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Top Ten Tips Palliative Care Clinicians Should Know About Solid Organ Transplantation

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Abstract

Solid organ transplantation (SOT) is a life-saving procedure for people with end-stage organ failure. However, patients experience significant symptom burden, complex decision making, morbidity, and mortality during both pre- and post-transplant periods. Palliative care (PC) is well suited and historically underdelivered for the transplant population. This article, written by a team of transplant specialists (surgeons, cardiologists, nephrologists, hepatologists, and pulmonologists), PC clinicians, and an ethics specialist, shares 10 high-yield tips for PC clinicians to consider when caring for SOT patients.

Keywords: allograft dysfunction; end-stage organ failure; palliative care; physician–patient communication; solid organ transplantation; symptom burden

Introduction

Solid organ transplantation (SOT) improves survival and quality of life (QoL) for patients with end-stage organ failure. However, patients with SOT experience significant morbidity and mortality before and after transplant, effectively exchanging one set of health limitations for another, and face challenges highly relevant to palliative care (PC) clinicians.

Pretransplant care involves complex coping and nuanced decision making due to heightened acuity, uncertain clinical courses of often comorbid serious illnesses, and stressful processes for distributing limited organs. In the post-transplant period, care is complicated by system pressures such as transplant program evaluation and unique physician–donor–recipient–caregiver relationship dynamics.[1] In addition, chronic allograft dysfunction is common, and

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Table 1. Solid Organ Transplant Metrics and Clinical Burden Pre- and Post-Transplant

Transplant organ	*Pretransplant bridge therapy*	*Transplant type*	*1- and 5-year post-transplant patient survival*	*Signs and symptoms of chronic allograft dysfunction*	*Success metrics*	*Common post-transplant complications*
Kidney	Hemodialysis	Deceased donor kidney transplant	95%–98% (1 year)	Chronic kidney disease	Off dialysis	Rejection, infection, cardiovascular complications, malignancy
	Peritoneal dialysis	Living donor kidney transplant	80%–85% (5 years)	Fluid overload, electrolyte abnormalities, fatigue, pruritis, restless leg		
	Conservative kidney management					
Liver	None	Deceased donor liver transplant	85%–90% (1 year)	Chronic liver disease	Resolution of liver failure	
		Living donor liver transplant	70%–75% (5 years)			
Heart	Mechanical support (LVAD, IABP)	Deceased donor heart transplant	85%–90% (1 year)	Heart failure	Off mechanical or inotrope support	
	Inotrope therapy		~75% (5 years)	Fluid overload		
Lung	Mechanical respiratory support	Deceased donor lung transplant	75%–80% (1 year)	Chronic lung allograft dysfunction	Off oxygen or ventilator support	
	ECMO	Living donor lung transplant	50%–55% (5 years)	Dyspnea		

ECMO, extracorporeal membrane oxygenation; IABP; intra-aortic balloon pump; LVAD; left ventricular assist device.

patients' needs change after transplant as they experience significant symptom burdens (Table 1) and communication needs.

Together, the unique medical, policy, and interpersonal dynamics of SOT require longitudinal and collaborative relationships to prepare for uncertain timing of complications and graft dysfunction. Despite multifaceted PC needs in SOT candidates and recipients, these patients tend to receive PC less frequently and often receive intensive care at end of life (EoL).[2] However, in a number of ways, the missions and passions of SOT and PC teams align.

This article aims to discuss some of the most important topics that PC clinicians should consider when providing care with transplant teams for SOT candidates and recipients. These 10 tips were written by a team of PC and transplant clinicians specializing in surgery, nephrology, hepatology, cardiology, and pulmonology, and ethics. Although the article is intended for an audience of PC clinicians, it is applicable to clinicians of all specialties who are caring for patients before and after SOT.

Tip 1: Patients and Their Transplant Teams Experience Obligations to the Organ Donor and Their Families; Grief, Frustration, and Remorse About the Loss of an Organ Graft and Subsequent Organ Failure May Complicate Efforts to Support Goal Concordant Therapy

Patients suffering end-organ failure often spend months or years with declining health on a waiting list. For these patients, transplantation offers a life free from supportive therapies such as dialysis or a left ventricular assist device (LVAD) and recurrent hospitalizations. Recipients regularly develop a sense of interconnectedness with their donor and reflect on their donor's generosity,[3] prompting a range of emotions after transplantation including gratitude, joy, anguish, and accountability. This indebtedness to the donor, despite being impossible to directly repay, may motivate recipients to develop a relationship with their donor's family.[4]

These relationships can be mutually beneficial and simultaneously burdensome for recipients with expectations of gratitude and sharing of the donor family's grief. When faced with loss of an organ graft, transplant recipients, in addition to having to relive the experience of end-organ illness, can also experience a failure to fulfill a perceived obligation to the donor.[5]

Transplant teams also recognize the essential role of organ donors and families. During organ recovery, surgical teams honor families at their darkest moment, and later connect with them at recognition ceremonies where they recount the positive impact of organ donation for donor and family.[6,7] Although transplant teams have a duty to respect the needs and priorities of the organ recipient, they have borne witness to and feel protective of the donor's gift. In incorporating PC for patients whose transplanted organ is failing, especially soon after transplant, the team's dual loyalties can be difficult to navigate when the goals of EoL are viewed as in conflict with their donor-honoring objectives.[8]

Tip 2: Patients with End-Stage Organ Disease Often Want, and Can Benefit, from Advance Care Planning and Goals-of-Care Conversations, which Require Clear, Complex, and Nuanced Communication and Partnership with Transplant Clinicians

Despite patient readiness to engage with advance care planning (ACP) and the high risk of hospitalization, intensive care, and death among patients with end-stage organ disease, <10% discuss ACP with their clinicians before transplant evaluation.[9–11] Early ACP can clarify patient preferences and goals before a need for urgent decision making.[12] ACP supports shared decision making and patient autonomy, which is important given the profound QoL implications and life-long care requirements transplant imposes.

Prognostic discussions are associated with more realistic patient expectations and have not been shown to harm patients emotionally or undermine patient–physician relationships.[11] ACP may lessen regret, reduce anxiety and depression, and improve the quality of EoL care.[13–15] For caregivers, ACP may reduce decision-making burden, especially for families of patients with end-stage liver disease (ESLD) and end-stage renal disease who frequently experience cognitive impairment and may require surrogate decision making.[16]

Partnership, trust, and clear communication between transplant and PC clinicians are essential to supporting patients pre- and post-transplantation. Role ambiguity, full code requirement for transplant candidates, time constraints, pressure related to clinical outcomes, and lack of awareness of the benefits of ACP represent barriers to ACP engagement among transplant clinicians.[17–20] Inclusive accessible materials to assist with decision making are critical, as low EoL-specific health literacy poses a challenge for patients with organ failure.[21]

Studies have also found pervasive racial and ethnic disparities in ACP and PC utilization among patients of color and non-native English speakers in ACP.[22] Providing culturally sensitive care and fostering partnerships with trusted community leaders, such as faith organizations, and with the transplant community may be crucial.

Tip 3: Transplant Programs' Incentives, with Outcomes Assessment and Payment Based on One-Year Survival, Creates a "Surgical and Medical Buy-In" for Organ Recipients and May Lead to Unintended Consequences and Conflict Over Continuation of Life-Sustaining Treatment

Although the Centers for Medicare and Medicaid Services has deemphasized one-year survival in transplant program assessment, private payors still benchmark one-year survival.[23] In addition, the Scientific Registry of Transplant Recipients provides a publicly available ''five tier'' program assessment that emphasizes one-year survival.[24] At-risk programs are more likely to discard marginal organs, less willing to consider higher risk candidates, more likely to inactivate the sickest candidates, and, at least in lung transplantation, more likely to continue life-sustaining treatment until after the one-year mark.[25,26]

As a result of the one-year survival benchmark, patients, families, and nontransplant health care professionals may worry that transplant team recommendations do not focus solely on patient health and well-being, particularly for recipients with prolonged hospital stays or multiple transplant-related complications.[27–29] In addition, the one-year survival benchmark contributes to transplant consent being conceptualized according to ''surgical and medical buy-in.''[30] In this model, patients interpret their consent to include not just the procedure itself but also ongoing intensive management without a clearly defined outcome. This can lead to a misalignment of patients' and transplant teams' goals in the postoperative period, particularly in the face of unexpected complications.

Especially among transplant recipients who experience graft failure, prior expectations that patients have committed to all measures after transplantation may undermine relationships and patient autonomy. Open and bidirectional discussion of risks, benefits, and goals of transplant as they pertain not just to survival but also to QoL, starting in the pretransplant setting and continuing after surgery, can help to enhance trust and optimize post-transplant outcomes and patient satisfaction.

Tip 4: For Patients with Advanced Heart Disease, Inotropic Support and LVADs Afford Survival and QoL Benefits but Come with Potential Tradeoffs

Palliative intravenous (IV) inotropes in advanced heart failure (HF) improve patients' New York Heart Association (NYHA) functional class without improving survival (Level of Evidence class IIb American College of Cardiology/American Heart Association).[31,32] However, IV inotropes increase the risk of mortality, hospitalization, central-line infection, and implanted cardioverter defibrillator shocks. Additional studies highlight IV inotrope-specific risks of medication tachyphylaxis, persistence of HF-related symptoms, myocardial ischemia, and central catheter withdrawal, occlusion, or thrombosis.[31]

One-year survival for NYHA class D HF patients is ~67%; for similar adults using continuous flow LVAD (cf-LVAD), mortality rates are similar to heart transplant patients (one year 86.6%, two years 79.0%).[33] Studies highlight ~80% of patients with cf-LVADs achieve NYHA functional class I or class II symptoms at two years, with doubling of six-minute walk test distance and significant improvement in QoL.[34] However, despite markedly decreased pump thrombosis and strokes with current cf-LVAD technology, persistent complications contribute to significant physical cost and lessened event-free survival when compared with transplantation.[33]

Use of either inotropes or cf-LVAD is associated with many challenges including frailty, anxiety, depression, reliable access to telephone and electrical services, financial stress, caregiver burden, and changes in sexuality and intimacy.[35] As EoL approaches, adults using these advanced therapies may also encounter limited options for hospice and lack of clear guidelines and protocols regarding device discontinuation.

Tip 5: Significant Symptom Burden May Be Present in Patients Who Are Awaiting or Are Postheart Transplant; Treatment Should Include Optimal Guideline-Directed Medical Therapy Along with Standard PC Assessment and Interventions

Patients with HF report a range of symptoms, many attributable to disease progression or illness exacerbation. The most frequently reported physical symptoms include

shortness of breath (56%–100%), lack of energy (66%–85%), edema (50%–72%), and pain (37%–84%).[36–40] These patients also experience greater than average rates of psychological symptoms including depression (21%–40%), anxiety (31%–50%), and sleep disturbance (44%).[36,37,41] Despite the high prevalence of burdensome symptoms compared with patients with other serious illness such as cancer, PC referrals are underutilized in this population and management strategies primarily focus on reduction in pulmonary congestion and optimization of guideline-directed medical therapy.[42]

Patients with advanced HF benefit from collaboration between cardiologists and PC clinicians to optimize the illness experience. Symptom management should begin with achievement of euvolemia, including use of IV inotropes if needed. The side effect profile of cardiac medications should be evaluated to determine any potential contribution to symptom burden.[43] Persistent symptoms despite these measures necessitate consideration of pharmacological and nonpharmacological strategies frequently employed in PC.[39,40,43]

Although the small subset of patients with advanced HF who successfully undergo cardiac transplantation experience improved HF-related symptom burden, they often trade living with one serious illness for another due to the intensity of the medication regimen and follow-up needs post-transplant.[44] Thus, patients remain at risk for significant symptom burden related to immunosuppressant regimen side effects, post-transplant complications, and overall illness experience and are likely to benefit from longitudinal PC engagement.

Tip 6: Kidney Transplantation Is a Complex Multistage Journey, from Wait Listing to Graft Failure, Each Period with Its Own Unique PC Challenges

PC is well suited to support the needs of patients navigating the kidney transplant journey, but successful integration of PC requires an understanding of the needs of these patients during two distinct different phases of their care—waiting list period and post-transplant period. Each phase presents with its own unique set of factors that contribute to lower QoL, as well as psychological and physical symptom burdens.

The waiting list period for kidney transplantation can be lengthy and is associated with deteriorating physical and psychosocial QoL, depending on time on waiting list, age, and gender.[45] Physical symptom burden parallels worsening renal function, and the most frequently reported symptoms are pruritis, fatigue, pain, and anorexia.[46] Patients also experience notable psychological stresses related to the uncertainty of transplantation and grief surrounding the possibility of future graft failure.

The post-transplant period also contains its own unique complexities. One meta-analysis revealed that the mortality after renal allograft failure was $\sim$3%–4% after one year,[45] and $\sim$40% of all patients lose their grafts within 10 years.[47–49] Maintenance immunosuppression decreases organ rejection and subsequent allograft loss but contributes to further pill burden and an increased risk of infection, cardiovascular disease,[50] and cancer.[51] Although QoL and symptomatology often improve post-transplantation,[46] recipients face another set of self-management challenges, including fear of complications (e.g., rejection and future morbidity), treatment expectations and responsibilities (e.g., medicalization, numerous hospital and doctor visits, and interventions), and clinical complexity.[52]

Tip 7: Kidney Allograft Dysfunction Is Common; As Graft Function Declines, Patients Will Have a Different Experience with Advanced Chronic Kidney Disease and Face Different Treatment Choices Than in Their Pretransplant Period

Nearly 40% of kidney transplant recipients experience allograft failure within 10 years post-transplant.[48] The course of allograft failure is complex and unpredictable,[53] ranging from a gradual decline in allograft function over years to a rapid decline over days or a few weeks due to severe acute rejection. Nationally, the majority of patients with allograft failure return to dialysis and only 15% receive retransplantation within 10 years of graft failure; wait time for retransplantation depends on the region where the patient lives.[54] The survival and QoL of the patients who return to dialysis after graft failure are worse than those undergoing dialysis for the first time.[55,56]

For patients with failing allografts, decision making around modalities of renal replacement therapy will be different from their prior experiences. Since time has passed, frailty and additional comorbidities add complexity for retransplantation, and treatment modality options may be more limited. In addition, patients' previous experience on dialysis may affect their values and decision making and facing allograft failure can be emotionally challenging.[5,57] Evidence demonstrates complexity, discordance, and regret in pretransplant decision making,[17,58] and those with failing allografts have additional experiences and serious illnesses that make decision making even more complex. Integrated specialty PC can help support patients, families, and transplant teams as they navigate choices in allograft failure.[59]

Tip 8: In the Immediate Post-Transplant Period, Liver Transplant Patients Can Develop Significant Critical Illness that Is Nevertheless Survivable and Does Not Necessarily Mean that Their Graft Will Fail

Liver transplantation differs from other SOTs. The liver transplantation operation may have two opposite effects on the recipient's physiological reserve. On the one hand, the major abdominal operation on a patient with ESLD can deplete physiological reserve and predispose to clinical worsening in the immediate postoperative period. On the other hand, the presence of a functioning liver will improve physiological reserve and clinical status. For many patients, the positive effect of the new liver will result in rapid resolution of any pretransplant critical illness and general clinical improvement within the perioperative period. Some patients, however, may experience severe postoperative complications and clinical worsening despite a functioning liver.

Although prolonged critical illness reduces overall survival rates compared with those who experience rapid recovery post-transplant, median overall survival and graft survival for patients with prolonged post-transplant critical illness exceed five years.[60] A focus group with transplant recipients and caregivers identified their post-transplant critical illness as a surprise, and several participants recalled being scared that it signified that their graft was failing and that they would soon die.[61]

PC engagement in the pretransplant setting provides an opportunity for anticipatory guidance about the possibility of post-transplant critical illness and subsequent recovery and ensures that patients' values are elicited and documented in the pretransplant period. PC clinicians consulting on critically ill patients after transplant should be cognizant of their potential for recovery, which is quite different from similarly ill patients suffering complications after nontransplant major surgery.

Tip 9: Frailty Is Common among Patients with Cirrhosis and Is Strongly Linked with Waitlist Mortality, Health Care Utilization, Health-Related QoL, and Post-Transplant Outcomes

Frailty is a clinical state of decreased physiological reserve across physical, psychological, social, and environmental domains that was first described in the geriatric population. Physical frailty, as defined by functional impairment, is highly prevalent among patients with cirrhosis with rates ranging from 17% to 43%.[62] Multiple factors contribute to physical frailty among patients with cirrhosis, including cirrhosis-related complications such as ascites and hepatic encephalopathy, sarcopenia, malnutrition, systemic inflammation, and physical deconditioning. In addition, as the average age of patients undergoing liver transplantation continues to rise, the prevalence of frailty among patients with cirrhosis is expected to increase due to the compounded effects of both disease-specific and aging-related factors.

Physical frailty, as a measure of increased vulnerability to health stressors, has emerged as a powerful predictor of adverse clinical outcomes for patients with cirrhosis independent of traditional prognostic metrics such as the Model for End-Stage Liver Disease-Sodium score. Measurements of physical frailty such as Karnofsky Performance Status and the Liver Frailty index are prognostic of waitlist mortality in patients with cirrhosis.[63] Physical frailty has also been associated with outcomes beyond mortality, including risk of cirrhosis progression, unplanned hospitalizations, symptom burden, depression, falls, debility, and health-related QoL.[62] Because of this complexity, frail patients with cirrhosis have substantial PC needs and may benefit from PC comanagement.

Unfortunately, physical frailty does not rapidly reverse after liver transplantation. On the contrary, <40% of all patients are physically robust by 12 months after liver transplantation, even if they were robust pretransplant.[64] Setting expectations for patients and families regarding recovery of physical function after liver transplantation is an important and underaddressed aspect of post-transplant survivorship care.[65]

Tip 10: Chronic Lung Allograft Dysfunction Is Not the End of the Road; Chronic Lung Allograft Dysfunction Is Common and Limits Long-Term Survival in Lung Transplantation but Patient Trajectories Are Variable

Chronic rejection or chronic lung allograft dysfunction (CLAD) presents with a persistent decline in allograft function and affects up to 50% of recipients by five years after lung transplant.[66] It is the leading cause of mortality after the first year and can impact physical and psychological QoL.[66,67] As lung transplant recipients with CLAD may benefit from PC for management of progressive respiratory failure, associated anxiety, and complex communication challenges, it is important for PC clinicians to understand the variable trajectories after CLAD onset.

Although a number of factors impact CLAD progression, the most important is CLAD phenotype. The two main phenotypes are bronchiolitis obliterans syndrome (BOS) and restrictive allograft syndrome (RAS), accounting for ~70% and 30% of CLAD, respectively.[66] Whereas BOS presents with obstructive spirometry and small airways disease, RAS presents with restrictive spirometry and upper lobe predominant fibrosis.

Median survival after diagnosis is ~2.5 years after BOS onset versus 1 year for RAS.[68,69] Beyond phenotype, timing also matters as those that develop CLAD within two years of transplant are at greater risk of mortality.[69] Individual trajectories of allograft function also vary within a given phenotype from an initial decline followed by stability to a gradual stair stepping decline or a relentless progressive decline.

Although treatment options for CLAD remain limited, recipients whose disease process stabilizes can experience continued high health-related QoL. In contrast, progressive CLAD often requires management of anxiety, dyspnea, and other sources of distress while preparing for repeat transplant or nearing EoL. For a PC clinician assessing a lung recipient with CLAD, understanding the potential trajectories and anticipating QoL impacts are essential to providing high-quality care.

Conclusion

Caring for patients with SOT carries unique challenges during both pre- and post-transplantation periods. With increasing acuity and medical complexity, enhancement of symptom management, communication, and coping are critical aspects for all clinicians working in SOT. PC teams can help facilitate better experiences for patients when aligned with transplant teams. To achieve this close collaboration, transplant teams should aim to see PC as more than EoL care and PC teams must be aware of the unique systems, policies, relationships, and medical pressures of SOT care.

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