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The Intersection of Aging and Lung Transplantation: its Impact on Transplant Evaluation, Outcomes, and Clinical Care

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Abstract

Purpose—Older adults (age ≥ 65 years) are the fastest growing age group undergoing lung transplantation. Further, international consensus document for the selection of lung transplant candidates no longer suggest a fixed upper age limit. Although carefully selected older adults can derive great benefit, understanding which older adults will do well after transplant with improved survival and health-related qualiy of life is key to informed decision-making. Herein, we review the epidemiology of aging in lung transplantation and its impact on outcomes, highlight selected physiological measures that may be informative when evaluating and managing older lung transplant patients, and identify directions for future research.

Recent Findings—In general, listing and transplanting older, sicker patients has contributed to worse clinical outcomes and greater healthcare use. Emerging evidence suggest that measures of physiological age, such as frailty, body composition, and neurocognitive and psychosocial function, may better identify risk for poor transplant outcomes than chronlogical age.

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Conflict of Interest

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Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

Summary—The evidence base to inform transplant decision-making and improvements in care for older adults is small but growing. Multipronged efforts at the intersection of aging and lung transplantation are needed to improve the clinical and patient centered outcomes for this large and growing cohort of patients. Future research should focus on identifying novel and ideally modifiable risk factors for poor outcomes specific to older adults, better approaches to measuring physiological aging (e.g., frailty, body composition, neurocognitive and psychosocial function), and the underlying mechanisms of physiological aging. Finally, interventions that can improve clinical and patient centered outcomes for older adults are needed.

Keywords

Lung transplantation; Aging; Frailty; Body composition; Neurocognitive function; Psychosocial function

The field of lung transplantation continues to quickly evolve. One of the most rapid evolutions has been the aging transplant candidate. Indeed, older adults are the fastest growing age group undergoing lung transplantation today [1, 2]. For example, the proportion of USA lung transplant recipients aged 65 and over at the time of donor offer increased from 3% two decades ago to nearly 36% in 2019 [1].

Although overall short- and long-term survival after transplant has not changed, (88.8%, 74.4%, and 59.2% at 1, 3, and 5 years respectively)[3], median survival for older transplant recipients (> 65 years) is substantially lower than younger transplant recipients (3.6 vs 6.5 years) [4]. Listing and transplanting older, sicker patients has also contributed to higher rates of hospitalization at the time of transplant, longer post-transplant lengths of stay, and higher likelihood of discharge to places other than home [5].

Despite these trends, many older patients derive substantial benefit from transplant, including improved survival, functioning, and health-related quality of life (HRQOL). In order to maximize individual and societal benefit of transplant, however, understanding *which* older patients will do well with transplant is a key knowledge and practice gap. Herein, we aim to review the epidemiology of aging in lung transplantation and its impact on outcomes and highlight selected physiological measures that may be informative when evaluating and managing older lung transplant candidates and recipients. We also suggest some directions for future research based on review of the literature and expert opinion.

Epidemiology of Aging in Lung Transplantation

Offering lung transplantation to older adults has been controversial. Historically, international consensus statements on the selection of lung transplant candidates identified older age (> 60 [6] and > 65 [7] years) as a relative contraindication to listing. However, recent international guidelines no longer suggest a fixed upper age limit but instead, support lung transplantation for carefully selected older adults [8].

Increased transplant rates for older adults are driven by the aging population worldwide [9], changes in lung allocation systems that prioritize idiopathic pulmonary fibrosis (IPF), the incidence and prevalence of which increases with age [10], and growing willingness on

behalf of transplant centers to list and transplant older adults [11]. In step with evolving transplant practices, thought leaders in the field of geroscience now embrace initiatives to identify and replicate biomarkers of aging, acknowledging explicitly the divergence between chronological and biological aging among many older adults [12]. One thing is evident—the rapidly aging lung transplant population has created a need for transplant centers worldwide to prepare for the complex decision-making and care required for this population.

Impact of Age on Outcomes

Listing and transplanting older and more medically complex patients for transplant has not come without consequences. Although overall 1-year post-transplant survival for adult lung transplant recipients has moderately improved over the past two decades, 5-year survival has remained relatively poor [2]. Stratified by age, older adults experience relatively similar 1-year survival rates (84% in ≥ 65 years vs 85% in 50–64 years and 86% in 18–49 years), but lower 3-year (65% in ≥ 65 years vs 71%-74% in recipients < 64 years) and 5-year survival rates compared to younger recipients (62% in ≥ 60 years vs 75% in recipients < 60 years) [2]. Beyond survival, listing older and more medically complex patients has contributed to worse pre-transplant outcomes, greater healthcare use, and complications.

The proportion of candidates who are hospitalized at the time of transplant is now more than twice (> 20%) [1, 2] the proportion it was before 2005 (9.2%) [2]. Over half of those who are hospitalized at the time of transplant are admitted to the intensive care unit and require mechanical ventilation and/or extracorporeal membrane oxygenation [1]. Overall, wait list mortality initially decreased for those countries who transitioned to allocation approaches that prioritize medical urgency, but in the years following implementation, mortality rates began to increase again [13]. Wait list mortality rates are highest for older adult candidates (> 65) [1]. In the USA, nearly 20% of adults awaiting lung transplants either die or are removed from the wait list because they become too ill to safely undergo transplant surgery [14]. After transplant, the median length of hospitalization is increasing [5]. After transplant surgery, the number of transplant recipients discharged to places other than home, such as a skilled nursing facilities, rehabilitation hospitals, or home with nursing care, is rising [15]. Higher rates of 30- and 90-day readmissions have been observed [10]. In sum, listing and transplanting patients who are older and sicker has increased healthcare utilization, contributing to substantial increases in cost and likely morbidity [5, 15].

In addition to greater healthcare use, older transplant recipients seem to be more susceptible to clinical complications and comorbidities including infections [16], malignancies [10, 17], drug toxicity [17], atrial fibrillation [18], delirium, and impaired neurocognitive function [19]. The pathophysiological changes associated with aging (e.g., immunosenscence, inflammaging, frailty) are likely to increase the risk of these complications [20].

Given the increased morbidity and mortality among older adult lung transplant patients, we might expect this population to suffer from worse patient centered outcomes, such as greater symptom burden, poor functional recovery and health-related quality of life, and more difficulty with self-care and management. However, evidence suggests that age does not have a major effect on the HRQOL benefits of lung transplantation; the majority of

recipients across all age groups achieve substantial improvements in HRQOL [21–23]. However, this evidence base is small; the increasing number of older adults undergoing lung transplantation provides an opportunity to more closely study outcomes for this vulnerable population. Undoubtedly, the care of older adult lung transplant candidates and recipients is complex, but carefully selected older adults can derive great benefit from lung transplantation.

Considerations in the Selection of Older Adult Candidates for Lung Transplantation

Advances in the field have allowed broader access to lung transplantation for historically higher risk patients, such as older adults. However, in light of a persistent shortage of organs, offering lung transplantation for increased risk patients remains an area with substantive ethical considerations. The current International Society for Heart and Lung Transplantation (ISHLT) consensus document for the selection of lung transplant candidates [8] is guided by the ethical principles of utility, justice, and respect for persons. According to utility, survival benefit at the patient and societal level is prioritized when selecting candidates for transplant. Offering lung transplantation to individuals in whom transplantation would be futile can be harmful not only to the transplanted patient, but also to potential alternative recipients who may never have the opportunity to undergo transplant. Justice requires that “all individuals with a potential survival benefit from lung transplant be given equal consideration and opportunity for transplant [8].” This warrants the use of objective criteria for the evaluation of transplant candidacy [13]. Respect for persons requires that all individuals be treated as autonomous persons with the right for self-determination [8]. In the context of continued donor shortages and persistently high morbidity and mortality in lung transplantation, it is critically important to identify which older adults will survive and thrive following lung transplant to maximize the individual and societal benefit of lung transplantation and to provide older adults with appropriate information to make informed decisions about their treatment plans.

Historically, deciding which older adults are suitable candidates for lung transplant has been guided by arbitrary chronological age cutoffs or subjective “eyeball” tests of physical fitness. There is growing interest in applying concepts from the field of geroscience to develop an evidence base for older adult transplant decision-making and clinical care. Here, we review important physiological measures of aging and their relevance in lung transplantation.

Physiological Biomarkers of Aging

Multiple interconnected molecular pathways have been identified as drivers of aging phenotypes. Chromosomal DNA across cells requires active maintenance, and imperfections in these maintenance systems allow problems to accumulate over time [24]. Specifically, genomic instability accumulates because of imperfections in DNA replication and repair enzymes. At the same time, nucleoprotein caps at the end of chromosomes, termed telomeres, tend to shorten because of insufficient activity of telomerase enzymes. Finally, the DNA methylation patterns that determine cellular phenotypes undergo characteristic changes with age, reflecting the activity of epigenetic maintenance systems [25]. Active

maintenance of these genetic and epigenetic codes requires constant use of physiological resources and helps explain how stressors have been linked to accelerated biological aging. Short telomeres, for example, are linked to multiple mental illnesses, obesity, smoking, trauma, and poor sleep [26]. These chromosomal alterations may be further exacerbated through oxidative stress, as aging mitochondria are associated with increased reactive oxygen species, which damage DNA and alter DNA methylation patterns [27]. Chromosomal abnormalities, oxidative stress, and other metabolic derangements, in turn, drive senescence pathways. For example, short telomeres activate the p16/p21/p53 pathways that cause cell cycle arrest [28]. Physiologically, these pathways act as a checkpoint to prevent cells with abnormal chromosomes from malignant proliferation and transformation, but these same pathways can block stem cell renewal leading to recognized hallmarks of aging.

While there is an intuitive sense that chronologic age in the donor and recipient inadequately capture the physiologic consequences of aging, the molecular mechanisms linking biologic aging to poor post-transplant outcomes are inadequately understood. In renal transplantation, recipient epigenetic age outperformed chronologic age in predicting infection risk [29]. Telomere dysfunction is highly prevalent within the lung transplant population, in part because telomere dysfunction can manifest as fibrotic lung diseases [30]. Short recipient telomeres are associated with poor lung transplant outcomes [31, 32], potentially through increased risk for infection, kidney injury, and medication intolerance. Patients with IPF and short telomeres have impaired immune responses to cytomegalovirus (CMV), potentially leading to life-threatening CMV infections [33]. There is similar impairment of donor-specific immune responses in IPF subjects potentially mediated by p53 activation through short telomeres. However, donor-specific immune responses in IPF lung transplant recipients do not differ substantially from the partial tolerance state that appears in non-IPF lung transplant recipients at two years, and the donor-specific anergic phenotype in IPF T-cells could be overcome by strong cytokine stimulation, as might happen following infection [34].

After transplantation, the lung allograft age differs from that of the recipient, allowing us to discern local and systemic effects of biologic aging. Allograft telomere length is determined by donor age [35], and allograft telomere dysfunction can lead to chronic lung allograft dysfunction pathology through senescence of airway progenitor cells [36, 37]. Similarly, airway epigenetic age is determined by the time from donor birth. However, this airway epigenetic age may be increased in recipients who experienced primary graft dysfunction (PGD), potentially relating to effects of hypoxia on the epigenetic maintenance system [38]. None-theless, the donor and recipient ages are not entirely independent, as transplanted senescent cells have the potential to transfer aging phenotypes to the recipient [39].

Practical implementation of these biological insights remains a challenge. Lung transplant recipients with severe telomerase dysfunction from germline mutations may have worse outcomes, but likely still derive a significant survival benefit from lung transplantation [40]. Reduced immunosuppression targets in the setting of aging immune systems may leave lung transplant recipients vulnerable to worse rejection in the setting of infections. The interactions between donor and recipient ages on outcomes remains uncertain [41].

Answering these questions will require careful clinical trials assessing immunosuppression strategies stratified by recipient age.

Frailty Assessment and Outcomes

Drawing from experiences in geriatrics, frailty emerged in lung transplantation in response to a need for an objective approach to evaluate “fitness” for transplant in an older, sicker, more medically complex cohort of patients. While conceptually, frailty is defined as a clinical state of decreased physiological reserve and increased vulnerability to stressors, there is much debate over how to operationalize it [42]. The two general operational models of frailty are the “physical”/”phenotype” [43] model and the “cumulative deficit” model [44]. Frailty was first studied in lung transplantation using the frailty deficit index [45]. However, recent frailty research in lung transplantation has predominantly focused on the study of physical frailty, measured using either the Short Physical Performance Battery (SPPB) or the Fried Frailty Phenotype (FFP) [46]. There is some data favoring the face, construct, and predictive validity of the SPPB over the FFP [14, 47]. However, both the FFP and SPPB were developed in cohorts of community dwelling older adults without known lung disease [48]. Refinements to frailty measures specific for lung transplantation may yield improvements in construct and predictive validity, as has been shown in liver transplantation [49].

Frailty appears highly prevalent in the lung transplant population, with estimates varying from 10–70% of lung transplant candidates [50] and recipients [48, 50–52]. Frailty is associated with death and delisting before transplant [14] and prolonged hospitalization [45], rehospitalization [53], and mortality after transplant [54]. As a result, some transplant centers are hesitant to list frail patients for transplant [50]. However, a single-center study of frailty before and after lung transplant found that in survivors, pre-operative frailty resolves in most patients (84%) within 6-months after transplant surgery [55]. These findings demonstrate that frailty is modifiable and suggest that restricting access to transplant based on frailty status alone may not be appropriate [55].

The high prevalence of frailty seen in lung transplant patients is likely due to both disease-related and age-associated changes that affect patients with lung disease [48]. However, the causal factors driving frailty in lung transplant patients are not well established. Previous studies have identified an association between frailty and protein biomarkers [54] (IL-6, tumor necrosis factor receptor 1, insulin-like growth factor I, leptin), sarcopenia (grip strength [52] and appendicular skeletal muscle mass index [54]), adiposity (BMI [52] and visceral adipose tissue), malnutrition (albumin [52]) and renal dysfunction (creatinine [52]). Defining the factors contributing to the development of frailty in patients with advanced lung disease could highlight targets for interventions.

Future frailty research should address several key areas. A novel measure to objectively quantify the construct of physical frailty in lung transplant patients with improved predictive validity, similar to the Liver Frailty Index, which was developed for patients with liver disease [49], may be helpful. A solid organ transplant frailty index has recently been developed that uses data routinely collected during transplant candidacy evaluation.

Worsening in this frailty index is associated with death before and after transplant [56]. Longitudinal studies to understand how frailty changes over time and factors that affect frailty trajectories could help inform the development of effective interventions and clinical care strategies [57]. Identification of the underlying pathobiology of frailty in lung transplantation is an ongoing, active area of research. Effective frailty interventions to reverse or prevent frailty in the lung transplant population are needed. Thus far, pulmonary rehabilitation is the most effective intervention in improving frailty, but patients face significant barriers in accessing and adhering to this therapy [48]. Using technology to deliver in-home-based interventions appears to be a promising alternative to in-person pulmonary rehabilitation, capable of improving frailty scores [58, 59], but larger-scale randomized control trials are needed [48]. Finally, clearer guidelines on how to incorporate frailty in transplant decision-making and care are needed.

Body Composition Measurement and Outcomes

Research has long shown lung transplant candidates with either a low or high body mass index (BMI) are at increased risk for death after lung transplant [59–62]. These findings informed ISHLT consensus recommendations for transplant candidate selection. However, BMI is an imprecise surrogate for the components of body composition—adiposity and sarcopenia—that likely underlie the causal relationship between BMI extremes and transplant complications [60, 63–66].

Sarcopenia, defined as the presence of low muscle mass with or without decreased muscle strength, is associated with increased disability and increased risk of death or delisting before transplant and with increased risk of tracheostomy, prolonged mechanical ventilation, and prolonged hospital length of stay after transplant [67–69]. Higher BMI and abdominal subcutaneous adipose tissue are associated with an increased risk of PGD after lung transplantation [63, 70]. Similarly, both low and high visceral adipose tissue mass are associated with increased likelihood of frailty in lung transplant candidates [64].

Changes in body composition are amplified as we age. Normal aging is associated with loss of bone density and muscle mass, decreased muscle strength, and increased adiposity [71–74]. Furthermore, loss in muscle mass is associated with decreases in strength that are disproportionate to the amount of mass lost, suggesting that muscle quality declines as well [75]. Aging is associated with increases in central or visceral obesity, along with increased adipose deposition in and around muscle [75, 76]. This redistribution of fat may contribute to decreases in muscle quality [75, 77] as the presence of adipose tissue in and around muscle contributes to insulin resistance and impairs mitochondrial function, protein production, and muscle regeneration [78–83]. Decreased physical activity with age further contributes to both the accumulation of fat, the loss of muscle mass and strength, and decreases in bone mineral density [84]. These changes in body composition increase the risk of developing frailty in older adults [64, 85–91], and may be accelerated in patients with chronic lung disease due to both exercise limitations and the use of medications which alter muscle, adipose, and bone deposition. These age-associated changes in body composition may put older adults at increased risk for poor outcomes after lung transplantation. However,

this remains unclear due to analyses limited by small sample sizes and selection bias given inclusion of highly selected older candidates for transplant [64].

Optimal assessment of body composition in lung transplantation remains an area of ongoing research. Recent guidelines focus on the importance of the evaluation of muscle mass, muscle function, and frailty [92]. However, further work is required to derive and validate standard metrics for body composition in this patient population. For patients whose body composition puts them at increased risk of poor outcomes, interventions and therapies are needed to help access lung transplantation. Pulmonary rehabilitation programs help preserve muscle function and quality of life in lung transplant candidates [93, 94]. While healthy eating should be encouraged, there is no evidence for any specific nutritional interventions or diets to optimize body composition in this patient population. And, although interest remains high in pharmaceutical therapies to improve physical function and body composition [95, 96], there is insufficient evidence to support their use for this indication in older adults or patients with advanced lung disease.

Cognitive Function and Postoperative Delirium

Neurocognitive function is recognized as an important consideration among lung transplant patients [97], in large part because of the increasing age of all solid organ transplant candidates and recipients [98–100]. Nearly half of transplant candidates exhibit at least mild neurocognitive impairments (26–45%) [101–103] which have been associated with worsening physiological functioning, such as poor gas exchange, and reduced exercise capacity [101]. In addition, poorer pre-transplant performance on two composite measures of executive functioning and memory performance are associated with post-transplant mortality (HR = 0.42 [0.19, 0.9]) [104]. Among those who exhibit mild pre-operative impairments, cognitive function often worsens following transplant [19, 103]. Preliminary data [19, 104, 105], have demonstrated that postoperative cognitive dysfunction (POCD) following lung transplant surgery is common, affecting more than half of recipients [19, 106]. Available evidence suggests that impairments are most commonly observed on tests of executive function, attention, and memory [21, 27], suggesting an important role for prefrontal and subcortical brain structures [105].

The mechanisms of post-transplant POCD are not fully understood. Data from other transplant and cardiothoracic surgical populations [107, 108] have informed our current understanding of POCD mechanisms. In these populations, occult white matter damage, alterations in brain functional connectivity [109], microembolic ischemic insult, vasogenic edema, intraoperative hypoxia, regional metabolic abnormalities, and neuroinflammation appear to underlie postoperative cognitive changes [110–113]. Older age and mild preoperative neurocognitive impairment have been identified as the strongest risk factors for POCD [102, 103]. These mechanisms and risk factors also appear predictive of POCD in lung transplantation [19, 102, 114]. Neuroimaging has been able to identify occult cerebrovascular changes in lung transplant recipients that are undetectable during standard neurobehavioral assessment [115–118]. Available evidence suggests that greater microvascular disease and systemic dysregulation of multiple brain networks are key contributors to POCD among advanced pulmonary disease patients [119]. Older age [120],

greater cerebrovascular disease, and pre-existing neurocognitive weaknesses [106, 121] have been consistently associated with POCD in lung transplant patients. Importantly, although older age is perhaps the strongest risk factor for POCD, evidence suggests that middle-aged transplant patients are also at risk [19, 122].

A closely related corollary of POCD is postoperative delirium (POD). POD is a common and prognostic complication following lung transplant. POD occurs in approximately 37–45% of recipients [102, 114, 123, 124], and this prevalence appears higher among older recipients. Consistent with data among geriatric patient samples, the risk of POD appears to be predicted by three dynamically interacting risk domains: (1) patient-related background and clinical characteristics (e.g., older age, comorbidities, pre-existing mild cognitive impairment), (2) intraoperative factors (e.g., restricted cerebral perfusion, microembolic load), and (3) perioperative complications (e.g., PGD). All three of these factors confer increased POD risk in lung transplantation, with preoperative executive function [102], intraoperative cerebral perfusion pressure [114], and postoperative PGD all associating with POD. The development of POD appears to be associated with subsequently increased risk of re-hospitalization and mortality, even when it occurs several years following POD during transplant hospitalization [124, 125].

Psychosocial Function

Poor psychosocial function and, more specifically depression, are associated with increased risk for adverse outcomes in transplantation [126, 127]. Depressive symptoms are common among lung transplant candidates (6–40% [128–133]) and recipients (3–21% [132–134]).

Notably, early research suggests that preoperative depression and lower perceived social support may only be associated with adverse post-operative outcomes in those who experience perioperative complications. In patients whose transplant surgery hospitalization lasted less than 1 month, no consistent associations with depression, social support, or mortality after transplant were found. Whereas, among those whose hospitalization lasted greater than 1 month, preoperative depression and low social support were both associated with markedly higher mortality after transplant [135].

Interestingly, both persistent and new onset post-transplant depressive symptoms appear to be most predictive of adverse transplant outcomes [107, 128, 136]. In a single center study, depression after transplant was associated with a two-fold higher risk of chronic rejection, a 75% increase in the risk of graft loss, and a 65% higher risk death [137]. We reported similar findings across multiple samples of lung transplant recipients at various follow-up time periods ranging from 3 to 18 months [107, 125, 130, 136, 138, 139]. Greater psychological distress and depression, even at subclinical levels, were independently and strongly associated with mortality [127]. The association between depressive symptoms and adverse clinical outcomes does not appear to be explained by overlapping differences in exercise capacity [130], physical activity [107], immunosuppressant adherence [139], or sleep quality [140].

International guidelines and consensus statements support an assessment of psychosocial function at transplant evaluation [141]. Repeated assessments while awaiting transplantation and after transplant may also be warranted, especially in older individuals who are at higher risk for cognitive dysfunction, delirium, and depression. Given the association between psychosocial function and outcomes, findings from the psychosocial evaluation should be used to inform transplant candidacy and clinical care [142]. Future research should aim to identify the biological and behavioral pathways linking psychosocial function and adverse outcomes. Tailored interventions that target these biological and behavioral pathways are needed in effort to improve psychosocial function and in turn, improve access to transplant and reduce the risk for adverse outcomes.

Conclusion

The rapid shift towards transplanting older adults has challenged our field to rethink transplant evaluation, candidacy and clinical care. A growing number of older adults are listed for transplant, but median survival after transplant is only half that of younger recipients [1] Therefore, identifying which older adults will do well after transplant with improved survival and HRQOL is key to informed decision-making and judicious use of a limited resource. There is growing evidence that measures of physiological age more accurately identify risk for poor transplant outcomes than chronlogical age. Evidence presented here suggest that measures of frailty, body composition, and neurocognitive and psychosocial function have improved our ability to identify which patients will dervive the greatest benefit from lung transplantation. The challenge is how to use these data to inform transplant decision-making, interventions, and clinical care for older candidates and recipients.

Future research should focus on how to measure physiological aging (e.g., frailty, body composition, neurocognitive and psychosocial function). This may require the development of tools specific for this population with improved construct and predictive validty. Longitudinal studies are needed to identify risk factors for and the underlying mechanisms contributing to physiological aging and how changes contribute to poor transplant outcomes. These findings will be particularly important for the development of personalized, effective, and timely interventions. Whether interventions that target physiological aging can increase access to transplant and improve outcomes remains unknown.

Equally important, current clinical care needs should be tailored for older transplant candidates and recipients. For example, given what we know about the physiological affects of aging on pharmacokinetics, pharmacodynamics, and the increased risk for toxicity of immunosuppressive drugs, personalized immunosupression protocols that account for age-related physiological changes may be beneficial. Evidence suggests that older adults are more susceptible to malignancies, drug toxicity, and atrial fibrillation as well as cognitive dysfunction, depression, and isolation. Thus, heightened surveillance to detect and provide prompt treatment for these clinical complications may improve outcomes. Finally, emerging work show that palliative care can improve patient centered outcomes, including symptoms and exercise tolerance, yet is infrequently incorporated into routine transplant management [143]. Palliative care consultations facilitate advanced care planning to ensure

goal-directed, patient-centered care, which is particularly important for older adults who may need additional help deciding whether to pursue advanced treatment options, such as transplantation versus alternatives that focus on comfort. Given the complex decision-making and care that older adult transplant candidates and recipients require, older adults may derive great benefit from early integration of palliative care.

The evidence base to inform improvements in transplant care for older adults is small but growing. Multipronged efforts at the intersection of aging and lung transplantation are needed to improve the clinical and patient-centered outcomes for this rapidly growing cohort of patients.

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