ISHLT consensus document on lung transplantation in patients with connective tissue disease: Part II: Cardiac, surgical, perioperative, operative, and post-operative challenges and management statements

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Patients with connective tissue disease (CTD) present unique surgical, perioperative, operative, and postoperative challenges related to the often underlying severe pulmonary hypertension and right ventricular dysfunction. The International Society for Heart and Lung Transplantation-supported consensus document on lung transplantation in patients with CTD standardization addresses the surgical challenges and relevant cardiac involvement in the perioperative, operative, and postoperative management in patients with CTD.

J Heart Lung Transplant 2021;40:1267–1278
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and supported by the International Society for Lung and Heart Transplantation, on cardiac, surgical, perioperative, operative, and post-operative challenges and management in patients with connective tissue disease (CTD).

Patients with CTD present unique surgical, perioperative, operative, and postoperative challenges related to the often underlying severe pulmonary hypertension and right ventricular dysfunction. The goals of this consensus paper are to address the surgical challenges, and relevant cardiac involvement in the perioperative, operative, and postoperative management in patients with CTD.

Methodology

As detailed in Part I of this consensus document, the strength of the agreement was based on Delphi method voting sent to the workforce members. The voting range for each participant was from 0 to 9, with 0 as no agreement with the statement and 8 to 9 as high agreement. A consensus agreement was considered to be present when ≥80% of workforce members voted 8 or higher. The final statement was done based on the results of the team’s survey voting and recommendations. A comprehensive literature search and review was performed to answer the identified questions based on the published evidence, and to provide guidance based on prevailing expert knowledge and experience.

Relevant cardiac involvement in the perioperative, operative, and postoperative management in patients with connective tissue diseases

Epidemiology and pathogenesis

Estimating the prevalence of cardiac involvement in CTD across subgroups is challenging, given a discordance between clinically evident disease and autopsy reports.2,3 The most notable association is for Group 1 pulmonary arterial hypertension (PAH), especially in those with limited cutaneous scleroderma (lSSc),2,7 which is well described in the guidelines of the world health organization/World Symposium on Pulmonary Hypertension (WSPH). Beyond this, patients with CTD are at risk for developing other types of pulmonary hypertension (PH), including left heart disease, interstitial lung disease, or chronic thromboembolic PH (CTEPH).8-11 Regarding PAH, CTD-associated PAH (CTD-PAH) accounts for over half of the cases of nonidiopathic PAH and has a worse survival, with the highest risk subtype being CTD-PAH from systemic sclerosis (SSc).12,13 The best estimate of PAH prevalence in SSc comes from the Detection of PAH in SSc (DETECT) study, where the prevalence of PAH was estimated at 19%.5 PH in the setting of systemic lupus erythematosus (SLE) and mixed connective tissue disease (MCTD) is less common than SSc-PH (CTD-PAH) accounts for over half of the cases of nonidiopathic PAH and has a worse survival, with the highest risk subtype being CTD-PAH from systemic sclerosis (SSc).12,13 The majority of SSc patients have such abnormalities as detected by CMRI, with a recent cross-sectional study reporting an abnormal CMRI in 43% of patients with SLE,33,34 including the presence of stress perfusion deficits, pericardial effusion, and late gadolinium enhancement. These findings didn’t correlate with the patient’s degree of clinical symptoms.34

Several studies in the SSc population have shown that while resting hemodynamics may be consistent with PAH, that is, low pulmonary artery wedge pressure or left ventricular end-diastolic pressure, performing a saline challenge or exercise can unmask occult left heart disease.5,35,36

While cardiac involvement in patients with CTD contributes significantly to their morbidity and mortality, limited data exist about routine screening for these entities.26,27

Diagnosis

As noted above, PH is often a driver or a significant comorbid condition in a patient with CTD who is being considered for a lung transplant (LTx) or heart-lung transplant (HLTx). According to the most recent European Society of Cardiology (ESC)/European Respiratory Society (ERS) guidelines, annual screening transethoric echocardiography (TTE), along with pulmonary function testing (PFT) with diffusing capacity of the lungs for carbon monoxide (DLCO) and serum biomarkers (i.e., NT-proBNP) is recommended for asymptomatic SSc-spectrum disease patients.28 In conjunction with the above, the adoption of the DETECT algorithm has also been suggested, whereby a score of weighted variables is generated to aid in the triage of patients for right heart catheterization.5

TTE serves as an important diagnostic modality across the broad spectrum of cardiopulmonary disease in patients with CTD. TTE is the initial diagnostic test of choice to assess myocardial systolic and heart failure with preserved ejection fraction (HFPeF) as well as valvular and pericardial dysfunction. HFPeF is prevalent in approximately 20% of patients and is associated with high mortality.29,30 Cardiovascular magnetic resonance imaging (CMRI) enables assessment of both biventricular function and evidence of pulmonary vascular disease and identification of myocardial fibrosis and inflammation.31,32 The majority of SSc patients have such abnormalities as detected by CMRI, with a recent cross-sectional study reporting an abnormal CMRI in 43% of patients with SLE,33,34 including the presence of stress perfusion deficits, pericardial effusion, and late gadolinium enhancement. These findings didn’t correlate with the patient’s degree of clinical symptoms.34

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In addition to the hemodynamic considerations, chest imaging including computed tomography (CT) scan of the chest, ventilation-perfusion scan, PFTs with DLCO are essential to clarifying the clinical classification of underlying PH (i.e., WSPH group 3 or lung disease-associated PH, and WSPH Group 4, or CTEPH, respectively).5,8,37,38 Additionally, pulmonary veno-occlusive disease (PVOD) and pulmonary capillary hemangiomatosis are increasingly appreciated in the SSc population and may explain worse prognosis and response to PH therapy.8,39,40 PVOD can be difficult to distinguish from PAH. The typical histological diagnosis shows diffuse involvement of venules and septal veins by intimal sclerosis, resulting in luminal narrowing or obliteration. The hallmark findings on high-resolution CT chest include mediastinal lymph node enlargement, interlobular septal thickening, enlarged pulmonary arteries (PA’s), normal caliber pulmonary veins, bilateral pleural
effusions, and centrilobular ground-glass opacities. Lastly, not all PH in CTD is PAH, and thus the etiology of PH needs to be well-elucidated as the treatment differs.

**Pulmonary hypertension and right ventricle dysfunction**

While severe PAH refractory to medical therapy is an indication for LTx, an elevated mean pulmonary arterial pressure has been associated with a higher risk of primary graft dysfunction (PGD) postlung transplantation, as well as right ventricle (RV) dysfunction. Patients with a diagnosis of PVOD require a prompt transplant evaluation, given the rapid progression of the disease and the absence of effective medical therapy.

In SSc-PAH, RV dysfunction occurs due to chronic pressure overload and SSc-related intrinsic RV cardiomyopathy. When compared to idiopathic pulmonary arterial hypertension (iPAH), RV contractile reserve is depressed in SSc-PAH at rest. Intrinsic RV dysfunction historically has been underappreciated in SSc patients without PH; however, with the recent advances of newer echocardiographic and CMRI techniques, it has gained recognition as a cause for worse outcomes and potential target of intervention in SSc-PAH. Most of the literature on CTD-PAH comes from studies performed on patients with SSc-PAH. SSc-PAH has worse survival than iPAH, even with less severely compromised right heart hemodynamics. In the US REVEAL registry, 5-year survival in newly diagnosed SSc-PAH was 39.6% compared to 68% in iPAH. SSc-PAH has worse survival compared to other CTDs such as SLE and MCTD associated-PAH, which have similar survival to iPAH.

**Left heart failure**

LV diastolic dysfunction or HFpEF is particularly common in SSc, with a reported prevalence of 20% to 35% and is associated with increased mortality. Evaluation and treatment for HFpEF is challenging, as LV ejection fraction (EF) is normal and dyspnea is masked by symptoms of the underlying lung disease. Patients with CTD, particularly those with SLE, SSc, and rheumatoid arthritis, have a higher incidence of valvular disease, myocardial ischemia, and microvascular endothelial disease, increasing the risk for HFpEF.

The presence of HFrEF with an EF < 40% is usually an absolute contraindication for LTx alone, and those patients may benefit from combined HLTx, particularly when associated with severe or fixed PH. Patients with CTD, particularly those with SLE or inflammatory myopathies (Polymyositis/Dermatomyositis), are at a higher risk of pericarditis and myocarditis, which can lead to HFrEF. CMRI is a very helpful tool to identify cardiac involvement, myocardial enhancement, and fibrosis. Patients with fulminant myocarditis should be treated for cardiogenic shock with inotropes while advanced HF therapies, like heart transplantation and ventricular assist devices (VADs) are reserved for patients that fail maximal medical therapy.

**Surgical, anesthesia, and ICU management in lung and heart-lung transplantation in patients with CTD**

**Selection of transplant procedure, support strategies as a bridge for transplant, surgical planning and conduct, and intraoperative management: discussions, recommendations, and agreement strength**

Patients with CTD present unique surgical challenges to LTx and HLTx and outcomes rely heavily on disease and patient-specific factors. Surgical planning and conduct, and postoperative management (Figure 1) are key components for a successful operation and adequate long-term outcomes. This section cover these aspects to clarify common practices in successful high-volume surgical programs. The consensus group acknowledges that the paucity of evidence precludes any strong conclusions regarding the best surgical transplant selection, extracorporeal life support (ECLS) strategies, anesthesia, and ICU management in the perioperative and post-transplant period in patients with CTD. The willingness to accept any risk may vary between centers, depending on local expertise.

**Discussion: Selection of transplant procedure**

Bilateral lung transplant (BLTx) is most frequently utilized (up to 85% of the patients), with the theoretical benefit of improved survival, postoperative RV function and better reserve to compensate for any decline in lung function due to chronic lung allograft dysfunction over time. Due to the lack of definite evidence to support BLTx exclusively, single lung transplantation continues to be offered successfully in some patients with CTD in the absence of secondary pulmonary hypertension when the clinical condition requires a shorter waiting time on the list.

Patients with severe structural or cardiac functional abnormalities or dysfunction, not likely to improve with normalization of pulmonary pressures, in conjunction with intrinsic lung disease or severe PAH, are considered for HLTx. This decision must be balanced with the likelihood of RV recovery after BLTx in the absence of objective assessment of infarcts or fibrotic changes of the RV. Importantly, the presence of moderate or severe LV dysfunction and/or profound RV dilatation and dysfunction on high doses of inotropic support should be considered high-risk conditions for lung transplantation alone.

**Discussion: Support strategies as a bridge to lung and heart-lung transplantation**

Patients with CTD can present with rapid clinical deterioration while awaiting transplantation resulting in progressive lung failure, and non-invasive means of supplemental support...
oxygen delivery alone may be ineffective. Veno-arterial extracorporeal oxygenation (VA-ECMO) provides both preoperative cardiovascular support and is a useful adjunct for continued intraoperative and postoperative support. Although ECLS has been used as a bridge to LTx in patients with CTD, the experience is limited, and a detailed analysis of outcomes in this setting is lacking. Even though ECLS bridge to transplant is becoming increasingly common practice, transplant center volume and ECLS expertise improve success rates pre-and post-operatively.

**Recommendations:** Early consideration should be entertained for placement if feasible of an awake venovenous extracorporeal oxygenation (VV-ECMO) system, via either an open or percutaneous technique. This may avoid the need for invasive mechanical ventilation or even tracheostomy. If prolonged invasive mechanical ventilation cannot be avoided, then there should be consideration for early tracheostomy. VV-ECMO may be less effective or inadequate support in patients with severe pulmonary hypertension and right heart dysfunction. In some patients this necessitates conversion of VV- to VA-ECMO or placement of VA-ECMO as the initial therapy.

The team consensus statement agreement strength on these recommendations was 83.33%.

**Discussion: Surgical planning and conduct**

There are several considerations in developing an optimized surgical plan (Figure 1).

Understanding the degree of RV dysfunction, pulmonary hypertension, and donor and recipient relative chest sizes are critical. This information determines optimum anesthesia techniques, type of intra- and post-operative and the likelihood of other required supportive measures.

The induction of anesthesia is an important step in these patients. The failing right ventricle is extremely sensitive to fluctuations in pre-load or increases in afterload. Principles of anesthetic management in the presence of pulmonary hypertension are essential to prevent hemodynamic collapse. In this case VA-ECMO provides both preoperative cardiovascular support and is a useful adjunct for continued intraoperative and postoperative support includes avoiding increasing pulmonary vascular resistance (PVR), maintaining pre-load while avoiding fluid overload, reducing RV afterload, and reducing tachycardia. The goal is to maintain forward flow and avoiding precipitating rapid hemodynamic decompensation.

**Recommendations:** The important considerations during the surgical LTx planning in patients with CTD includes understanding of the degree of RV dysfunction, PH, and donor and recipient relative chest sizes to determine the optimum anesthesia techniques, type of intra- and postoperative and the likelihood of other required supportive measures. The induction and management of anesthesia is also an important step and includes avoiding increasing PVR and maintaining pre-load while avoiding fluid overload, reducing RV afterload, with the goal is to maintain forward flow and avoiding precipitating rapid hemodynamic decompensation. The presence of a pulmonary artery catheter is essential to monitor pulmonary pressures, and CO throughout the procedure, and an extra right internal jugular venous access should be obtained in case postoperative VV-ECMO support is considered. Femoral access (arterial and venous) may be necessary soon after or even prior to induction in case a rapid deterioration is expected to initiate extracorporeal circulation or ECMO.

The team consensus statement agreement strength on these recommendations was 90.38%.

**Intraoperative care and anesthesia challenges: Decisions, recommendations, and agreement strength**

**Discussion: Vascular access: Challenges and concerns**

Patients with CTD may be at increased risk of vascular complications including, pseudoaneurysms, hematomas, arteriovenous fistulas, and limb ischemia. Pre-existing vasculopathy related to Raynaud’s phenomenon creates a higher risk of complications related to arterial line placement such as digital embolization or hand ischemia. Given this, it has been recommended to avoid radial artery cannulation in this population. However, there are no consistent data regarding the optimal arterial line site. Modification of the usual intraoperative monitoring techniques should also be considered given the associated Raynaud’s phenomenon using topical nitroglycerin as tolerated, warm gloves, warm blankets, and limiting the duration of use of radial arterial lines or consideration of femoral or brachial arterial lines based on institutional protocols may be preferred.

The working group recommends close monitoring for signs of digital ischemia and prompt removal of the arterial line if there is suspicion of early ischemia to prevent digital necrosis and the need for amputation.

Alterations of the skin and neck stiffness in patient with SSc increases the difficulty of skin nicking and dilation for central venous cannulation. Experienced proceduralists and ultrasound guidance results in fewer mechanical complications. Randomized controlled trials report fewer insertion attempts with the use of ultrasound for both internal jugular and subclavian vein central lines. The group recommends avoiding the subclavian site for large bore central cannulation to prevent venous stenosis, a factor that may limit successful arteriovenous fistulas in cases of prolonged renal failure.

**Discussion: Intubation: Challenges and strategies**

The combination of microstomia with advanced lung disease poses a unique challenge for airway management. Also, patients with connective tissue disorders may have decreased salivary gland flow and tongue fibrosis. Having extra time to maneuver and secure the airway is unlikely as these patients also have parenchymal lung disease and will
suffer rapid oxygen desaturation. Early evaluation of micro-
stoma by the anesthesiology team is essential, and a diffi-
cult airway cart should be located near the patient. We
recommend the treatment team to have both a detailed pri-
mary plan and a backup plan for securing the airway. We
also recommend an awake technique, if possible. The com-
bination of high-flow nasal oxygen therapy (e.g., Vapo-
therm, Exeter, NH) with fiberoptic bronchoscopic
intubation is often utilized. A final consideration is the
maintenance of appropriate minute ventilation. Patients
with interstitial lung disease commonly have high pulmo-
nary artery pressures and impaired right ventricular
function. Any increase in CO₂ retention may precipitate
and subsequent cardiopulmonary collapse.

Discussion: Ventilation management
intraoperative

In general, CTD patients undergoing transplantation for
fibrotic lung disease have restrictive pulmonary physiology. If transplantation is performed without ECLS support, the
ventilator strategy will need to account for the poor lung
compliance. Optimal ventilator settings include relatively
low tidal volumes and a high respiratory rate. Following perfusion of the first allograft, efforts should be made to revert to a lung-protective strategy to avoid ventilator-induced allograft lung injury. Intra-operative FiO2 should be minimized to maintain peripheral arterial oxygen saturation (SPO2) > 90% and arterial oxygen tension (PaO2) > 60 mm Hg to avoid potential detrimental effects of hyperoxemia and oxidative stress.75

The decision of the first lung to be transplanted is made based on the degree of ventilation and perfusion contribution of each lung (transplanting the lung contributing less) or on anatomical consideration where the left lung is frequently transplanted first since it will be the most difficult to implant and require heart retraction to expose the retracted left hilum. After implantation, if ECLS or cardio-pulmonary bypass (CPB) are used, we encourage some pulsatility in the pulmonary artery (PA) waveform to ensure adequate lung perfusion. Following implantation, surgical sizing and staged closure or post-operative mechanical circulatory support (MCS), is considered based on hemodynamics and domain issues. A small-bore enteral tube is also placed to ensure early postoperative enteral feeding.

Considerations during lung transplantation: Decisions, recommendations, and agreement strength

Discussion: Surgical approach and cardio-pulmonary support

The ideal surgical approach has not been determined in patients with CTD. Bilateral thoraco-sternotomy (Clamshell) or bilateral sequential thoracotomies are appropriate approaches based on the centers’ experience.

In a recent study in patients undergoing LTx for SSC, 56% of the patients underwent LTx with the use of extracorporeal circulatory support vs 32% in the control group with pulmonary fibrosis.76 Recent studies favor ECLS over standard CPB, although these benefits have not been specifically studied in the CTD population. The advantages of intra-operative VA-ECMO include reduced bleeding complications, less primary graft dysfunction, and diminished renal dysfunction compared to CPB.61,62 Specifically, in patients with SSc, central aortic cannulation (aorta to the right atrium or aorta to right femoral vein) is the preferred approach to prevent ischemic limb complications. If ECMO is needed into the postoperative period due to severe primary graft dysfunction, converting to peripheral VV-ECMO or maintaining the patient on central VA-ECMO configuration depending on the physiological needs are the best support choices in this population.

The team consensus agreement strength on these recommendations was 90.5%.

Recommendations: Special attention should be considered while using TEE in patients with CTD and underlying esophageal disease to avoid any esophageal injury. The use of smaller caliber probes is recommended whenever available. It is unclear what the degree of additional risk is in patients with CTD.

The team consensus agreement strength on these recommendations was 88.46%.

Discussion: Hemodynamic monitoring and support

At the end of the procedure, the use of vasoconstrictors should be minimized to avoid peripheral and coronary spasm, and optimal evaluation of fluid status and CO using a TEE and a Swan-Ganz catheter can aid in the immediate postoperative management. Awareness should be taken for those patients with a history of Raynaud’s phenomenon who develop postoperative chest pain, as they are prone to coronary arterial spasm, which could be lethal if not promptly disrupted.15,18

Following LTx, SSc-specific cardiac complications can include: (1) LV diastolic dysfunction60 and PH/SSc-related

| Table 1 Absolute and Relative Contraindications to Transesophageal Echocardiogram |
|-----------------|-------------------------------|
| Absolute        | Relative                      |
| Perforated viscus | History of head, neck or mediastinal radiation |
| Esophageal stricture or tumor | History of upper gastrointestinal surgery |
| Esophageal diverticulum or laceration | Recent upper gastrointestinal bleed |
| Active upper gastrointestinal bleed | Barret’s esophagus or dysphagia |
|                 | Restricted neck mobility     |
|                 | Symptomatic hiatal hernia    |
|                 | Esophageal varices           |
|                 | Coagulopathy                |
|                 | Active esophagitis or peptic ulcer disease |

Since many of these patients have some degree of right ventricular dysfunction, intraoperative use of TEE is useful.76 Complications associated with TEE probe insertion in the general population include mortality (<0.01%-0.02%), major bleeding (<0.01%), and esophageal perforation (<0.01%).79,80 Patients should be screened for any absolute or relative contraindications to TEE placement listed in Table 1. TEE in patients with a known relative contraindication such as esophagitis or esophageal varices can be successfully performed.81,82

Recommendations: It is important to keep in mind that small chest cavities, a common finding in patients with CTD, may lead to limited surgical exposure, and incisions providing the optimal surgical field are preferred. During the transplant procedure, cardio-pulmonary support is frequently required due to high pulmonary artery pressures and small chest cavities requiring significant cardiac retraction. In patients with SSc, central aortic cannulation (aorta to the right atrium or aorta to right femoral vein) is the preferred approach to prevent ischemic limb complications. If ECMO is needed into the postoperative period due to severe primary graft dysfunction, converting to peripheral VV-ECMO or maintaining the patient on central VA-ECMO configuration depending on the physiological needs are the best support choices in this population.
RV dysfunction, (2) PAH-related post-lung transplantation LV systolic dysfunction, (3) supraventricular and ventricular tachyarrhythmias, and less commonly (4) bradyarrhythmia or (5) unsuspected constrictive pericarditis.27

**Recommendations:** Vasodeconstrictors should be minimized in patients with CTD to avoid peripheral and coronary spasm, and optimizing evaluation of fluid status and CO is warranted. Hemodynamic monitoring together with blood products and fluid administration and avoidance of inotropes and vasoconstrictors at high doses are preferable post-operative resuscitative techniques that could have a deleterious effect on distal skin perfusion and renal function. Special attention should be taken for those patients with a history of Raynaud’s phenomenon who develop post-operative chest pain. Limiting postoperative bleeding with early re-operations and liberal use of “open chest strategy” in patients with a small chest, or a significant coagulopathy or in patients with significant RV or LV dysfunction are critical to minimize peripheral and systemic effects of perfusion insufficiencies frequently compromised in patient with CTD. The liberal use of early postoperative VA-ECMO in cases of severe post-operative RV dysfunction or VV-ECMO in patients with early signs of PGD should be considered.

The team consensus statement agreement strength on these recommendations was 90.56%.

**Management of primary graft dysfunction, ventilation and weaning, hemodynamics, and renal failure prevention: Discussions, recommendations and agreement strength**

**Discussion: Primary graft dysfunction management**

The reported incidence of Grade 3 PGD varies in the medical literature but is estimated at approximately 30% early after transplant and 15-20% at 48 to 72 hours post-transplant.82,84 The incidence of PGD in LTx recipients with CTD has not been specifically studied. However, given the high prevalence of PAH in CTD and the association between PAH and PGD, it is likely that CTD patients are at higher risk for PGD.83 The impact of PGD on both short and long-term outcomes is well established, and has been associated with increased duration of mechanical ventilation, ICU and hospital length of stay, increased resource utilization and hospital costs.84,85

**Discussion: Postoperative ventilator management and ventilator weaning**

Consensus regarding the optimal ventilator strategy following lung transplant is lacking. A single randomized controlled trial of thirty patients comparing “open-lung protective ventilation” to a control arm is the only prospective study performed to date.85 Given this, no consensus regarding the optimal ventilator strategy following lung transplant exists. As mentioned above, the use of lung-protective ventilator strategies has been extrapolated from our knowledge of acute respiratory distress syndrome (ARDS) to the care of lung transplant recipients. An international survey of early postoperative management found that a lung-protective strategy is commonly employed by lung transplant centers, with 65% of respondents using tidal volumes ≤ 6 ml/kg of ideal body weight (IBW) and all respondents using ≤ 8 ml/kg of IBW.35 In these patients, the traditional parameter of rapid-shallow breathing index (RSBI) utilized by many clinicians as a tool to assess readiness for extubation may suggest patients are not ready to liberate from mechanical ventilation.86 Further studies on the predictors of extubation failure in transplant recipients are warranted.

**Recommendations:** A lung-protective strategy using tidal volumes ≤ 6 ml/kg of ideal body weight (IBW) is recommended. IBW should be calculated using the donor rather than the recipient’s height. A spontaneous breathing trial can be performed in patients with adequate oxygenation and ventilation in lung-protective settings. Anecdotally, many patients with restrictive lung disease before transplant seem to maintain a pattern of rapid shallow breathing in the early post-transplant period. Patients who maintain adequate oxygenation and ventilation without signs of distress when undergoing a spontaneous breathing trial should be considered for a trial of extubation regardless of RSBI.

The team consensus agreement strength on these recommendations was 84.90%
baseline blood pressure. Norepinephrine and vasopressin are the most commonly selected vasopressors. RV dysfunction deserves special attention as PH is common in CTD patients. The presence of PH prior to transplantation does not predict the need for significant RV support post-operatively, as the pulmonary vascular resistance is substantially reduced following the procedure. Conversely, overly aggressive support of the RV may lead to the development of PGD or pulmonary edema by unmasking LV dysfunction or increasing RV output.84 Inhaled nitric oxide (iNO) or inhaled epoprostenol are effective vasodilators in the setting of persistent PH associated with reduced CO. Hypoxemia and hypercapnia should be corrected together with diuresis to reduce right atrial pressure and correct RV distention. Inotropes, such as dobutamine or milrinone, can also be used to reduce RV afterload and improve RV contractility. If significant RV dysfunction persists despite these measures, extracorporeal support can be considered.

**Recommendations:** Clinicians should consider the patient’s pre-transplantation hemodynamics, particularly the presence of pulmonary hypertension when developing a post-operative management plan. The primary goal of hemodynamic management is to ensure adequate end-organ perfusion while avoiding overly aggressive support that may be detrimental to the allograft. A conservative fluid strategy is typically recommended following LTx. However, volume or appropriate resuscitation with blood products should not be withheld at the expense of end-organ hypoperfusion in the setting of hypovolemic or hemorrhagic shock. Inotropes can be utilized if patients have an inadequate cardiac output despite adequate preload due to LV or RV dysfunction. RV dysfunction deserves special attention as PH is common in CTD patients. Inhaled epoprostenol or iNO are effective vasodilators in the setting of persistent PH associated with reduced CO. If significant RV dysfunction persists despite these measures, extracorporeal support can be considered.

The team consensus agreement strength on these recommendations was 87.75%.

**Discussion: Renal failure prevention strategies and management**

Renal failure is a relatively common complication after LTx and HLTx that has both short and long-term consequences. The risk of transient or persistent acute kidney injury (AKI) early after transplantation can be as high as 68%.90 Calcineurin inhibitors toxicity is associated with both a risk for AKI early after transplantation and the development of chronic kidney disease and the need for dialysis in longer-term survivors. Patients requiring hemodialysis after transplant have a high mortality rate.92 Other potential risk factors for AKI post-transplant are severe pre-transplant PH and cardio-renal syndrome or low glomerular filtration rate and pre- or post-transplant ECMO requirement.90,91

Scleroderma renal crisis (SRC) can occur in up to 5% to 10% of SSc patients.93-95 Patients with CTD, particularly SSc, are more at risk for developing AKI post-transplant. Raynaud’s phenomenon and systemic vasospasm in SSc outside of the peripheral circulation might be playing a role in the pathogenesis of SRC and AKI post-transplant.95 The use of high-glucocorticoids, (>15 mg/day of prednisone or equivalent) is an independent risk factor for developing SRC.96,97 There have also been reports of patients developing hypertensive AKI with the use of cyclosporine.98

**Recommendations:** The group recommendations for renal protection post-transplantation in patients with CTD are: optimize low calcineurin inhibitors goal levels, avoid dehydration, nonsteroidal anti-inflammatory medications, and hypotension. Although scleroderma renal crisis is rare after transplant, the corticosteroid maintenance dose should be reduced to the minimal amount possible.

Team consensus agreement strength on these recommendations was 77.77% indicating poor agreement on renal preservation strategies.

**Summary and future recommendations**

Cardiothoracic transplantation in CTD recipients requires a comprehensive knowledge of the extrapulmonary manifestations of the particular disease states. The evaluation and the management of the extrapulmonary manifestations are critical to the care of this patient population compared to other patients undergoing lung transplantation since these conditions require special management and interventions both early and later after transplantation. In addition, CTD patients may be maintained on a complex biologic immunosuppressive regimen before transplantation. Although only a limited amount of data exists in the literature to support the use of many of these agents in this patient population before discontinuation of these agents should carefully take into account a risk-benefit analysis. Therefore, a multidisciplinary team must be involved early in the management of these patients during the evaluation phase and throughout the subsequent phases of transplantation.

In the future, with gained knowledge through clinical experience, a more refined approach to the management of the biologic regimen and the extrapulmonary manifestations including management of the gastrointestinal complications will be more standardized.

**Disclosure statement**

No specific funding was available for this project. Each workforce member disclosure their conflict of interest. The funding sources for each workforce member had no role in study design, data collection, data analysis, or writing of the report.

We thank Mrs Megan Barrett for providing administrative support and for helping with the preparation and distribution of the surveys used for this project.

We also thank the expert reviewers Dr. Jason Christie, Dr. Joseph Pilewski, and Dr. Paul Corris for their input.
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