

Palliative care in cardiac transplantation: an evolving model

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Published online: 5 May 2017

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Abstract It is currently estimated that 5.7 million Americans live with heart failure. Of these, less than 3000 will receive a heart transplant this year, according to the US Department of Health and Human Services Organ Procurement and Transplantation Network. With successful transplantation can come significant emotional and physical symptoms that are not always addressed. Although palliative care is an interdisciplinary subspecialty designed to alleviate multiple domains of suffering in serious illness, many mistakenly associate it solely with the end of life. Traditionally associated with cancer, research into the role of palliative care in other chronic illnesses and complex life-changing therapies such as solid organ transplantation remains scarce but is nonetheless developing. Here, we try to investigate a potential role for palliative care for heart transplant recipients. Early research thus far has demonstrated importance of early involvement of palliative care teams and the significant improvement of physical and emotional symptoms in the pre- and post-transplant period. Nevertheless, more research is warranted to determine the ideal timing of palliative care integration, the effects on health care resource utilization, and whether improving quality of life can affect morbidity and mortality. By understanding these critical elements and others we may be able to develop a model for the role of palliative care for heart transplant patients.

Keywords Palliative care · Heart transplant · LVAD · Cardiac transplant

Introduction

It is currently estimated that 5.7 million Americans live with heart failure (HF) [1]. Of these, about 10% have advanced heart failure (AHF) with AHA/ACC stage D disease refractory to standard medical management [2]. Of all patients with AHF, only a select group will be eligible for listing for orthotopic heart transplantation. In 2015, according to the US Department of Health and Human Services Organ Procurement and Transplantation Network (OPTN), 2804 patients received a heart transplant in the USA. Of those, 2347 were over the age of 18, and 1620 were over the age of 50. Heart transplant recipients have an expected 1 year survival of 86%, an impressive improvement over alternative therapeutic options of medical therapy alone (25%) seen in the REMATCH trial or mechanical circulatory support (MCS) such as left ventricular assist devices (LVADs) (80%) [3].

The burdens experienced by patients with HF and their caregivers continue to be elucidated, including elsewhere in this journal. Professional organizations such as the American Heart Association and the American College of Cardiology endorse the inclusion of supportive care expertise such as palliative care (PC) into routine clinical care of patients with AHA/ACC stage C/D HF as well as hospice referral when indicated [4]. As the incidence of HF continues to rise worldwide, the role of PC specialists notably increases, aiming to prevent or attenuate suffering related to the illness experience and to improve patient and caregiver quality of life (QOL). Most of this clinical focus understandably falls on patients with end-stage disease not eligible for AHF therapies including transplantation. More recently, with the rapid growth in

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LVAD implantation and Joint Commission requirement for MCS certification that centers include PC input for LVAD implantation as destination therapy (LVAD-DT), considerable attention has shifted to PC support in patients receiving MCS [5–7]. One outcome of this relatively new attention to PC needs in HF is a growing interest in and acceptance of clinical collaboration between HF and PC specialists [8].

The role of PC in the care of heart transplant candidates and recipients remains obscure. What PC needs do heart transplant recipients have? What do we understand about how to prevent or alleviate transplant-related suffering or distress in this population? Physical symptoms including dyspnea and pain, the mental, emotional, and spiritual needs of patients are often under-addressed and under-treated in transplant recipients [9]. While the drive for transplantation may understandably focus on lengthening lifespan and increasing patient function, for some this may still come at an important cost to quality of life warranting the attention of PC expertise. Indeed, although PC is commonly misinterpreted as an appropriate intervention only around transitions to end-of-life care, early evidence suggests a positive supportive role through cardiac transplantation [10, 11].

To date, there is insufficient evidence to draw strong conclusions about the role PC plays in cardiac transplantation. Instead, we attempt to excavate what evidence exists to date regarding PC in solid organ transplantation and what PC needs might be present in the solid organ (specifically heart) transplant recipient population.

Palliative care and models of integration with disease-modifying therapies

As a concept, PC has been defined as interdisciplinary care for patients with life threatening illnesses and their families that aims to prevent or alleviate suffering, whether it be physical, social, emotional, or existential [12]. PC's inclusion of facets beyond just the patient's physical ailments allows it to be a patient and family centered way of medical care that complements traditional disease-centered care. This reinforces the idea that PC is not contradictory to life extending therapies, but rather a way to develop and provide better medical care that should not only be utilized at the end of life. High-quality PC is most likely achieved with clinical expertise representing these different domains of suffering, including but not limited to specially-trained physicians, nurses, social workers or psychologists, and chaplains; palliative-trained clinical pharmacists may provide additional expertise navigating complex polypharmacy in advanced illness and symptom management-directed pharmacotherapies [13].

In clinical implementation, PC has traditionally centered around transitions from aggressive disease-modifying therapy to care focused on QOL or comfort. Historically developing around cancer care, the discipline PC has broadened its focus to other serious, progressive illnesses including HF [14, 15]. Perhaps in large part because of this strong association

between PC and end of life, patients and clinicians alike have historically demonstrated resistance to PC referral even in the face of notable suffering and distress [16].

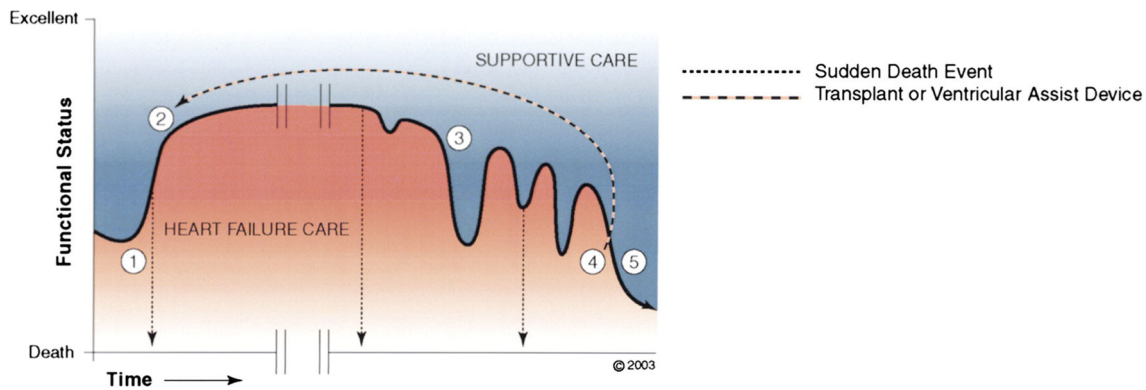
Nonetheless, the timing of PC introduction in the disease trajectory has continued to shift further upstream to a more concurrent care model, where PC has a complementary collaborative role alongside disease-modifying therapies. (Fig. 1) Again, this concurrent model is most evident in cancer care; nevertheless, it also continues to develop in non-malignant diseases, including advanced renal disease, pulmonary disease, and of course, heart failure [15, 18–20]. Beginning in 2014, The Joint Commission required CMS-certified LVAD-DT programs to include PC in the patient selection process. In terms of a hybrid disease-modifying therapy/PC model, this type of collaboration shifts the palliative focus from exclusively managing suffering around disease progression to providing support through a period of high risk but nonetheless a potentially positive outcome.

Integration specifically with transplantation

In transplantation medicine, this collaborative PC model has developed most prominently in bone marrow transplantation (BMT) although it still remains very limited [21]. Depending on the underlying disease, PC expertise may alleviate distress while maintaining the possibility of favorable prognosis. For example, in one trial of patients undergoing high-risk hematopoietic stem cell transplantation and early PC (defined as pre-transplant consultation), most reported stable or improved mood and sense of hope with a median of three PC visits and 82% reported feeling “very comfortable” with the early PC intervention [22].

Shifting attention to solid organ transplantation, studies have shown that patients awaiting transplant experience considerable multi-modal distress, including dyspnea, pain, fatigue, weight loss, decreased exercise tolerance, and frequent hospitalizations that interfere with daily activities [23, 24]. Clinical uncertainty, wait periods that increase limitations in work/leisure activities, anxiety regarding likelihood of transplant success, major lifestyle changes after organ transplant, and financial strain due to prolonged illness contribute to psychological distress for both transplant patients and caregivers [24–26]. Similar to other clinical settings, house staff and nurses on transplant teams are more likely to recognize needs/benefits of PC consultation than attending physicians [27].

PC's role continues to positively evolve in both the pre- and post-transplant phases of care. In one study of lung transplant candidates, 20% were referred to PC consultation, most of whom received opioids for safe management of dyspnea. Of these patients, nearly half went on to receive lung transplants successfully, highlighting that concomitant PC in the transplant process does not impede this care trajectory [20]. Post-lung transplant, PC referral also improves symptom management and clarifying goals of care appropriately in the context of organ



Schematic course of Stage C and D heart failure. Sudden death may occur at any point along the course of illness. (1) Initial symptoms of heart failure (HF) develop and HF treatment is initiated. (2) Plateaus of variable length may be reached with initial medical management or after mechanical support or heart transplant. (3) Functional status declines with variable slope, with intermittent exacerbations of HF that respond to rescue efforts. (4) Stage D HF, with refractory symptoms and limited function. (5) End of life.

Fig. 1 Comprehensive Heart Failure Care (adapted with permission from Goodlin et al. [17])

failure [28]. Similar early findings of better symptom management and holistic support prior to transplantation and appropriate clarification of goals and code status post-transplantation have also been established in liver transplant care [29, 30]. In each of these settings, PC referrals address high symptomatology associated with both end-organ failure and then with organ transplantation and long-term management [29, 31].

Palliative care intervention pre-heart transplant

The needs of patients with heart failure for holistic supportive care are well documented [13, 32, 33]. Patients with ACC/AHA stage C or D heart failure develop a high symptom burden, particularly dyspnea but also significant levels of chronic pain, fatigue, insomnia, and/or depression, to name only a few sources of distress [34, 35]. Spiritual distress may be considerable and responds positively to spiritual care interventions [36, 37]. Complex medical decision making, including advanced care planning and prognostication, requires expert communication that can be facilitated by PC providers [38, 39].

Among this larger group of advanced heart failure patients is the select population being evaluated or even actively listed for heart transplantation. Thus far, studies aimed specifically at heart transplant candidates are few and small, but generally point to consistencies with studies examining supportive care needs in larger heart failure populations. With medical care focused on work-up and preparation for organ transplant, common physical, emotional, and spiritual sources of distress prior to transplant are often overlooked. Unsurprisingly, quality of life, including vitality and functional capacity for patients is

typically worse prior to heart transplant and perhaps worse than other disease processes [40–42]. One study found that patients waiting for transplant experience dyspnea, pain, and fatigue that not surprisingly correlated positively with higher stress, less life satisfaction, lower quality of life, and more functional disability [22]. Another study found high symptom burden in heart transplant candidates that responded well to PC interventions, often resulting in lower opioid use but improved quality of life and less anxiety associated with waiting; patients and family members noted increased satisfaction with medical care, decision making, and continuity of care [9].

Palliative care intervention post-heart transplant

While quality of life improves and caregiver burden decreases after transplant, [43, 40] there continues to be physical symptoms, including pain [44] and an increase in emotional and psychosocial-spiritual burdens [45].

One study conducted showed that liver, kidney and heart transplant patients continue to suffer from pain after surgery [46]. The same study showed that heart transplant patients had the highest rate of pain with up to 69% endorsing continued symptoms [46]. More research, however, is needed to delineate how much physical pain causes a decrease in quality of life and how much of that is due to pain as a symptom of psychological distress [44].

Like other solid organ transplant patients, heart recipients continue to experience pain. Up to 67% of patients reported mild to severe pain after heart transplant [44]. Bone pain secondary to osteoporosis, fatigue, mental confusion, fatigue, and

dizziness are some of physical symptoms that prevented post-transplant patients from returning to work [45].

Many develop psychological disorders and while physical health improves, many continue to suffer significant cognitive deficits. Patients often find difficulty with returning to normalcy including work and personal relationships [47]. Anxiety and depression were common among patients after heart transplant and depression often arose within the first 2 weeks of surgery [48]. One study showed that up to 11% of patients are diagnosed with PTSD 1 year after transplant and up to 8% of caregivers were diagnosed with PTSD secondary to the transplant experience [49]. It is estimated that up to 20–30% of heart transplant recipients experience depression [50–52]. Heart transplant recipients with depression had higher all cause hospitalizations than their non-depressed counterparts and depression has been linked with higher medical noncompliance raising the risk of serious consequences in a transplanted patient [53]. Addressing these issues early and mobilizing a strong support system help to alleviate some of the anxiety that comes after transplant [54].

One study looking to see whether a web-based intervention could improve post-heart transplant outcomes showed that those patients and caregivers who visited and utilized a web program more often had better compliance with diet, doctor appointments, and improved anxiety which subsequently results in better physical outcomes [47]. Among patients who utilized the web-based program anxiety improved and among caregivers, hostility improved. Improvement in hostility is relevant as it is associated with improved medical compliance [47]. This illustrates the importance of continued support and resource for post-heart transplant patient.

Other problems that arise are a patient's inability to cope with the losing of their own heart and having another patient's heart keeping them alive. Unlike other solid organ transplants, the recipient feels the heart's beat and with it a constant reminder of the donor. We hear and read stories of heart transplant recipients who finally meet the mother of the heart donor after 25 years [55] or the bride being walked down the aisle by the man who received her father's heart [56]. There has even been discussion regarding whether a recipient's personality begins to change to that of the donor [57]. Current literature suggests that facilitated communication between donor family and recipient can positively impact both parties. Learning of the successful organ transplant can help assure the donor family that the decision to donate was right and make meaning from the bereaved loss [58]. Similarly, organ recipients are able to directly express gratitude, dissipating a common sense of guilt that one's life was saved through the death of another [59, 60]. In fact, close relations between donor family and recipient may enhance transplant success [61].

Besides physical and emotional symptoms, many patients have spiritual needs before and after transplant that are often times not addressed. Death, the suffering they endure, and the impact their disease and its implication has for their loved

ones are some of the thoughts many transplant patients have before and after surgery [62].

An evolving flexible model

Both patients and clinicians alike tend to exhaust all medical options prior to engaging PC seeing it as a last resort rather than a resource that can be utilized concurrently [26]. While it is understood and even recommended by organizations like the ACCP that palliative should be involved early and concurrently with other medical services for patients with advanced disease including those who are being referred for transplant, there still remain many barriers to implementing this practice [14]. Despite the fact that PC involvement results in better symptom management, and studies have advocated for earlier involvement of PC [29] there continues to be a lack of involvement of PC in the care of solid organ transplant patients because of confusion about the optimal time to include their services and of a lack of open communication during rounds with various team members [50]. A survey published in *CHEST* looked to understand that barriers existed in having palliative involved for lung transplant patients showed that there was limitation of access to PC consultants, lack of understanding among physicians on the role of PC, and limited resources [14]. Other identifiable barriers include the contradictory role of palliative and transplant, the unrealistic expectations of patients of transplant and the belief that care would be compromised once palliative is consulted [14, 63].

Studies in heart failure patients have shown that despite the benefit of PC, it is often delayed because of unknown trajectory of the disease and the misunderstanding of PC versus hospice [34, 64]. There is also a lack of evidence and a need for additional studies on the role of PC and how to integrate it in caring for heart failure patients [34]. Of the limited data available on the role of PC in patients awaiting transplant, there is evidence that PC should be involved early in the care [9]. With PC involvement, pain was better managed and patients were able to show more exertion during exercise sessions [7].

Conclusion

Over time, we are learning the importance of the palliative team in the care of cancer and non-cancer patients both at the end of life and those awaiting life saving procedures like transplants. Studies have already shown that PC involvement is best early and is integral in improving a patient's physical, emotional, and spiritual needs. Furthermore, PC not only impacts a patient's life, but their caregivers as well. They are often best at facilitating discussions about goals of care and maintaining continuity of care [11]. While there is some data on PC for patients awaiting transplant, more research needs to be conducted on PC for patients who have already received a heart transplant. Patients post-transplant continue to exhibit symptoms and needs that can best

be addressed by PC team who can improve the quality of life of patients and their caretakers. It is still to be seen whether by improving quality of life, there may be a positive impact on the quantity of life as well. Not only would PC improve subjective aspects of medical care for heart transplant patients, but may also lower cost and decrease hospitalizations. Studies have already shown that inpatient palliative consultation lowers costs [65]. Not only do we need to know whether this finding is also true for heart transplant recipients, but explore the differences between inpatient and outpatient PC and how each can be most effective. With the AHA Heart Disease and Stroke Statistics predicting an increase of 46% in heart failure prevalence between 2012 and 2030, and therefore more transplant candidates and transplant recipients, it is imperative that we study and develop a model for the role of PC in caring for heart transplant patients.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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