

# Palliative care in lung transplantation

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Abstract: The role of palliative care in lung transplantation has grown exponentially in the past two decades. From assisting with evaluating and optimizing candidates for transplant, to playing a crucial role in patients requiring extracorporeal cardiopulmonary life support (ECLS) as a bridge to lung transplant, perioperatively, or even during their first year post-transplant, palliative care has been shown to be an effective if underutilized tool in the armamentarium used to care for lung transplant patients. For patients being considered for primary transplantation and for lung transplant recipients, palliative care can decrease symptom burden and help to lessen the psychological distress experienced by patients and family members. For older patients listed for transplant, palliative care can help address cognitive impairment, depression, and frailty. Patients listed for lung re-transplant also benefit from palliative care involvement to address frequent symptom exacerbations, hospitalizations, and higher morbidity and mortality. Even for organ donors and their families, palliative care can facilitate communication and provide support to the family. While palliative care use in lung transplantation may be gradually increasing, further work is necessary to optimally integrate palliative care into lung transplantation. Barriers to lung transplant patients receiving palliative care are multifactorial and include physician, patient, and institutional factors. The potential role of palliative care in every aspect of lung transplantation has made a knowledge of palliative care principles crucial for the lung transplant practitioner. In this review, we will clearly delineate the potential benefit of palliative care for the perioperative lung transplant patient and make an argument for its increased use in this patient population.

Keywords: Palliative care; lung transplant

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#### Introduction

The existence of this review article, and indeed, an entire journal issue dedicated to palliative care and surgery, demonstrates how far our understanding of the potential role for palliative care in lung transplantation has come in the past two decades. Since 2005, when Drs. Molmenti and Dunn published their manuscript entitled "Transplantation and Palliative Care: The Convergence of Two Seemingly Opposite Realities", it has become clear that palliative care has important roles in organ donation, organ failure management, and pre- and post-transplant care (1). The potential role of palliative care in every aspect of lung transplantation has made a knowledge of palliative care principles crucial for the lung transplant practitioner. In this review, we will clearly delineate the potential benefit of palliative care for the perioperative lung transplant patient and make an argument for its increased use in this patient population.

# The argument for palliative care in lung transplantation

In 1990, the World Health Organization defined palliative

care as "the active total care of patients whose disease is not responsive to curative treatment" in which "control of pain, of other symptoms, and of psychological, social, and spiritual problems, is paramount" (2). The definition was subsequently expanded to describe "an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual" (3). Over the past few decades it has become clear that palliative care improves quality of life and reduces symptom burden for patients with serious illness including cancer and chronic organ failure (4).

There are perhaps few patient populations who stand to benefit more from palliative care than solid organ transplant candidates, who as Crone *et al.* note, must "balance the hope of prolonged survival, vastly improved health, and optimized quality of life against the possibility of decline and death" (5). Further, lung transplant recipients are a group that stand to particularly benefit, as they experience frequent hospitalizations, respiratory exacerbations, and higher levels of psychological distress including anxiety and depression, compared to other organ recipients (6,7). These patients manage an average of 17 symptoms and, in addition to their family members, report high levels of subjective burden, stress, and need for better communication and access to psychosocial support (8,9).

# The potential of palliative care in lung transplantation

Lung transplant patients can therefore greatly benefit from palliative care involvement, even before they are listed for transplant. As Crone *et al.* argue, "given that the majority of potentially eligible patients never receive a donor organ, it is reasonable to offer palliative care" to patients awaiting transplant (5). Both the American College of Chest Physicians and the American Thoracic Society recommend that specialty palliative care occur simultaneously with curative or life-extending care (10,11).

In addition, as many have noted, opioid use, an important component of palliative care, has been recommended for end-stage lung disease by multiple societies including The Canadian Thoracic Society, British Thoracic Society, the American Thoracic Society and the American College of Chest Physicians, as well as the National Institute for Health and Care Excellence (11-14). The American Thoracic Society in their Clinical Policy Statement Regarding Palliative Care recommends that palliative care should begin when a patient becomes symptomatic (11).

However, although many like McKenna *et al.* have argued that palliative care should be considered an integral part of the treatment of patients undergoing lung transplantation, few programs have incorporated palliative care into the routine evaluation or management of these patients (15). In addition, palliative care has not been written into the guidelines for the treatment of lung transplant patients for any of the major transplant societies. Much work remains to be done before the potential of palliative care in the perioperative care of lung transplant patients has been reached.

#### **Palliative care in lung transplantation**

# Patients awaiting lung transplantation

Patients listed for lung transplantation remain a particularly challenging group of patients, with high symptom burden as well as psychological distress associated with both the disease and the uncertainty of being on the waitlist. They experience what Freeman *et al.* call "a complex constellation of physical, psychosocial, and emotional symptoms, including dyspnea, cough, anxiety, depression, and insomnia" (16). The particular benefits of palliative care in this patient population include the providing of better coping skills, support for caregivers, the ability to address this existential distress, as well as a focus on symptom management. This is especially important in the highest risk populations, including older patients, hospitalized patients awaiting lung transplantation, patients mechanically bridged to transplantation, and re-transplant candidates.

However, many barriers remain to the routine use of palliative care in lung transplant candidates. Colman *et al.* name several specific barriers, including patient fear of abandonment by the transplant team, lack of access to supportive services, and concern over use of opioids by palliative care in symptom management, both due to the potential for opioid dependence and opioid-related respiratory depression (17). These perceived barriers result in delays to consultation of palliative care until the end of a patient's life and result in many end-stage lung disease patients dying in intensive care units receiving aggressive care (6,18-20).

In contrast to this widespread belief, Colman et al.

#### Annals of Palliative Medicine, Vol 11, No 2 February 2022

have shown that outcomes of lung transplant candidates referred for co-management by palliative care can be safely provided without compromising eligibility or exercise tolerance (17). In their review of 308 lung transplant candidates, 20.7% were referred to palliative care, and of these, 92% were prescribed opioids for dyspnea. Many providers are hesitant to consider transplantation in recipients with moderate or greater amounts of opioids because of concerns for challenging postoperative pain management with respiratory suppression or increasing rates of opioid dependence. However, of the 47% of patients who went on to receive a lung transplant, only 7 patients (23%) required an opioid prescription one month post-discharge. Colman et al. therefore argue that not only does palliative care not compromise a patient's ability to go on to lung transplantation, it may also improve a patient's baseline condition, improving their chance of a successful perioperative course (17).

Colman *et al.* describe an algorithm for symptom management with a palliative care consult involving attention to symptom control, advance care planning, and emotional as well as spiritual support. For the control of dyspnea in patients listed for lung transplant, they utilize a low-dose oral opioid regiment (morphine 2.5–5 mg or hydromorphone 0.5 to 1 mg PRN) with a planned transition to standing immediate-release opioids or sustained-release opioids over days to weeks, titrating the total daily dose to subjective symptom relief and side effects (17). Their routine palliative care efforts also include patient valuescentered discussions that encompass cardiopulmonary resuscitation and life-sustaining treatments (17).

Transplant clinicians have recently advocated for increased utilization of outpatient palliative care for patients with end-stage non-malignant lung disease awaiting transplantation. Freeman et al. recently evaluated the effect of an outpatient transplant palliative care clinic on patients awaiting transplantation and found that symptom burden was improved (16). As seen in other studies, there were no opioid-related morbidities, and the majority of patients prescribed opioids as part of the palliative care treatment (62/65 patients) discontinued opioids post-transplant; the three patients who did not were chronic pain patients on opioids prior to palliative care consultation (16). Wentlandt et al. argue that an ambulatory palliative care clinic is a useful model to improve symptom burden in lung transplant patients prior to transplantation and have outlined the development and structure of a Transplant Palliative Care Clinic (21). They argue that there is a need for palliative

care teams that span the inpatient and outpatient settings and recommend early referral to palliative care services as well as full integration of transplant and palliative care programs (21).

#### Patients who are hospitalized pre-transplant

Transplanting acutely ill patients is becoming more common, with as many as one-third of patients who receive a lung transplant being hospitalized prior to transplantation (22). In Singer et al's recent study, of the 33% of patients already hospitalized prior to transplant, 11% were intubated and 9% received extracorporeal cardiopulmonary life support, or ECLS (23). Importantly, acutely ill patients had the same likelihood of benefit in quality of life from lung transplantation as patients coming in from home (23). Nevertheless, given that patients hospitalized pre-transplant are likely to have more severe symptomatology and greater risk of death on the waitlist, they would stand to greatly benefit from the involvement of palliative care. As noted by Colman et al., palliative care involvement has often been delayed in these patients until almost the very end of life, suggesting there is much room for improvement in the involvement of palliative care in this patient population (17).

# Patients on extracorporeal cardiopulmonary life support as bridge to lung transplant

Extracorporeal cardiopulmonary life support, or ECLS, is increasingly used among patients awaiting lung transplant and deserves special mention (24). In some cases, ECLS can be initiated using a dual lumen cannulation strategy, allowing these patients to be bridged nonintubated, as well as ambulatory, and for physiotherapy to be performed while waiting for transplant (24,25). For these patients at our institution, a bicaval dual lumen catheter is inserted into the right jugular vein using echocardiographic guidance, usually bedside in the intensive care unit. We have used both Avalon and Crescent cannulas (VV ECMO, Avalon Cannula, Maquet, Germany and Crescent Jugular Dual Lumen Catheter, manufactured by MC3 Cardiopulmonary, Dexter, Michigan and distributed by Medtronic, Dublin, Ireland). The ability to avoid cannulating the groin with this technique allows patients to ambulate and work with physical and occupational therapy while awaiting lung transplantation.

Many have advocated for palliative care to be routinely involved in ECLS consults, in order to reduce symptom 930

burden, facilitate communication and decision-making, and alleviate patient and family suffering (25). As the use of ECLS bridge to lung transplant increases, palliative care utilization for these patients has increasing potential to improve the care of these patients.

### Older patients listed for lung transplant

The average age of lung transplant recipients is increasing (22). Moreover, patients aged 65 and older have been shown to have a median survival after lung transplantation of only 3.5 years, which is three years less than that for patients younger than 50 (22). Singer et al. have also shown that patients older than 65 derive less health-related quality of life (HRQL) from lung transplantation (23). They point to recent studies while postulating that frailty, depression, and cognitive impairment may play a role (26-28). Importantly, almost one-fourth of Singer et al.'s patient cohort was age 65 or older (23). With their known shorter life expectancy and smaller gains in quality of life after lung transplantation, the elderly patient population may benefit even more from the involvement of palliative care in the perioperative period.

### Patients listed for lung re-transplantation

Although they represent a small subset of lung transplant patients, patients who are listed for lung retransplantation may need additional support from palliative care services. They have higher morbidity and mortality compared to patients undergoing primary transplant, and experience frequent hospitalizations and symptom exacerbations (29,30). Ivarsson *et al.* followed the experiences of supportive care for seven patients listed for lung retransplantation, four of whom went on to die on the waiting list (31). They conclude that while hope for the future is paramount for these patients, ongoing support with "all facilities of palliative care" is crucial for both patients and their family members, particularly those patients with dependent children who may have additional emotional needs (31).

With both more elderly and acutely ill patients, including those requiring re-transplantation, being listed and undergoing lung transplant, there is great potential for palliative care principles of providing coping skills, support for caregivers, symptom management and quality of life discussions to make an impact in patient outcomes.

#### The early postoperative period

Early after transplantation, palliative care can have a significant impact on patient well-being, and in fact, this may be a key period during which the involvement of palliative care can improve patient outcomes. While posttransplant patients usually enjoy a temporary improvement in their symptom burden as well as quality of life, their psychosocial health can still suffer (27). While Rosenberger et al. characterized early postoperative lung transplant psychosocial health as below average, Singer et al. showed that most lung transplant recipients had enduring improvements in quality of life and psychological quality of life remained on average within population norms (23). However, Singer et al. found that one-fifth of patients experience a decline in mental quality of life in the first post-transplant year, with older patients being at greatest risk (23). These studies suggest that the early postoperative period is a crucial time for the involvement of palliative care, with the potential to alter difficult patient trajectories.

Further strengthening this argument is the knowledge gained from recent studies examining the early posttransplant course, which have concluded that a difficult early postoperative period is associated with longitudinally worse quality of life, and in particular a worse mental quality of life. Seiler *et al.*'s recent work demonstrated the difficulty of the early post-transplant adjustment period, during which severe adverse effects of treatment, physical complaints or medication side effects, fear of organ rejection, and restriction in everyday life emerged as the most common patient concerns (32). These concerns were shown to be consistent over the first six months after transplant, and the difficulty of this initial post-transplant period has been seen in other studies (33,34).

In addition, psychological co-morbidities of post traumatic stress disorder, depression, and anxiety are common in this patient population, and depression in particular is worrisome as it is associated with worse outcomes, including survival. Smith *et al.* have shown that survival is linked to psychosocial well-being in lung transplant patients (35), and this pattern can be seen in other transplant patients: importantly, bone marrow transplant recipients for AML follow a similar pattern of declining quality of life and increasing psychological and symptom burden (36,37). One recent randomized controlled trial of integrated palliative care for bone marrow transplant recipients demonstrated reduced decline in quality of life and improvement in psychological burden both in the immediate perioperative period, and the benefits of palliative care were still seen 6 months later (36,37).

#### The first post-transplant year

Nolley *et al.* reviewed 597 lung transplant patients at a tertiary medical center over five years, for whom 2,818 specialty palliative care encounters were undertaken (38). 64% of these occurred within the first year, with a median time of consultation 0.53 years post-transplant and the majority of consultations were for symptom management and psychosocial support (38). The majority of palliative care consults occurring within the first year after transplantation belies the distress that many transplant recipients experience immediately after transplantation, including from side effects related to immunosuppression, pain, postoperative cognitive dysfunction, depression and post-traumatic stress disorder. This, as well as the distress associated with adjusting to the challenges of post-transplant life, has been seen in many recent studies (23,35,38,39).

The majority of lung transplant patients are rehospitalized during the first transplant year, and palliative care remains crucial as re-hospitalization is associated with lower perception of general health, lower physical and social functioning, and greater bodily pain (40). Pneumonia, bronchitis, shortness of breath, graft rejection, respiratory failure, and pleural effusions have been shown to be leading causes of unplanned readmissions (41). The first year after lung transplantation is high risk for unplanned readmissions regardless of the initial indication for transplant, and patients readmitted within 60 days after their index hospitalization for lung transplantation were 1.6 times more likely to die than those readmitted later than 60 days (41). The high rate of re-hospitalization in the first posttransplant year, as well as the psychological distress that accompanies it, provides many opportunities for palliative care to improve patient outcomes.

#### Palliative care in organ donation

Palliative care has been shown to be effective in the treatment of organ donors and the care of their families. Kelso *et al.* describe the use of palliative care for end-of-life care and family support in organ donation after cardiac death (DCD), with palliative care skills including communication, coordination of care and skillful ventilator withdrawal proving beneficial (42). Once the DCD protocol

is initiated at their institution, the palliative care team is consulted with the goals of managing the patient's physical care, advocating for and providing comfort for the family, and to continue the care of the patient if they survive beyond 90 minutes (42).

In addition to palliative care providing support to patients who become donors and their families, the Hospice and Palliative Nursing Association (HPNA) supports palliative care practitioners promoting organ and tissue donation when possible (43). In their position statement, they argue that palliative care providers and hospices should both educate patients and families on the need for organ and tissue donation and partner with organ procurement organizations to help improve organ and tissue donation as appropriate (43).

# Continued barriers to thoracic transplant patients receiving palliative care

While transplant candidates and recipients likely have significant palliative care needs, they still rarely receive palliative care. Barriers to lung transplant patients receiving palliative care pre or post-transplant are multifactorial, including physician, patient, and institutional factors. In their survey of 74 transplant and palliative care clinicians from 18 transplant centers in 2009, Song et al. identified multiple barriers to post-transplant palliative care (30). Barriers for transplant clinicians included the misconception that palliative care was equivalent to end-of-life care, uncertainty about recipients' prognoses, the perception that palliative care precludes further aggressive treatment, and difficulty discussing palliative care with families. For the palliative care clinicians, barriers included a perceived lack of understanding by referring colleagues regarding the scope of palliative care services and the misconception that palliative care precludes further treatment (30).

Similarly, in 2013 Colman *et al.* assessed barriers to palliative care referral pre-transplant, identifying patient and family factors (unrealistic expectations of patients and family regarding survival, unwillingness to plan end-oflife care, concerns about abandonment or inappropriate care after enrollment in a palliative care program, and family disagreements about care goals), physician factors (competing time demands and seemingly contradictory goals of transplant versus palliative care), and institutional factors (requirements for weight loss or specific BMI requirements) (44). Additional barriers to referral may include concerns about 1 year post-transplant survival and 932

Table 1 Palliative care in lung transplantation

Groups that can benefit	Palliative care treatment
Patients awaiting lung transplant and patients hospitalized pre-transplant	Need for emotional and spiritual support
	High levels of psychological distress
	Need for advance care planning
	High symptom burden
Patients on ECMO bridge to transplant	Facilitate communication and decision-making
	Alleviate patient and family suffering
Older patients listed for transplant	Cognitive impairment
	Depression
	Frailty
Patients listed for lung re-transplant	High emotional needs for patients, dependent children and other family members
	Frequent symptom exacerbations
	Higher morbidity and mortality
	Frequent hospitalizations
Patients in the early postoperative period after transplant	Decline in mental quality of life
	PTSD, depression, and anxiety
	Medication side effects
	Fear of organ rejection
Patients in the first year post-transplant	Side effects related to immunosuppression
	Postoperative cognitive dysfunction
	PTSD
	Symptom management
	Psychosocial support
	Depression
	Pain

ECMO, extracorporeal membrane oxygenation; PTSD, post-traumatic stress disorder.

concerns about potentially addicting medications (38).

Interestingly, a recent in-depth interview study of transplant pulmonologists view of palliative care suggests that some barriers have changed. In contrast to the earlier work of Song, Nolley *et al.* found that transplant pulmonologists accurately distinguish between palliative care and hospice care as they describe palliative care as a specialty that aims to improve quality of life and hospice care as end of life care (38). Moreover, transplant pulmonologists views of transplant, and not their views of palliative care, were associated with different referral practices. Those that referred to palliative care while pursuing disease directed therapies described transplant as a temporary solution while those that referred once disease directed therapies were exhausted described transplant as survival focused. This finding echoes that of Colman *et al.* and suggest that despite differentiating between palliative care and hospice care, some transplant providers may still consider the treatment goals of palliative care and transplant.

Both Colman and Song recommend several strategies to overcome these barriers, including more collaboration between transplant and palliative care programs, the development of ambulatory services, and routine advanced care planning for listed patients (30,45). While palliative care likely remains widely underutilized, some recent trends are encouraging. Nolley et al. reported increasing utilization of palliative care for lung transplant recipients at a center with robust inpatient and outpatient palliative care services, with inpatient utilization increasing from 23% in 2010 to 42% in 2015, and outpatient utilization increasing from 2% in 2010 to 16% in 2015 (38). As has been argued for lung transplant candidates on ECLS, and given the clear benefit of palliative care perioperatively as has been delineated here, an argument can be made for routine use of palliative care to relieve symptoms, improve communication and decision-making, and alleviate psychological distress for the patient and family in all lung transplant candidates (25). We would argue that embedding palliative care into the lung transplant team, often referred to as integrated palliative care, offers the greatest opportunity to improve the use of palliative care in these patients, and would provide the greatest impact for this patient population.

#### Conclusions

We have shown the wide potential benefit of palliative care for perioperative lung transplant candidates, both broadly as well as for the highest risk populations, including older patients, hospitalized patients awaiting lung transplantation, patients mechanically bridged to transplantation, and retransplant candidates (*Table 1*). This care can be provided across patient settings, both inpatient and outpatient, and the argument for routine palliative care for these patients is bolstered by recent studies demonstrating a link between a difficult early postoperative period and longitudinally worse quality of life, including psychosocial quality of life (28,32,33). While there is still significant work to be done, the great potential for palliative care to further improve perioperative outcomes for lung transplant recipients justifies a robust continued effort to optimally integrate palliative care into lung transplantation.

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## 934

#### Annals of Palliative Medicine, Vol 11, No 2 February 2022

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