NARRATIVE REVIEW

PM&R

# Heart transplantation and the role of inpatient rehabilitation: A narrative review

**Leslie Rydberg MD**[1] ⓘ | **Kim Barker MD**[2] | **Julie Lanphere DO**[3] |
**Laura Malmut MD**[4] ⓘ | **Jacqueline Neal MD**[5,6] | **Sarah Eickmeyer MD**[7]

[1]Shirley Ryan AbilityLab, Department of Physical Medicine and Rehabilitation, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

[2]Department of Physical Medicine and Rehabilitation, UT Southwestern Medical Center, Dallas, Texas, USA

[3]T12 Neuro Specialty Rehab Unit at Intermountain Medical Center, Murray, Utah, USA

[4]MedStar National Rehabilitation Network, Washington, District of Columbia, USA

[5]Jesse Brown VA Medical Center, Chicago, Illinois, USA

[6]Department of Physical Medicine and Rehabilitation, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

[7]Department of Rehabilitation Medicine, University of Kansas Medical Center, Kansas City, Kansas, USA

**Correspondence**
Leslie Rydberg, Shirley Ryan AbilityLab, Department of Physical Medicine and Rehabilitation, Northwestern University Feinberg School of Medicine, Chicago, IL, USA.
Email: lrydberg@sralab.org

## Abstract

Heart transplantation is a definitive treatment option for patients with end-stage heart failure. Medical and functional complications are common after this procedure, and rehabilitation is often needed postoperatively. Physiatrists caring for persons who have received a donor heart must appreciate the surgical background, the physiologic changes expected, as well as the potential medical complications for which they are at risk after heart transplantation. This review summarizes various topics in heart transplantation including the history of the procedure, exercise physiology and functional outcomes, postoperative medical therapy, medical complications, and special considerations for inpatient rehabilitation in this patient population.

## INTRODUCTION

Heart failure affects more than 6.5 million people in the United States[1]; up to 500,000 individuals have advanced or end-stage disease.[2] The physical toll on these persons and impact on their functional health can be profound. Heart transplantation can improve survival and quality of life for some; however, between 1990 and 2010, only 2200 heart transplants occurred in the United States due to a limited availability of donors. The paucity of available donor hearts has caused implantation of mechanical circulatory support (e.g., a left ventricular assist device or LVAD) to become more common as a bridge to transplantation or as a destination therapy.[2] Despite this, heart transplantation remains the "gold standard" in treatment.

Rehabilitation is often needed postoperatively because medical and functional complications are common after heart transplantation. Inpatient rehabilitation (IPR), led by a physiatrist or physical medicine and rehabilitation physician, has been shown to be beneficial for people who have undergone LVAD placement,[3] and is one option to improve functional outcomes after heart transplantation. The purpose of this review is to discuss the history of the procedure, exercise physiology of the transplanted heart, functional outcomes after heart transplantation, medications used for immunosuppression and prophylaxis, medical complications seen after transplantation, and special considerations for IPR in this patient population.

### Literature search strategy

A literature search was performed in the PubMed, Medline, and Scopus databases using the search terms "heart transplant guidelines," "heart transplant complications," "heart transplant physiology," "heart transplant AND inpatient rehabilitation." Inclusion criteria were studies in humans and articles published in the

**TABLE 1** Indications and absolute contraindications to heart transplantation

| Indications | Absolute contraindications |
| --- | --- |
| Cardiogenic shock with inadequate organ perfusion requiring either continuous intravenous inotropic support or circulatory support from a device such as an intra-aortic balloon pump counterpulsation device or an implanted circulatory device such as a left ventricular assist device[2] | Life expectancy of <2 years despite heart transplantation[2] |
| Dilated cardiomyopathy with persistent New York Heart Association (NYHA) class IV heart failure refractory to optimal medical and surgical therapy[2] | Irreversible pulmonary hypertension[2] |
| Intractable angina with coronary artery disease not amenable to percutaneous or surgical revascularization[2] | Severely symptomatic cerebrovascular disease[2] |
| Intractable life-threatening arrhythmias unresponsive to medical therapy, catheter ablation, surgery, and/or implantable cardioverter-defibrillator[2] | Active substance abuse[2] |
| Congenital heart disease with NYHA class IV heart failure that is not amenable to palliative or corrective surgery, with severely symptomatic cyanotic heart disease not amenable to palliation, or with pulmonary hypertension that is still potentially reversible[4] | Multiple demonstrations of non-compliance with drug therapy[2] |
| Selected restrictive and hypertrophic cardiomyopathy with a NYHA class of III to IV[4] | Multisystem extra-cardiac organ involvement (e.g., amyloidosis)[2] |

English language without any restrictions on the publication date. Exclusion criteria were an inappropriate topic, case reports, or letters to the editor. The first author screened the abstracts and identified relevant articles related to the topic. Subsequently, complete articles with full text were gathered. The reference lists of these publications were scrutinized for other studies that might be relevant. This search strategy resulted in 40 total articles, which included original research and review articles. Published abstracts were considered if the content was relevant and not available elsewhere. Three authors reviewed this list for appropriateness and acceptance in the final list of articles. In addition, several textbook chapters were referenced to include relevant background knowledge for the topic and audience.

# DISCUSSION

## History and background

After several decades of preliminary work in orthotopic and heterotopic heart transplantation, the first interhuman heart transplant occurred in South Africa in 1967 by Dr. Christian Barnard. The early human-to-human heart transplants demonstrated limited survival of hours to days. Despite the short survival time, there continued to be great interest in heart transplantation in the late 1960s, with continued attempts. It was not until the 1980s, when cyclosporine became available as an immunosuppressant and was given after heart transplantation, that survival improved and the number of surgeries rapidly increased. The year 1980 is credited as the start of the modern era of heart transplantation.[4]

There are several indications for cardiac transplantation in a person with advanced heart failure. Risks and benefits are weighed based on the individual. Table 1 lists the indications and absolute contraindications to heart transplantation, per the major national and international cardiology society guidelines.

Relative contraindications include age >70 years, body mass index (BMI) >35, diabetes mellitus with poor glycemic control with evidence of end-organ damage, irreversible renal dysfunction with GFR <30, cancer, infection, inadequate social support, conditions that increase risk of perioperative complications, conditions that may limit tolerance of immunosuppression, and frailty.[2] For those who have absolute or significant relative contraindications, mechanical circulatory support via an LVAD may be recommended.[5] Alternate therapy should also be considered for patients with potentially reversible or treatable conditions.

Several steps are involved in the heart transplantation process. Only 30% of hearts from deceased donors ultimately meet criteria for donation and are listed for transplant. The Organ Procurement and Transplantation Network/United Network for Organ Sharing utilizes an allocation algorithm that prioritizes organs based on geographic location, then medical urgency and blood type compatibility.[6] United Network for Organ Sharing scoring was updated in 2018 for heart transplant and is now scored between 1 and 6.[7] Other parameters for match include comparable body size/weight of the donor to the recipient.[6]

## Immunosuppression after heart transplantation

Although a patient's transplant team often manages the immunosuppression regimen, it is important for physiatrists, who are a key team member participating in the post-transplantation care, to understand the typical medications used, as well as the potential complications resulting from these medications.

**TABLE 2** Complications of immunosuppressive drugs for heart transplantation

| Drug | Complication |
| --- | --- |
| Calcineurin inhibitors: tacrolimus and cyclosporine | Cardiovascular: hypertension, edema<br>Neurologic: headache, tremor, neuropathy, seizure<br>Hematologic: anemia, leukopenia, thrombotic microangiopathy<br>Dermatologic: fibrovascular polyps, alopecia, hirsutism<br>Gastrointestinal: nausea, diarrhea, steatohepatitis, jaundice<br>Metabolic: electrolyte abnormality, hyperglycemia<br>Renal: nephropathy |
| Mycophenolate | Infectious: herpes simplex virus, cytomegalovirus<br>Cardiovascular: hypertension, edema<br>Neurologic: headache, tremor<br>Hematologic: leukopenia, thrombocytopenia<br>Dermatologic: rash<br>Gastrointestinal: nausea, constipation, diarrhea, dyspepsia<br>Metabolic: hyperglycemia, hyperlipidemia, gout<br>Renal: nephropathy<br>Respiratory: dyspnea, cough |
| Corticosteroids | Neurologic: headache, labile mood<br>Dermatologic: bruising, fragile skin, impaired wound healing<br>Gastrointestinal: dyspepsia, esophagitis, pancreatitis<br>Metabolic: diabetes, hyperlipidemia, edema, adrenal suppression<br>Musculoskeletal: osteoporosis, myopathy<br>Ocular: glaucoma, cataracts |

The International Society of Heart and Lung Transplantation published guidelines for the care of heart transplant recipients in 2010.[8] Induction treatment in the perioperative period consists of polyclonal (thymoglobulin) and/or monoclonal antibodies (anti-CD25 or anti-CD52).[9] Calcineurin inhibitors, including tacrolimus and cyclosporine, are the mainstay of maintenance immunosuppression regimens after heart transplantation.[8] Sirolimus or everolimus may be used in place of tacrolimus. Adjuvant immunosuppression medications, such as mycophenolate, and corticosteroids are also used for maintenance immunosuppression, with individualized plans based on the characteristics and risks associated with each patient.[8] Immunosuppressive drugs have many interactions with other medications, and close monitoring of therapeutic drug trough levels is necessary. The therapeutic range of these medications varies depending on time after transplantation, concomitant medications, and toxicity concerns, so close coordination with heart transplant physicians and pharmacists is needed.

Cyclosporine and tacrolimus can cause many acute and chronic side effects, as listed below in Table 2. Importantly, calcineurin is involved in muscle growth, so both cyclosporine and tacrolimus can lead to muscle weakness during recovery from transplantation. Compared to cyclosporine, tacrolimus can cause more hyperglycemia but less hypertension, dyslipidemia, renal dysfunction, hirsutism, and gingival hyperplasia.[9] Neurologic side effects may include tremor, seizure, or posterior reversible leukoencephalopathy.[8] Electrolyte monitoring is key, as tacrolimus can cause hypomagnesemia and lead to QTc prolongation and torsades de pointes. As time increases from transplantation, the therapeutic range and dose often decrease for calcineurin inhibitors, which can help reduce toxicity and side effects.

Mycophenolate has been associated with an increased risk of infection, particularly from viruses such as herpes simplex virus and cytomegalovirus (CMV).[9] Common side effects also include nausea, vomiting, and diarrhea, which may require a dose reduction.[9]

Common acute side effects of corticosteroids include labile mood, insomnia, dyspepsia, and hyperglycemia. Corticosteroids may also increase the risk of infection, hypertension, and adrenal insufficiency, as well as long-term metabolic and skeletal disease. Corticosteroid myopathy may lead to proximal weakness and is often a reason for referral to a rehabilitation specialist. Corticosteroids can be eventually weaned at 3 to 6 months after transplantation in many low-risk patients, which minimizes the risk of long-term adverse effects.[8]

The International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients states that prophylaxis against CMV should be started 24 to 48 hours after heart transplantation, usually with ganciclovir for intermediate- and high-risk patients or acyclovir for low-risk patients.[12] Prophylaxis against mucocutaneous candidiasis should be initiated once extubated with nystatin or clotrimazole.[8] *Pneumocystis jirovecii* and *Toxoplasma gondii* prophylaxis should be initiated in the early postoperative period, usually with trimethoprim/sulfamethoxazole or alternatives in the setting of a sulfa allergy or glucose-6-phosphate dehydrogenase deficiency such as aerosolized pentamidine isethionate, dapsone, or atovaquone.[8] Due to the high risk for infection, care should be taken on the IPR unit to reduce the risk of hospital-acquired infections.

# Medical complications after heart transplantation

Over the decades, advancements in surgical techniques, immunosuppression, and postoperative management have improved survival and has reduced complications following heart transplantation.[10] Nevertheless, complications are common and range from mild to critical in severity.[11] Although patients are under

the care of physiatry postoperatively, it is important to monitor for and assist with medical management of these complications, while maintaining communication with the transplant team. Being knowledgeable about potential complications over the continuum of transplant care can facilitate timely treatment as well as patient education about the hospitalization period and anticipated recovery course.

Primary graft dysfunction is a significant cause of morbidity and mortality in the first 24 hours after transplantation and manifests through left and/or right ventricular dysfunction, pulmonary hypertension, or hyperacute rejection. Secondary early graft dysfunction is due to an identifiable cardiac insult, such as acute rejection or pulmonary hypertension. Certain donor and recipient characteristics and perioperative factors such as prolonged ischemic time, increase the risk.[11] Treatments include medical therapy or, in severe cases, mechanical circulatory support.[10] Late graft dysfunction develops weeks to years after transplantation and is typically caused by rejection or cardiac allograft vasculopathy.[11]

Organ rejection is the result of the transplant recipient's immune response to the donor heart's foreign alloantigens.[10] Rejection is one of the leading causes of death in the first year after transplantation,[11] with about 50% of rejection episodes occurring in the first 6 weeks.[10,11] In most cases of rejection, patients are asymptomatic or may experience mild symptoms such as fatigue, weight gain, reduced exercise tolerance, or fever.[10,11] Decreased systolic function and signs of hemodynamic compromise occur late in the rejection process and need to be addressed urgently. Endomyocardial biopsy is the gold standard for diagnosis. Most transplant centers perform surveillance biopsies weekly for the first several weeks following transplantation, progressively increasing the interval between biopsies according to the patient's clinical course. Immunotherapy is used to treat rejection when it is diagnosed.[10]

Cardiac allograft vasculopathy, a complication unique to heart transplantation, is an accelerated form of diffuse and obliterative arteriosclerosis resulting in thickening of the vascular intima and narrowing of the vessel lumen along its entire length. The etiology is immune- and non–immune-mediated endothelial damage and is progressive in nature.[10,11] Cardiac allograft vasculopathy has been detected in up to 70% of patients within the first year.[10] Due to denervation of the transplanted heart, patients rarely present with angina or other classic symptoms of coronary artery disease, which can result in silent clinical events such as myocardial ischemia and infarction, congestive heart failure, ventricular arrhythmias, and sudden death. Medical management includes administration of aspirin,[10] statins, and

immunosuppression.[11] Revascularization procedures benefit a minority of cases with proximal focal disease. Re-transplantation is the definitive treatment in select patients.[10]

Immunosuppression increases the risk of infection by suppression of the host's immune response.[11] Infection is a major cause of hospital readmission and the leading cause of death in the first post-transplant year.[10] In the first postoperative month, infections are typically due to nosocomial infections of the respiratory system, urinary tract, and the skin. Commonly reported infections include CMV, herpes simplex virus, Epstein–Barr virus, varicella zoster virus, tuberculosis, and pneumonia. Severe infections may necessitate reduction in immunosuppression, which can increase risk of rejection. Providers must maintain a high degree of suspicion, as symptoms can be masked by the effects of immunosuppressive drugs.[10]

The most frequent postoperative cardiac complications include pericardial effusion (61.5%), arrhythmia (41.8%), and mediastinal bleeding (8.4%).[12] The incidence of venous thromboembolism is high after heart transplantation, even with appropriate thromboprophylaxis. The frequency has been reported to be 9.3% for deep vein thrombosis, with pulmonary embolism occurring in 1.9%.[13]

Neurologic complications in heart transplant recipients include cerebrovascular events (3%–10%), seizures (2%–22%), delirium or encephalopathy (17.1%), and central nervous system infections (3%). Although most neurological complications are transient, strokes and central nervous system infections are associated with high mortality and morbidity.[14] Delirium and encephalopathy can be persistent and require close attention during rehabilitation. Complications related to the peripheral nervous system were reported in 30% of transplant recipients in one study.[15] The most frequent diagnoses were polyneuropathy (33%), muscle disease (26%), mononeuropathy (17%), and radiculopathy (13%). Risk factors include prolonged surgery, suboptimal patient positioning, and prolonged admission to the intensive care unit.[14,15]

Depression is common (almost 24%) in patients awaiting heart transplantation,[16] with similar rates reported following transplantation.[17] Premorbid depression is a strong predictor of poor medication compliance and higher rates of rehospitalization in transplant recipients.[16] Depression following transplantation is an important independent risk factor for all-cause mortality during a 6-year follow-up period.[17] Screening and treatment of depression should be considered in patients awaiting transplantation and in transplant recipients.[16,17]

Comprehensive assessment and careful management of complications is important and can help minimize adverse effects and ultimately improve longevity and quality of life after heart transplantation.[10]

# Physiologic changes before and after heart transplantation

Prior to transplantation, patients with heart failure typically have lower stroke volume, cardiac output, and aerobic capacity. Patients with heart failure often become symptomatic with activity and over time reduce their activity levels due to these symptoms, resulting in a steady decline in aerobic capacity and functional performance. Prolonged bed rest, such as occurs during a hospitalization for heart failure or transplant surgery, also causes a significant decline in aerobic capacity. Resting tachycardia with an exaggerated heart rate response to a lower level of activity is common. This physiologic change is due to reduced vagal tone and enhanced sympathetic response from circulating catecholamines.[8]

Outside of cardiac function, patients with heart failure prior to transplantation are also noted to have altered skeletal muscle cellular structure, commonly experiencing muscle fiber atrophy, reduced mitochondrial counts, and depletion of oxidative capacity.[18] Vasomotor changes with increased vasoconstriction and impaired arterial dilatation with exercise are noted. Following heart transplantation, patients continue to demonstrate these changes with skeletal muscle cellular structure and vasomotor changes.[18]

Due to sinoatrial node denervation that occurs with the transplantation, there is further loss of vagal tone to the sinoatrial node, which results in further resting tachycardia and elevated systolic and diastolic blood pressure while at rest. Also due to the sinoatrial node denervation, the rate of increase in heart rate and therefore cardiac output with exercise (and oxygen consumption) is diminished, because the newly transplanted heart is now reliant on responses to increases in circulating catecholamines. With these changes, peak heart rate is typically about 25% lower than in age-matched controls, and the $VO_2$ max is typically about 33% predicted. At maximum effort, there is a significantly reduced peak cardiac output and systolic blood pressure, as well as lower oxygen consumption at the anaerobic threshold. The lower oxygen consumption at the anaerobic threshold is also due in part to the persistent changes in skeletal muscle. Furthermore, there is a prolonged time for the heart rate to return to baseline after exercise.[19–23] All of these changes necessitate patient education about a gradual ramping up of activity during exercise routines. In addition, due to heart transplant recipients relying on catecholamine response to increase heart rate, exercise prescriptions based on target heart rate are not recommended, and rather other measures may have more utility such as Borg Rating of Perceived Exertion, Modified Borg Scale, Dyspnea Index, or defined exercise tasks and pace.

**TABLE 3**    Cardiac rehabilitation phases[27,28]

| | |
|---|---|
| Acute phase (Phase 1) | • Education about cardiopulmonary risk factor modification<br>• Acute mobilization should be done with cardiac monitoring<br>• Post-MI heart rate should be within 20 beats/min of baseline, SBP within 20 mmHg of baseline<br>• A decrease of 10 mmHg or more is indicative of medical issues<br>• Target intensity is 4 METs<br>• Mobilization in the ICU and while mechanically ventilated is safe and can be helpful |
| Inpatient rehabilitation phase (Phase 1B) | • For those who require acute or subacute rehabilitation treatment prior to discharge home<br>• Exercise guidelines are the same as for Phase 1, but with a longer recovery period extending their acute hospitalization |
| Training phase (Phase 2) | • Exercise with a target heart rate of 85% of the maximum heart rate<br>• Exercise with a lower for target heart rate of 65%–75% in patients at higher risk or with underlying conditions (such as arrhythmias or angina) has been found to be safe and effective<br>• Oxygen saturation is kept at >90%<br>• Typically 8 to 12 weeks long |
| Maintenance phase (Phase 3) | • Focuses on patient education of the importance of making exercise part of new healthy habits<br>• Emphasis on maintaining exercise capacity with target moderate intensity of at least 30 min, 3 times a week versus low-intensity frequency of 5 times a week |

Abbreviations: ICU, intensive care unit; MET, metabolic equivalent; MI, myocardial infarction; SBP, systolic blood pressure.

Following implementation of an aerobic training program emphasizing endurance tasks, heart transplant recipients demonstrate an increase in cardiac output at higher work intensities due to an increase in stroke volume. However, cardiac output at rest has been noted to remain unchanged. Furthermore, the arteriovenous-$O_2$ difference increases with aerobic training. Given these changes, based on the Fick equation (oxygen consumption = cardiac output x arteriovenous oxygen difference), an increased oxygen consumption ability is noted, with an improvement in the anaerobic threshold and $VO_2$ max increasing by 12% to 49%.[24] These changes have been demonstrated to improve functional capability and strength in addition to the improved aerobic capacity.

## Outpatient cardiac rehabilitation

Given the physiologic changes with heart failure, a rehabilitation program is typically recommended prior

to, and following, heart transplantation. Cardiac rehabilitation focuses on the reduction of cardiac risk factors in combination with education and exercise for patients. A review article by Mampuya notes early studies supporting cardiac rehabilitation being associated with reduced coronary events.[25] The standard model of cardiac rehabilitation was first described by Wenger et al. in 1971[26]; this has been modified over time with changes in treatment of coronary artery disease and revascularization techniques. The three phases of cardiac rehabilitation[27,28] are detailed in Table 3. The use of cardiac rehabilitation has broadened with time as well; it is now used in a wide variety of settings from revascularization to cardiac transplantation to stroke.[27] Various studies more recently also note a potential cost-effectiveness of cardiac rehabilitation compared to other treatments such as lipid-lowering medications, thrombolytics, and coronary artery bypass grafting.[25] Patients who undergo cardiac rehabilitation continue to demonstrate improvements in skeletal muscle structure and vasomotor changes after transplantation.

Cardiac rehabilitation is generally safe for patients receiving intravenous inotropic support awaiting transplantation.[29] Prior to transplantation, undergoing cardiac rehabilitation may prolong the window of eligibility for transplant and likely assist with tolerance of postsurgical rehabilitation and operative recovery. Prescribing aerobic exercise training in patients with heart failure, prior to transplantation, is a class I recommendation by the American Heart Association, as it decreases risk of all-cause mortality and improves exercise capacity and health-related quality of life.[30] Exercise training has even been described as safe and feasible in patients awaiting heart transplantation in the intensive care unit who are mechanically supported by intra-aortic balloon pumps.[31]

Although not explicitly described in the literature specific to post-heart transplantation patients, early mobility has been studied in the postoperative cardiothoracic surgical intensive care unit (including after heart transplantation) and has demonstrated a clinically significant reduction in hospital length of stay, intensive care unit days, intensive care unit readmission rate, and pressure ulcer prevalence.[32] Although almost every person who has had cardiac transplantation faces episodes of graft rejection at some point, it is rarely necessary to curtail exercise routines, unless there are signs of new arrhythmias, or abnormal vital signs such as new hypotension or fever.[33,34]

## Inpatient cardiac rehabilitation and outcomes

Transplant rehabilitation has been a growing field within the IPR scope over the last 10 to 15 years. Physiatry is well-suited to participate in managing the rehabilitation process starting prior to transplantation.

Rehabilitation ideally starts before transplantation, followed by early mobilization in the acute care hospital. From the acute care hospital, many patients can safely transition directly to home. For those who are not functionally or medically ready to return home, the IPR unit may offer an ideal setting. Postoperative transplant recipients who demonstrate a significant change in function from their baseline, require ongoing medical management and oversight by a physician at least 3 days per week, can tolerate intensive rehabilitation, require services by at least two skilled therapy domains (physical therapist [PT], occupational therapist [OT], speech therapist [SLP]), and have appropriate functional goals that can be addressed by the interdisciplinary team during IPR, are ideal IPR candidates. Facilities that are unable to obtain timely lab values for dosing immunosuppressants or unable to provide close medical oversight, whether IPR or skilled nursing facilities, are not optimal for rehabilitation after heart transplantation.

The IPR team should communicate with the transplant coordinators and the cardiac transplant surgical and medical teams to coordinate care around medication management, lab testing, follow-up care, family training, and other preventative care needs post-transplant. The rehabilitation focus is to improve overall endurance and conditioning for daily activities, promote independence with all basic mobility and self-care, and focus on gait, based on the capability of each patient.

Heart transplant recipients are a small transplant subpopulation, and outcomes have been followed in only a handful of studies. IPR heart transplant programs were built off the evidence for outpatient cardiac rehabilitation and IPR programs for other transplant groups, such as liver and kidney. A number of small retrospective studies have demonstrated the benefits of IPR following orthotopic heart transplantation, the findings of which are summarized in Table 4.[35,36,37,38]

## Considerations for inpatient rehabilitation programs

Based on their medical complexity, as outlined earlier, patients who enter IPR programs after heart transplantation require special attention and consideration. Given the pre-morbid heart failure that most patients experience, they start with significant deconditioning, as well as cardiorespiratory and skeletal muscle dysfunction. Heart transplant recipients can develop deconditioning and numerous physical impairments related to end-stage disease prior to transplantation in addition to complications during the surgery or postoperative course. Prolonged bed rest, nutritional deple-

**TABLE 4**  Outcomes after inpatient rehabilitation for patients with heart transplant

| Study | Type of study | Functional independence measure (FIM) | Other outcome measures |
|---|---|---|---|
| Gupta (2016)[35] | Retrospective study $n = 17$ | Mean admission and discharge motor FIMs were 51.5 (±14.6) and 74.4 (±12.0). Mean cognition admission and discharge FIM were 30.9 (±3.2) and 32.9 (±1.7). Mean total FIM gain was 26.9 ± 13.3 with a $p$ value <.05. Mean FIM efficiency was 3.2 (±2.0) | 82% discharge to home rate |
| Shiner (2019)[36] | Retrospective study $n = 116$ all transplant patients *$n = 49$ heart transplant patients | Mean admission and discharge total FIM were 79.8 (±20.3) and 101.8 (±29.1). No significant difference between heart and other transplant recipients | 6 MWT improved from 103.6 ± 80.1 to 183.2 ± 104.8 m ($p < .001$). TUG was decreased from 26.4 ± 18.3 s to 16.5 ± 14.1 s ($p < .001$). Berg Balance Scale scores increased from 26.8 ± 17.1 to 45.0 ± 9.4 ($p < .001$). 94% discharge to home rate |
| Patcai (2013)[37] | Retrospective study $n = 173$ all transplant patients *$n = 10$ heart transplant patients | Transplant patients (all groups) had a lower total FIM gain compared to the general rehab population (8.9 vs. 20.9, $p < .001$); and a lower FIM efficiency (1.1 vs. 1.4, $p < .001$) | Compared to general rehab inpatient population, transplant rehab inpatients had more transfers <3 days to acute care (5.2% vs. 1.9%, $p < .001$); higher rate of readmission to an acute hospital after first 3 days (19.1% vs. 1.9%, $p < .001$); a longer mean LOS (27 ± 19 vs. 20 ± 18 days, $p < .001$) |
| Joshi (1997)[38] | Retrospective study $n = 12$ | NA | Modified Barthel Index mean admit score of 57 (range 31–75), discharge was 86.5 (range 55–100, $p < .001$) |

*Subset of study population that had heart transplantation specifically.
Abbreviations: LOS, lenght of stay; 6 MWT, 6 minute walk test; TUG, timed up and go.

tion, and exercise intolerance are important factors before and after heart transplantation. Side effects related to cardiopulmonary pulmonary bypass that occurs during transplantation include diffuse generalized weakness, sternal dehiscence, poor endurance, denervation incompetence, neuropathies, myopathies, dysphagia, and cognitive impairment.[35]

## Goals of inpatient rehabilitation

The mains goals for patients in the IPR setting after heart transplantation are to improve overall endurance, improve strength, reduce falls, ensure adequate mobility to navigate the home environment, achieve independence with self-care and activities of daily living, and improve conditioning for community ambulation, community reintegration, and outpatient therapy programs (PT, OT, speech therapy, and/or cardiac rehabilitation).

## Physiatrist

The physiatrist serves as the leader of the rehabilitation team and is the physician responsible for the medical oversight of the transplant recipient during IPR and for prescribing and overseeing the patient's therapy course. An example of a guided therapy prescription is included in Table 5. From a medical standpoint, the physiatrist must closely monitor fluid status including daily weights, intake and output, peripheral edema, and renal function. Assessment of relevant signs and symptoms such as chest pain, shortness of breath, and changes to vital signs is crucial, as these findings can signify cardiac impairment. The team must also monitor for and address anxiety and depression that frequently occurs and may affect the rehabilitation process. The incidence of venous thromboembolism is high even with appropriate thromboprophylaxis.

Rejection is one of the leading causes of mortality after heart transplantation, with many rejection episodes happening in the first 6 weeks after transplantation while the patient participates in IPR. The physiatrist must monitor closely for signs and symptoms of rejection as well as coordinate care for the monitoring of rejection such as cardiac biopsies, which may interfere with therapy scheduling.

Infections are common during rehabilitation given the immunocompromised status of heart transplant recipients. Because these patients are immunocompromised, they may require special isolation or precautions for safety, based on the hospital protocols. Physiatrists must maintain a high index of suspicion for infections as classic infectious signs/symptoms may be obscured by the effects of the immunosuppressant medications.

The physiatrist must pay close attention to the medications to ensure that their patients are being given the correct immunosuppression medications and infection

**TABLE 5**　Sample therapy prescription within inpatient rehabilitation

| Discipline | Speech language pathology | Physical therapy | Occupational therapy | Psychology | Dietitian |
|---|---|---|---|---|---|
| Prescription | Dysphagia assessment, voice assessment, respiratory muscle strength assessment | Mobility assessment, assessment for mobility device aides, warm up/cool down periods, endurance training, monitor exertion/exercise intensity with Borg scale, assessment for home modifications | Assessment of independence with activities of daily living, assessment for integration of adaptive equipment, energy conservation/pacing strategies, assessment for home modifications | Assess for anxiety or depression | Nutritional assessment |
| Frequency | 3 days/week | 5 days/week | 5 days/week | | |
| Precautions | Sternal precautions, maintain Borg RPE 11–14 (moderate intensity), blood pressure and heart rate monitoring (contact physician if HR >150 or <70, or systolic BP >180) | | | | |

Abbreviation: RPE, rate of perceived exertion.

prophylaxis. All medications ordered for these patients must be double-checked for medication interactions. There must be a clear plan for ensuring that patients have access to all the transplant medications at the time of discharge including extensive medication education. This can be accomplished by day of discharge, in-person education or a follow-up appointment at the transplant clinic to see transplant pharmacy where the education and the first month of medication are provided.

## Social work/care manager

The social worker and/or care manager is integral to ensuring a smooth discharge plan in terms of follow-up, insurance approval, durable medical equipment, and medical follow-up appointments.

## Psychology

A psychologist or social worker is integral to assisting with the diagnosis and management of depression, delirium, or anxiety.

## Dietitian

A dietitian is often involved to assist with providing adequate nutrition, minimize nutrition-related side effects of immunosuppressants such as nausea and anorexia, optimize caloric intake, and assess weight gain or weight loss.

## Allied health team

A highly skilled allied health team is integral to the success of the recovery of this patient population. During therapy, it is important to monitor blood pressure, heart rate, and oxygen saturation changes with activity, as well as monitor for symptoms of chest pain, light-headedness, or shortness of breath. Physiatrists may provide guidance for specific cardiac parameters. It is important that sternal precautions as prescribed by the surgical team are followed. Classic sternal precautions include no reaching over head, out to the side, behind the back, lifting more than 5 to 10 pounds, no pushing or pulling with the arms, and no driving. Newer sternal precautions attempt to consider both reducing sternal complications as well as the functional impact that these precautions can have on an individual's life. Cahalin et al.[39] proposed the use of an algorithm based on individual risk factors and the Sternal Instability Scale. Another sternal precaution that is becoming more frequently followed is move in the tube precautions in which patients are permitted to perform all activities as long as they are symptom-free and push up with their arms only when their arms are close to their bodies. Studies have noted that patients using move in the tube are not at greater risk of sternal disruptions compared to following traditional sternal precautions.[40]

Heart rate does not accurately reflect activity intensity due to the lack of vagus nerve innervation. A common solution is to use the Borg Rating of Perceived Exertion or the Modified Borg Scale.[41,42] This is a 6–20 rating scale that uses the patient's perception of how hard their body is working. It allows the subjective physical sensations a person experiences during therapy to estimate the amount of work a patient is doing. Therapy should generally be targeted to a goal of a Borg scale of 11 to 14 (or "somewhat hard"). In addition, with the delayed heart rate response to exercise, it is important to incorporate warm-up and cool-down time for all exercise sessions.

## Physical therapy

The PT focuses on mobility and a cardiac rehabilitation program and additionally includes endurance training such

as gait intervals and circuit training. Cardiopulmonary rehabilitation integrates pulmonary hygiene tasks for those patients who have also experienced respiratory failure or were intubated for a prolonged period.

## Occupational therapy

The OT is important to integrate adaptive equipment for patients with limitations due to tremor or hand weakness (i.e., built-up foam handles to increase independence with eating and grooming, long-handled reacher, sock aid, shoe horn, elastic shoelaces). OT can also use energy conservation, pacing strategies, and sternal precautions adherence to help with the safe completion of activities of daily living.

## Speech therapy

The SLP can address any concerns regarding dysphagia, vocal cord pathology, and hypophonia, which can be seen with vocal fold abnormalities. Any neurocognitive impairments can be assessed and treated by the SLP to maximize cognitive capabilities with compensatory strategies and education. Cognitive impairments may have a direct effect on discharge planning and safety.

The entire interdisciplinary rehabilitation team works together to safely transition the patient to the next level of care, including setting up ongoing therapies via home health or in the outpatient setting.

## CONCLUSION

Functional impairments and medical complications such as infections and medication side effects are common after heart transplantation. Many IPR units offer an ideal setting for postoperative transplant recipients to receive therapies to improve functional status while allowing for close medical oversight. Physiatrists must understand the procedure itself and potential medical complications to provide comprehensive and anticipatory care in IPR. A comprehensive rehabilitation program can significantly improve physical function, mobility, and independence for debilitated transplant recipients with a high likelihood of achieving community discharge.

### DISCLOSURE
The authors declare no conflict of interest.

### ORCID
*Leslie Rydberg* https://orcid.org/0000-0001-5817-4861

*Laura Malmut* https://orcid.org/0000-0003-1122-845X

## REFERENCES

1. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics—2012 update: a report from the American Heart Association. *Circulation*. 2012;125:e2-e220.
2. Mancini D, Lietz K. Selection of cardiac transplantation candidates in 2010. *Circulation*. 2010;122(2):173-183.
3. Eickmeyer SM, Barker KD, Sayyad A, Rydberg L. The rehabilitation of patients with advanced heart failure after left ventricular assist device placement: a narrative review. *PM&R*. 2019;11(1):64-75.
4. Stolf NAG. History of heart transplantation: a hard and glorious journey. *Braz J Cardiovasc Surg*. 2017;32(50):423-427.
5. Mehra MR, Canter CE, Hannan MM, et al. The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: a 10-year update. *J Heart Lung Transplant*. 2016;35(1):1-23.
6. Krandsdorf EP, Kobashigawa JA. Chapter 44: heart transplantation. *Heart Failure: A Companion to Braunwald's Heart Disease*. 4th ed. Elsevier; 2020:631-648.
7. Goff RR, Uccellini K, Lindblad K, et al. A change in heart: preliminary results of the US 2018 adult heart allocation revision. *Am J Transplant*. 2020;20(10):2781-2790.
8. Costanzo MR, Dipchand A, Starling R, et al. The International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*. 2010;29:914-956.
9. Goldraich LA, Leitão SAT, Scolari FL, et al. A comprehensive and contemporary review on immunosuppression therapy for heart transplantation. *Curr Pharm Des*. 2020;26(28):3351-3384.
10. Hoffman FM. Outcomes and complications after heart transplantation: a review. *J Cardiovasc Nurs*. 2005;20(5 Suppl):S31-S42. doi:10.1097/00005082-200509001-00005
11. Alba C, Bain E, Ng N, et al. Complications after heart transplantation: hope for the best, but prepare for the worst. *Int J Transplant Res Med*. 2016;2:22. doi:10.23937/2572-4045.1510022
12. Kim HJ, Jung SH, Kim JJ, et al. Early postoperative complications after heart transplantation in adult recipients: Asan medical center experience. *Korean J Thorac Cardiovasc Surg*. 2013;46(6):426-432. doi:10.5090/kjtcs.2013.46.6.426
13. Elboudwarej O, Patel JK, Liou F, et al. Risk of deep vein thrombosis and pulmonary embolism after heart transplantation: clinical outcomes comparing upper extremity deep vein thrombosis and lower extremity deep vein thrombosis. *Clin Transplant*. 2015;29(7):629-635. doi:10.1111/ctr.12566
14. Sakusic A, Rabinstein AA. Neurological complications in patients with heart transplantation. *Semin Neurol*. 2021;41(4):447-452. doi:10.1055/s-0041-1726285
15. Mateen FJ, van de Beek D, Kremers WK, et al. Neuromuscular diseases after cardiac transplantation. *J Heart Lung Transplant*. 2009;28(3):226-230. doi:10.1016/j.healun.2008.12.004
16. Delibasic M, Mohamedali B, Dobrilovic N, Raman J. Pre-transplant depression as a predictor of adherence and morbidities after orthotopic heart transplantation. *J Cardiothorac Surg*. 2017;12(1):62. doi:10.1186/s13019-017-0626-0
17. Havik OE, Sivertsen B, Relbo A, et al. Depressive symptoms and all-cause mortality after heart transplantation. *Transplantation*. 2007;84(1):97-103. doi:10.1097/01.tp.0000268816.90672.a0
18. Bussières LM, Pflugfelder PW, Taylor AW, Noble EG, Kostuk WJ. Changes in skeletal muscle morphology and biochemistry after cardiac transplantation. *Am J Cardiol*. 1997;79(5):630-634. doi:10.1016/s0002-9149(96)00829-6
19. Givertz MM, Hartley LH, Colucci WS. Long-term sequential changes in exercise capacity and chronotropic responsiveness

after cardiac transplantation. *Circulation*. 1997;96(1):232-237. doi:10.1161/01.cir.96.1.232

20. Kavanagh T, Yacoub MH, Mertens DJ, Kennedy J, Campbell RB, Sawyer P. Cardiorespiratory responses to exercise training after orthotopic cardiac transplantation. *Circulation*. 1988;77:162-171.

21. Lord SW, Brady S, Holt ND, Mitchell L, Dark JH, McComb JM. Exercise response after cardiac transplantation: correlation with sympathetic reinnervation. *Heart*. 1996;75:40-43.

22. Marconi C, Marzorati M. Exercise after heart transplantation. *Eur J Appl Physiol*. 2003;90(3–4):250-259. doi:10.1007/s00421-003-0952-x

23. Osada N, Chaitman BR, Donohue TJ, Wolford TL, Stelken AM, Miller LW. Long-term cardiopulmonary exercise performance after heart transplantation. *Am J Cardiol*. 1997;79(4):451-456. doi:10.1016/s0002-9149(96)00785-0

24. Baroud I, Niset G, Vachiery JL, et al. Long-term follow-up of heart transplant patients. *Acta Cardiol*. 1996;51:315.

25. Mampuya WM. Cardiac rehabilitation past, present and future: an overview. *Cardivasc Diagn Ther*. 2012;2(1):38-49.

26. Wenger N, Gilbert C, Skopora M. Cardiac conditioning after myocardial infarction: an early intervention program. *J Cardiac Rehabil*. 1971;2:17-22.

27. Braddom R. *Physical Medicine and Rehabilitation*. Third ed. Saunders Elsevier; 2007.

28. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: an updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Circulation*. 2007;39:1423-1434.

29. Karapolat H, Engin C, Eroglu M, et al. Efficacy of the cardiac rehabilitation program in patients with end-stage heart failure, heart transplant patients, and left ventricular assist device recipients. *Transplant Proc*. 2013;45(9):3381-3385. doi:10.1016/j.transproceed.2013.06.009

30. Bottiger BA, Nicoara A, Snyder LD, et al. Frailty in the end-stage lung disease or heart failure patient: implications for the perioperative transplant clinician. *J Cardiothorac Vasc Anesth*. 2019; 33:1382-1392.

31. Chen S, Lester L, Piper GL, et al. Safety and feasibility of an early mobilization protocol for patients with femoral intra-aortic balloon pumps as bridge to heart transplant. *ASAIO J*. 2022; 68(5):714-720. doi:10.1097/MAT.0000000000001557

32. Floyd S, Craig SW, Topley D, Tullmann D. Evaluation of a progressive mobility protocol in postoperative cardiothoracic surgical patients. *Dimens Crit Care Nurs*. 2016;35(5):277-282. doi:10.1097/DCC.0000000000000197

33. Anderson L, Nguyen TT, Dall CH, Burgess L, Bridges C, Taylor RS. Exercise-based cardiac rehabilitation in heart transplant recipients. *Cochrane Database Syst Rev*. 2017;4(4): CD012264. doi:10.1002/14651858.CD012264.pub2

34. Kobashigawa JA, Leaf DA, Lee N, et al. A controlled trial of exercise rehabilitation after heart transplantation. *N Engl J Med*. 1999;340(4):272-277. doi:10.1056/NEJM199901283400404 (Erratum in: N Engl J Med 1999 Mar 25;340(12):976).

35. Patcai JT, Disotto-Monastero M, Gomez M, Adcock L. Inpatient rehabilitation outcomes in solid organ transplantation: results of a unique partnership between the rehabilitation hospital and the multi-organ transplant unit in an acute hospital. *Open J Ther Rehabil*. 2013;1:52-61.

36. Gupta S, Larsen E, Garg A, et al. Functional effectiveness of inpatient rehabilitation after heart transplantation. *PM&R*. 2016; 8(9):855-859.

37. Shiner CT, Woodbridge G, Skalicky DA, Faux SG. Multidisciplinary inpatient rehabilitation following heart and/or lung transplantation-examining cohort characteristics and clinical outcomes. *PM&R*. 2019;11(8):849-857.

38. Joshi A, Kevorkian C. Rehabilitation after cardiac transplantation. *Am J Phys Med Rehabil*. 1997;76(3):249-254.

39. Cahalin LP, Kinney LaPier T, Shaw DK, Min D. Sternal precautions: is it time for change? Precaution versus restrictions—a review of the literature and recommendations for revision. *Cardiopulm Phys Ther J*. 2011;22(1):5-15.

40. McKenna H, Jones J, Harmon EY. Move in the tube sternal precautions: a retrospective analysis of a single inpatient rehabilitation facility. *Cardiopulm Phys Ther J*. 2022;33(3):108-115.

41. Borg GAV. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc*. 1982;14:377-381.

42. Keteyian S, Ehrman J, Fedel F, Rhoads K. Heart rate-perceived exertion relationship during exercise in orthotopic heart transplant patients. *J Cardiopulm Rehabil*. 1990;10(8): 287-293.