction may predominate in addition to increased cardiac contractility.[4]
- Dopamine: endogenous central neurotransmitter and precursor to norepinephrine that produces a dose-dependent response by acting on dopaminergic and adrenergic receptors. At low doses, it produces vasodilation of coronary, renal, mesenteric, and cerebral beds via D_1 and D_2 stimulation. At intermediate doses, β_1 agonism promotes norepinephrine release and inhibits presynaptic reuptake, producing increased cardiac contractility and chronotropy with mild increase in systemic vascular resistance (SVR). At high doses, α_1-mediated vasoconstriction predominates.
- Epinephrine: endogenous catecholamine that acts predominantly on β_1 and β_2 receptors,

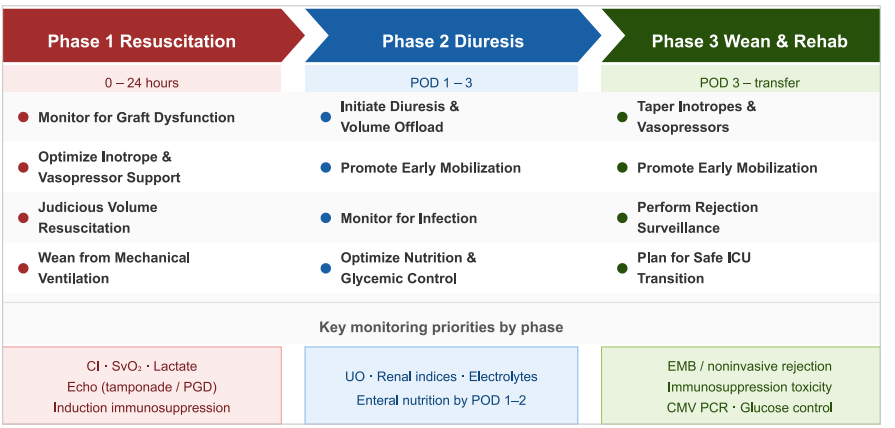

Fig. 1. Phases of post–heart transplantation ICU care. POD, postoperative day; UO, urine output.

with more α_1 agonism at higher doses. It increases cardiac contractility in addition to increasing SVR and pulmonary vascular resistance (PVR).
- Milrinone: phosphodiesterase-3 inhibitor with a longer half-life than other inotropes. It inhibits intracellular cyclic adenoside monophosphate (cAMP) breakdown, increasing myocardial contractility and systemic and pulmonary vasodilation. Additionally, improves diastolic relaxation (lusitropy) and reduces preload, afterload, and SVR.
- Isoproterenol: potent nonselective β-adrenergic agonist with powerful chronotropic and inotropic properties, with both systemic and pulmonary vasodilatory effects.

Vasoactive agents

- Norepinephrine: endogenous neurotransmitter, potent α_1-adrenergic receptor agonist with some $\beta_1 > \beta_2$ agonism, rendering it a powerful vasoconstrictor with some inotropic properties. Increases systolic, diastolic, and pulse pressure with minimal effect on CO or chronotropy.
- Vasopressin: nonapeptide synthesized in the hypothalamus that activates V_1 receptors in vascular smooth muscle leading to vasoconstriction, and V_2 receptors in the renal collecting duct system to promote water reabsorption in the renal collecting duct. Results in increased SVR, though spares the pulmonary vascular beds to avoid increases in PVR. The pressor effects of vasopressin are generally preserved in hypoxic and acidotic conditions.
- Angiotensin II: synthetic peptide activating primarily AT-1 receptors causing vasoconstriction, aldosterone release by the adrenal gland, sodium and water reabsorption in the renal proximal tubule, and vasopressin secretion.

Goals

1. *Restore and maintain adequate perfusion:* Target cardiac index (CI) greater than or equal to 2.2 L/minute/m^2 and mean arterial pressure (MAP) 65 to 80 mm Hg using individualized inotrope–vasopressor combinations.
2. *Prevention and early recognition of PGD:* Recognize risk factors for PGD with management and treatment escalation plan using inotropes and/or MCS.
3. *Protect pulmonary function:* Use low–tidal volume ventilation (6–8 mL/kg ideal body weight [IBW]) with positive end-expiratory pressure (PEEP) 5 to 8 cm H_2O and limit plateau pressure less than 28 cm H_2O.
4. *Continue comprehensive monitoring:* Frequent assessment of CI, SvO_2, MAP, SVR, and other data points of end-organ perfusion.

Complications

Primary graft dysfunction PGD is the leading cause of early mortality after heart transplantation, reported in 10% to 30% of cases.[5] It is defined as single- or biventricular allograft failure with hypotension and reduced CO within 24 hours of transplant, unrelated to rejection, pulmonary hypertension or surgical complications.[6] Severity is classified as mild, moderate, or severe based on inotropic needs and use of MCS.[5,6] Although the etiology is not fully understood, multiple risk factors have been identified, enabling better donor–recipient matching, and earlier recognition. Segovia and colleagues[7] proposed the RADIAL score, which includes: right atrial pressure greater than 10 mm Hg, age of recipient greater than or equal to 60 years, diabetes in recipient, inotropic requirement preoperatively, age of donor greater than or equal to 30 years, length of ischemic time greater than or equal to 240 minutes. Additional contributors include preoperative MCS, congenital heart disease, pulmonary hypertension, allosensitization, donor–recipient sex mismatch, and large volume transfusion intraoperatively.[8,9]

Initial management relies on inotropes, vasopressors, and pulmonary vasodilators. If CO remains inadequate, temporary MCS—most commonly venoarterial extracorporeal membrane oxygenation (VA-ECMO)—is indicated. Although optimal timing for ECMO initiation is unclear, delayed initiation is associated with higher in-hospital mortality and greater end-organ injury.[8] Recent analyses suggest that peripheral VA-ECMO carries fewer device-related complications and offers a higher rate of graft recovery and survival than temporary biventricular assist devices.[10,11] Among patients who survive to hospital discharge, those treated with VA-ECMO have the same conditional 1-year survival as patients without PGD.[12] Outstanding questions remain regarding the timing of escalation to MCS, device selection, central versus peripheral VA-ECMO, and the role of left ventricular unloading, with current practice largely shaped by institutional expertise.

Vasoplegic syndrome Vasoplegia—severe refractory systemic arterial hypotension with low systemic vascular resistance despite adequate CI and volume resuscitation—occurs in 15% to 34% of recipients.[13,14] Mechanisms include excess nitric oxide release, inflammatory cytokine-mediated smooth muscle desensitization, systemic inflammation,

and relative vasopressin deficiency.[13] Risk factors include preoperative MCS (including durable left ventricular assist device [LVAD]), recurrent driveline infections, prolonged cardiopulmonary bypass, older age, impaired renal function, prolonged ischemic time, preoperative angiotensin-converting enzyme (ACE) inhibitor use, and high transfusion volumes.[5,13,15]

After restoring euvolemia and correcting electrolytes and acid–base disturbances, first-line management is typically norepinephrine with the addition of vasopressin to restore vascular tone. Angiotensin II has emerged as a rescue therapy in catecholamine-resistant cases, though evidence remains limited, and may be associated with increased risk of thromboembolism.[16,17] Other rescue methods to treat refractory vasoplegia include methylene blue (1–2 mg/kg) or high-dose hydroxocobalamin (vitamin B12). Both work to reduce cyclic guanosine monophosphate (cGMP)- and nitric oxide (NO)-guanylyl cyclase-mediated vasodilation: methylene blue inhibits soluble guanylyl cyclase, while hydroxocobalamin binds nitric oxide, preventing it from binding to guanylyl cyclase. Methylene blue carries risks, including contraindications in glucose-6-phosphage dehydrogenase deficiency, preoperative serotonergic therapy due to the risk of serotonin syndrome, and potential worsening of hypoxemia due to blunted hypoxic pulmonary vasoconstriction. Glucocorticoids may also help by increasing adrenergic receptor expression and inhibiting biosynthesis of NO synthase.[16]

Right ventricular failure Acute right ventricular (RV) dysfunction often coexists with PGD, or may be a cause of secondary graft dysfunction.[16] It presents with rising central venous pressure (CVP) (usually defined as > 15 mm Hg) and low CI less than 2.0 L/minute/m^2. The ISHLT recommends inhaled pulmonary vasodilators (nitric oxide or prostacyclins), maintaining perfusion pressure (SBP > 85 mm Hg) with vasoactive agents, optimizing contractility with inotropes, and careful preload and afterload management. In cases of severe RV dysfunction especially if refractory to the prior recommendations, VA-ECMO or percutaneous right ventricular assist device (RVAD) should be considered.[5,8]

Bleeding and coagulopathy Heart transplant recipients are at high risk of bleeding due to systemic inflammation, cardiopulmonary bypass, transfusion needs, and mechanical support-related coagulopathies (platelet dysfunction and acquired von Willebrand syndrome). Many are also anticoagulated preoperatively. Heart transplant recipients are poorly represented in prospective trials investigating bleeding and transfusion practices, thus current guidelines generally follow the general cardiac surgery recommendations, including a restrictive red blood cell (RBC) transfusion strategy (hemoglobin 7.5–8 g/dL), guided by end-organ perfusion parameters and SvO_2.[8]

Preoperative coagulation screening and viscoelastic testing can guide intraoperative and postoperative replacement and correction.[5] Warfarin reversal should follow institutional protocols using IV vitamin K, fresh frozen plasma (FFP), and 4-factor prothrombin complex concentrates. Postoperative care for bleeding and coagulopathies in a heart transplant recipient is critical and involves frequent assessment of output and appropriate, timely blood product replacement considering rate, volume, and product choice. Judicious monitoring for progression to tamponade is essential, requiring the immediate availability of transesophageal echocardiography and the expertise needed for bedside sternal re-entry if required.[5]

Challenges

Phase 1 requires a careful balance of preload optimization, maintenance of perfusion pressure, and graft support. Under-resuscitation jeopardizes graft and organ perfusion, while volume overload exacerbates pulmonary edema and RV strain. Excessive beta-agonist use can trigger arrhythmias, increase myocardial oxygen demand, and promote myocyte apoptosis. PGD, bleeding, and vasoplegia can necessitate escalation of pharmacologic support and contribute to end-organ dysfunction, increasing mortality. Early signs of PGD within the first 24 hours should prompt a multidisciplinary discussion regarding optimal support—either pharmacologic or mechanical—though evidence guiding timing and device choice is limited. The primary goal is to stabilize hemodynamics, maintain perfusion, and ensure adequate graft function postcardiopulmonary bypass (**Fig. 2**).

Recommendations

- Initiate goal-directed therapy using CI, SvO_2, and lactate as targets.
- Favor *conservative fluid administration* with early transition to loop diuretics once stability achieved.
- Use *norepinephrine* ± *vasopressin* as first-line pressors; continue inotropic support with minimal titration before phase 2.
- Begin *infection prophylaxis* (bacterial, fungal, and cytomegalovirus (CMV) per institutional protocol).[18]

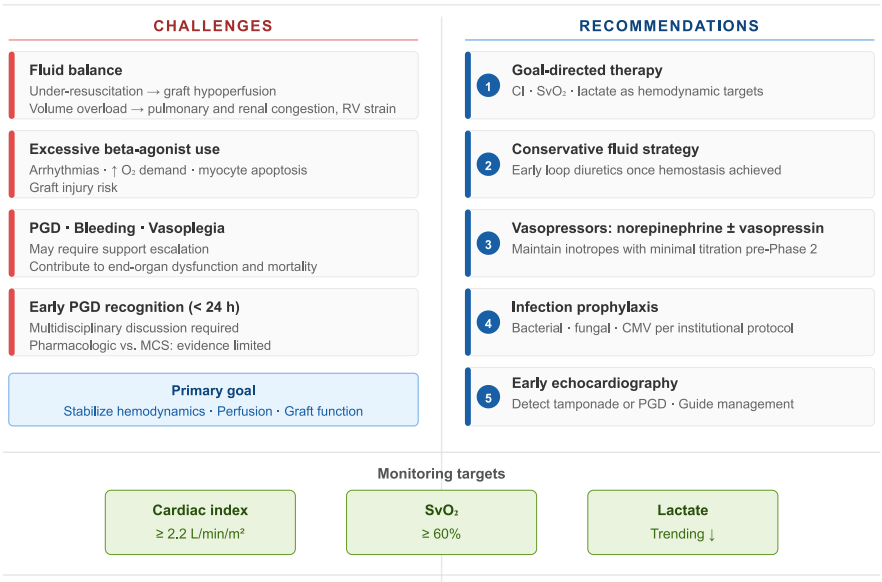

Fig. 2. Phase 1 (0–24 h): challenges and recommendations.

- Conduct *early echocardiography* to guide management and detect tamponade or PGD.

Once perfusion and oxygenation stabilize and sedation lightens, the focus shifts to volume removal and ventilator liberation.

Phase 2: Diuresis

Clinical presentation

After hemodynamic stabilization, attention turns to optimizing cardiac loading and minimizing complications in critically ill, immunocompromised patients. The main goal is managing volume overload and venous congestion while preserving renal function. Achieving euvolemia enhances CO, supports pulmonary mechanics and ventilator weaning, and reduces edema-related complications—lowering the risk of infection, delirium, ileus, and immobility. Simultaneously, systematic infection surveillance is initiated for early detection of potential infectious complications in the newly immunocompromised patient (Fig. 3).

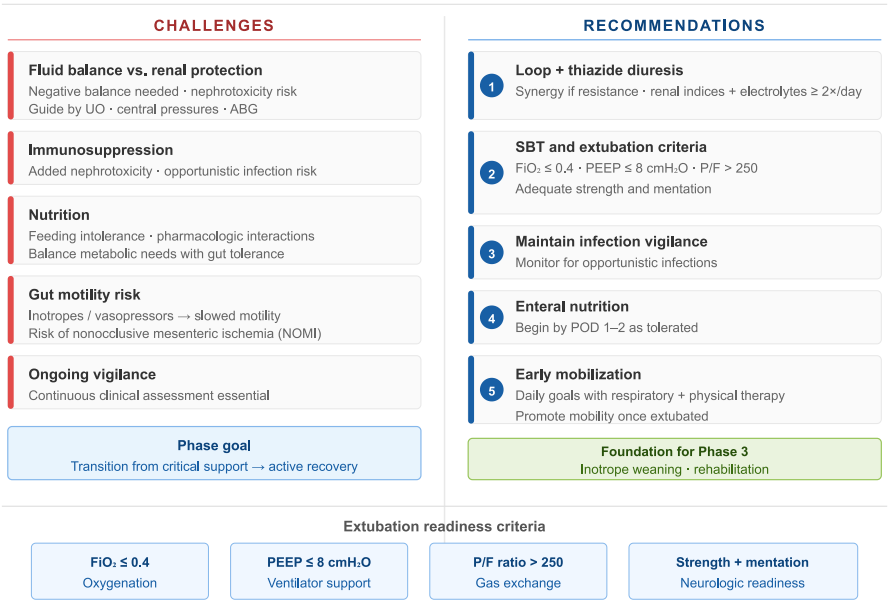

Fig. 3. Phase 2 (diuresis): challenges and recommendations. ABG, arterial blood gas; NOMI, nonocclusive mesenteric ischemia; P/F, PaO_2/FiO_2 ratio; POD, postoperative day; UO, urine output.

Goals

1. *Achieve net-negative fluid balance while preserving renal function* through established diuresis protocols with a target CVP goal of 5 to 12 mm Hg to optimize RV filling and afterload reduction. Monitor for decreased creatinine clearance, electrolyte disturbances, and need for escalation to renal replacement therapy (RRT).
2. *Liberate from mechanical ventilation* once gas exchange, mental status, and hemodynamics permit. Extubation to high-flow nasal cannula can allow for continuation of inhaled pulmonary vasodilators.
3. *Institute infection surveillance* with daily chest radiographs, standard vital monitoring, daily evaluation of white cell counts, and use a low threshold for infectious workup.
4. *Initiate early enteral nutrition* with trophic feeds within the first 48 hours post-transplant unless severe hemodynamic instability or enteral intolerance.

Complications

Volume overload Heart transplant recipients are prone to volume overload due to large intraoperative resuscitation, capillary leak, acute kidney injury, and physiologic limitations of the transplanted heart. ISHLT guidelines recommend targeting a CVP of 5 to 12 mm Hg to optimize filling pressures and reduce venous congestion.[5] Volume overload—excess sodium and water with expanded extracellular fluid—is linked to increased mortality.[19]

Diuretic resistance Prolonged neurohormonal activation and renal tubular injury can blunt response to loop diuretics. Intravenous (IV) loop diuretics (furosemide, torsemide, bumetanide) are first-line, typically started at 2 to 2.5 times the prehospital dose.[20,21] If inadequate, therapy may escalate to continuous infusion—furosemide first, then bumetanide if needed—which can improve fluid removal and tolerability.[22]

If maximal dosing fails and the patient becomes diuretic resistant, thiazides (eg, metolazone, chlorothiazide) or carbonic anhydrase inhibitors for metabolic alkalosis may be added.[23] Persistent resistance warrants consideration of RRT. Early post-transplant diuretic resistance is often driven by impaired renal perfusion from low CO, venous congestion, or an evolving acute kidney injury.[23] Renal function is strongly linked to long-term outcomes, with early RRT use predicting higher mortality and chronic RRT dependence.[24] Preservation of renal function should guide diuretic strategy, antimicrobial selection, and other early postoperative management decisions.

Respiratory failure or failed extubation Mechanical ventilation supports gas exchange but can have mixed effects on RV afterload. Positive-pressure ventilation raises intrathoracic pressure and compresses pulmonary vessels, increasing PVR. Conversely, it can reduce RV strain by correcting hypoxia, hypercarbia, and acidemia—key contributors to elevated PVR.[5] Patients should undergo daily assessment for extubation with the goal of safe and early liberation from mechanical ventilation to minimize risks such as ventilator-associated lung injury, ventilator-associated pneumonia, tracheal trauma, oropharyngeal dysfunction, and ICU-associated weakness.[25] Reproducible across multiple studies, daily spontaneous awakening and spontaneous breathing trials (SBTs) in eligible patients improves survival and reduces time on a ventilator.[26–28]

Heart transplant patients follow standard SBT criteria—manageable secretions, adequate gas exchange on minimal support (PEEP $\leq$ 8 cm H2O, $FiO_2 \leq 0.4$, $PaO_2/FiO_2 > 250$), adequate strength and mentation, and relative hemodynamic stability—but vasopressors, inotropes, inhaled pulmonary vasodilators, and even VA-ECMO are not absolute contraindications to extubation.[26] Volume status and RV function are critical, as extubation changes inspiratory pressure from positive to negative, increasing RV preload and RV strain if not optimized. Common causes of failed extubation include volume overload, phrenic nerve injury, residual neuromuscular blockade, and recurrent laryngeal nerve palsy.[16] Assessment should include diaphragm ultrasound and laryngoscopy when needed.

Infection Immunosuppression is initiated at the time of transplant, placing patients at elevated high risk for opportunistic infections.[5] Indwelling lines and mechanical ventilation further predispose to ventilator-associated pneumonia and sepsis. Bacterial infections predominate in the early post-transplant period, with most recipients experiencing at least one infectious complication within the first 6 months following transplant.[29] Surgical site infections are typically caused by coagulase-negative *Staphylococci* or *S. aureus*, while bloodstream and respiratory infections are often gram-negative (*Enterobacteriaceae, Pseudomonas, Klebsiella*).[30,31]

There are no published guidelines or expert consensus to guide acquisition of surveillance cultures and/or labs beyond minimum monthly quantitative CMV viral load monitoring recommended by the American Society of Transplantation.[32] Routine screening for bacterial or fungal pathogens is not recommended, though daily clinical screening for signs and symptoms of infection

may be prudent.[32] In the ICU, chest radiographs are routinely performed daily and can partly serve as radiologic screening for pneumonia, as respiratory infections account for approximately one-third of infectious complications over this time period.[30,33] Traditional infectious biomarkers such as C-reactive protein and procalcitonin are not capable of distinguishing between an infection and generalized inflammatory response associated with transplantation in the early postoperative period, and are not routinely recommended.[34]

The threshold to perform surveillance cultures should be low. Any fever (>38°C), new productive cough and/or respiratory compromise, leukocytosis, or unexplained hypotension should result in blood and sputum cultures, consideration of urinalysis, *C. difficile* assays and/or viral panels, potentially alongside empiric antibiotic administration.

Electrolyte disturbances Aggressive diuresis causes hypokalemia and hypomagnesemia, precipitating arrhythmias if uncorrected.

Risk of malnutrition Early enteral nutrition within 48 hours of transplant is considered safe, and is endorsed by the American Heart Association (AHA) Scientific Statement on Prevention of Complications in the Cardiac ICU, and may reduce infection risk by preserving gut integrity and preventing bacterial translocation.[1,35–37] Because catabolism climbs for the first 48 hours following transplant, and malnutrition is an independent predictor of postoperative complications and mortality after heart transplant, initiating early enteral nutrition is recommended.[38–40]

For patients extubated within 24 hours, enteral feeding should start with clear liquids and advance as tolerated. Intubated patients or those with dysphagia should start trophic feeds (10–20 mL/hour) and advance as able.[36,37] Gastrointestinal symptoms such as pain or distension warrant slowing or pausing feeds; prokinetics or post-pyloric feeding tubes may be used for gastroparesis.[35,36] Causes of intolerance include ileus, bowel obstruction, colonic pseudo-obstruction, or mesenteric ischemia.[41] Enteral nutrition should be withheld in shock with high or escalating vasopressors or significant lactic acidosis. Once hemodynamics stabilize, trophic feeds can be restarted and advanced as tolerated.[36,37]

Challenges

Balancing negative fluid balance with renal protection is paramount, guided by urine output, central pressures, and arterial blood gases. Immunosuppressive therapy adds risks of nephrotoxicity and infection. Nutritional needs must be balanced with feeding intolerance and pharmacologic support patients require. With ongoing inotrope and vasopressor requirements, there may be slowed gut motility and risk of nonocclusive mesenteric ischemia, though the benefits of early enteral nutrition are well known. As in phase 1, vigilant monitoring and continuous clinical assessment remain essential.

Recommendations

- Use *loop plus thiazide synergy* if resistance develops; monitor renal indices and electrolytes at least twice daily.
- Advance to *SBT and extubation* when $FiO_2 \leq 0.4$, PEEP $\leq$ 8 cm H_2O, PaO_2/FiO_2 greater than 250, and adequate strength and mentation are present.
- Maintain *infection vigilance.*
- Begin *enteral nutrition by postoperative day 1 to 2* as tolerated.
- Coordinate daily goals with respiratory therapy and physical therapy (OT) to promote early mobilization once extubated.

The diuresis phase marks the transition from critical support to active recovery, laying the foundation for successful inotrope weaning and rehabilitation.

Phase 3: Inotrope Wean & Rehabilitation

Clinical presentation

Most patients are extubated or on minimal oxygen support, hemodynamically stable, and beginning to participate in early mobilization. The pulmonary artery catheter usually remains in place for monitoring trends as inotropes are tapered. Graft function is typically preserved, though mild RV dilation and septal flattening may persist as pulmonary vascular tone normalizes.[42]

Typical findings include the following:

- CI 2.4 to 3.0 L/minute/m^2
- CVP 8 to 12 mm Hg
- Lactate less than 2 mmol/L
- Stable rhythm, often sinus tachycardia or junctional rhythm at 80 to 100 bpm

The immunosuppressive regimen, commonly a calcineurin inhibitor (tacrolimus and cyclosporine), cell cycle inhibitor (mycophenolate mofetil and mycophenolic acid), and corticosteroids, is typically now fully initiated, introducing new considerations such as infection susceptibility, renal dysfunction, and metabolic derangements.[5,8]

Goals

1. *Wean inotropes and vasopressors* safely, maintaining CI greater than or equal to 2.2 L/minute/

m^2 and/or SvO_2 greater than 55% and evidence of adequate end-organ perfusion.
2. *Initiate and intensify rehabilitation* including ambulation, pulmonary hygiene, and incentive spirometry.
3. *Continue infection and rejection surveillance* through laboratory, imaging, and biopsy-based strategies.
4. Optimize nutrition, metabolism, and immunosuppression.

Complications

Chronotropic incompetence and bradyarrhythmias The denervated heart has a fixed intrinsic rate with limited chronotropic stress response.[43] In the early postoperative period, junctional rhythms and transient atrioventricular (AV) block are common. Persistent bradycardia (heart rate < 70 bpm) reduces CO and may require temporary pacing, usually via surgically placed temporary epicardial pacing wires in the immediate postoperative period. Dual-chamber permanent pacemakers are indicated for sustained sinus node dysfunction or AV block beyond 5 to 7 days.

Rejection (acute cellular rejection and antibody-mediated rejection) Acute cellular rejection typically occurs within the first month, mediated by T-cell activation, while antibody-mediated rejection arises from donor-specific antibodies causing microvascular injury.[44] Both may present with allograft dysfunction, low-grade fever, malaise, or subtle respiratory changes, and imaging may mimic pneumonia or edema. Routine surveillance endomyocardial biopsies (EMBs)—weekly for the first month—remain the diagnostic standard, supplemented by echocardiography and donor-derived cell-free DNA assays.[5,44] It is important to balance the immunosuppressive regimen against infectious risk.

Steroid-associated myopathy and critical Illness weakness Reduced muscle mass and frailty are common in advanced heart failure and transplant recipients, increasing mortality, length of stay, and risk of nonhome discharge.[45–47] ICU-acquired weakness affects about one-third of ICU patients and worsens outcomes.[48] While post-transplant patients rarely gain strength during hospitalization, preventing decline is critical. Corticosteroids, neuromuscular blockade, and bed rest synergize to produce profound weakness, delaying recovery in these patients. Early, stepwise mobilization—from passive motion to ambulation—is safe, reduces ICU stay, delirium and functional dependence, and should continue after discharge.[48–50] Participation in post-transplant cardiac rehabilitation improves 1-year readmission rates and quality of life.[51,52]

Renal dysfunction and tacrolimus toxicity Acute kidney injury is common following OHT, up to 40% to 76%, with the need for RRT in up to 7% to 19% of patients.[8] Risk factors include preoperative chronic kidney disease, diabetes, prolonged cardiopulmonary bypass time, postoperative VA-ECMO, and significant bleeding.[8,53] Additionally, calcineurin inhibitors cause afferent arteriolar vasoconstriction, leading to acute kidney injury. Strategies to reduce renal injury include maintaining adequate perfusion with inotropes or MCS, minimizing renal congestion, and minimizing nephrotoxic antibiotics.

Challenges

The principal challenge in this phase is tapering pharmacologic support without precipitating graft dysfunction, often while patients remain on dual inotropes. Gradual weaning guided by hemodynamic indices, lactate, and urine output reduces recurrent PGD.

Rehabilitation can reveal inadequate chronotropic response due to denervation, with CO relying on stroke volume and baseline rate; pacing or low-dose theophylline may improve chronotropic competence in select patients. Immunosuppression adds complexity, as corticosteroids can cause hyperglycemia and myopathy, and calcineurin inhibitors worsen nephrotoxicity and hypertension. Close coordination with transplant cardiology and pharmacy teams is essential to balance immunologic safety with metabolic stability.

Recommendations

- *Wean inotropes sequentially.*
- *Maintain heart rate* and consider using temporary pacing or permanent device if bradyarrhythmia persists.
- *Initiate formal rehabilitation* (PT/occupational therapy) targeting daily ambulation and respiratory exercises.
- *Perform frequent rejection surveillance per institutional protocol.* While EMB remains the gold standard for rejection monitoring, many programs are reducing the number of routine biopsies in favor of noninvasive monitoring in patients at low risk for acute rejection, or at prohibitively high risk for EMB (difficult vascular access, tricuspid valve replacement.
- *Implement gradual corticosteroid taper* to prevent myopathy and glycemic instability.
- *Optimize nutrition* with 1.5 to 2.0 g/kg/day protein intake and strict glucose control.

- *Continue infection prophylaxis and CMV monitoring* through daily labs or polymerase chain reaction.[18]

By the end of this phase, the patient should have adequate CI and SvO_2, minimal oxygen requirements, and sufficient mobility for transfer, either off all inotropes or on a single inotrope that can be safely weaned without invasive hemodynamic monitoring on the step-down unit (**Fig. 4**).

MECHANICAL SUPPORT CONSIDERATIONS

MCS serves both as rescue therapy in PGD and as bridge to recovery in complex hemodynamics. Early recognition of graft failure and prompt initiation of MCS are imperative for survival.

Venoarterial Extracorporeal Membrane Oxygenation

VA-ECMO provides complete cardiopulmonary support and remains the mainstay for severe PGD unresponsive to maximal pharmacologic therapy. Early initiation—ideally within 2 hours of diagnosis—lowers mortality.[6] Central cannulation in the operating room allows immediate deployment, while peripheral femoral access is suitable for delayed deterioration. Central ECMO cannulation can be considered when separation from cardiopulmonary bypass is unsuccessful and may be the preferred modality in patients with severe peripheral arterial disease or small-caliber peripheral vessels. Peripheral ECMO, however, permits primary chest closure and may reduce the risk of mediastinal infection. Current evidence is insufficient to demonstrate superiority of central versus peripheral ECMO, or to establish ECMO as the unequivocally preferred temporary MCS modality in this setting. However, ISHLT guidelines recommend prompt institution of ECMO when progressive allograft dysfunction occurs despite maximum medical therapy in the postoperative period.[5] The level of support should be carefully titrated to ensure adequate systemic perfusion and oxygen delivery while providing sufficient time for myocardial recovery. Left-sided cardiac distension during ECMO support should be addressed aggressively, as it may worsen pulmonary function and impede left ventricular recovery, though no particular strategy of LV venting or unloading has been recommended for the post-transplant population.[11,12]

Weaning from Venoarterial Extracorporeal Membrane Oxygenation

No standardized guidelines exist for weaning from temporary MCS and decisions are based on an integrated assessment of clinical status, hemodynamic parameters, and echocardiographic

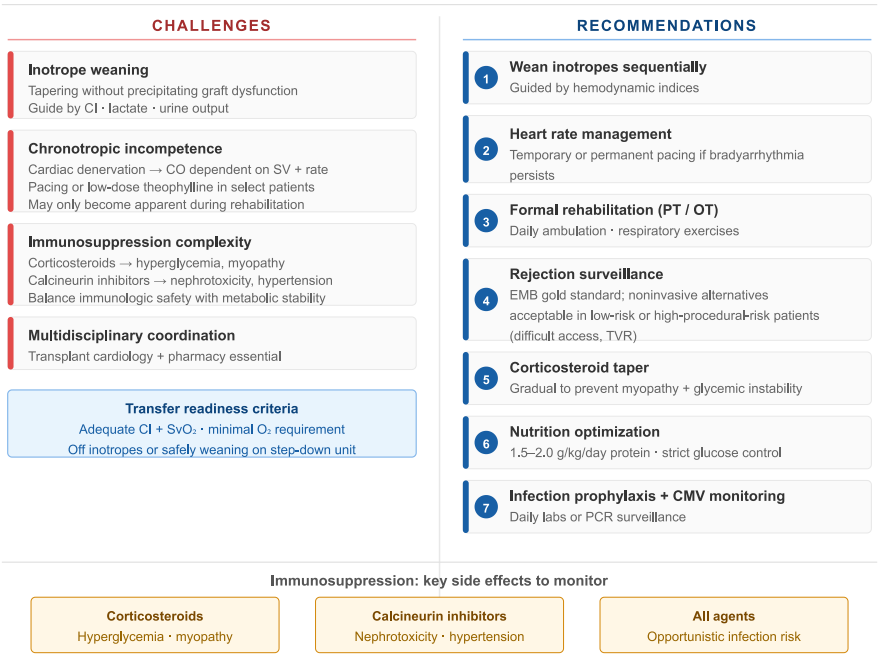

Fig. 4. Phase 3 (weaning): challenges and recommendations. OT, occupational therapy; PCR, polymerase chain reaction; SV, stroke volume; TVR, tricuspid valve replacement.

evidence of myocardial recovery. In the absence of demonstrable myocardial recovery, transition to durable MCS, retransplantation or withdrawal of life-sustaining therapies should be considered, with input from a multidisciplinary team. Prolonged ECMO (>7 days) predicts poor recovery and may prompt transition to durable LVAD or retransplant evaluation.[5] The evolving ISHLT consensus emphasizes structured criteria for both initiation and discontinuation, incorporating hemodynamic, echocardiographic, and biochemical markers.[54]

Intra-aortic Balloon Pump

Though less common in the modern era, intra-aortic balloon pump can temporize moderate PGD-LV by reducing afterload and augmenting coronary perfusion. It remains valuable in resource-limited or hybrid ECMO settings.

Emerging Trends and Technologies

Technological advances such as normothermic regional perfusion for donation after circulatory death (DCD) hearts and portable ECMO platforms have expanded the role of temporary support.[54] Early extubation and ambulation on ECMO are increasingly feasible in high-volume centers, emphasizing rehabilitation even in mechanically supported patients. Artificial intelligence–based monitoring and predictive modeling are being explored to optimize timing of MCS initiation and weaning.

SUMMARY

Post–heart transplant recovery in the ICU is a dynamic continuum of physiologic adaptation. The proposed *phase-based framework*—Resuscitation, Diuresis, and Inotrope Wean & Rehabilitation—provides a reproducible roadmap for clinicians navigating this complexity. Each phase emphasizes distinct but interlocking goals and this structure improves communication across disciplines and ensures that transitions of care, both physiologic and operational, occur deliberately.

FUTURE DIRECTIONS

Ongoing refinements in perfusion technology, donor management, and immunologic monitoring are reshaping early post-transplant care. Machine learning–driven hemodynamic prediction, portable ECMO, and minimally invasive biopsy alternatives are poised to further improve outcomes. The next evolution will emphasize not only survival but quality of recovery—functional capacity, freedom from chronic organ injury, and reintegration into life.

CLINICS CARE POINTS

- *Recognize and treat primary graft dysfunction early.* Low cardiac output or escalating inotrope requirements within 24 hours should prompt early consideration of temporary mechanical circulatory support, as delayed escalation is associated with increased mortality.[5,6]
- *Differentiate vasoplegia from graft dysfunction.* Vasoplegia is best treated with norepinephrine plus vasopressin, while concomitant right ventricular failure requires preload optimization, pulmonary vasodilators, and tailored inotropic support.[5,13]
- *Pair diuresis with ventilator liberation.* Achieving net-negative fluid balance while pursuing early extubation improves pulmonary mechanics and reduces ICU complications, but requires close monitoring of renal function and right ventricular loading conditions.[5,37]
- *Expect infection risk despite sterile inflammation.* Early immunosuppression may mask infection, and C-reactive protein or procalcitonin are unreliable in the immediate post-transplant period; management should rely on vigilant clinical surveillance and protocolized prophylaxis.[5,32]

DECLARATION OF AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this work, the authors used gen AI. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

DISCLOSURE

The authors report no conflicts of interest related to the content of this article.

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