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Outcomes of Lung Transplantation after Allogeneic Hematopoietic Stem Cell Transplantation

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Other than lung transplantation (LT), no specific therapies exist for end-stage lung disease resulting from hematopoietic stem cell transplantation (HCT)-related complications, such as bronchiolitis obliterans syndrome (BOS). We report the indications and outcomes in patients who underwent LT after HCT for hematologic disease from a retrospective case series at our institution and a review of the medical literature. We identified a total of 70 cases of LT after HCT, including 9 allogeneic HCT recipients from our institution who underwent LT between 1990 and 2010. In our cohort, the median age was 16 years (range, 10 to 35 years) at the time of HCT and 34 years (range, 17 to 44 years) at the time of LT, with a median interval between HCT and LT of 10 years (range, 2.9 to 27 years). Indications for LT-included pulmonary fibrosis (n = 4), BOS (n = 3), interstitial pneumonitis related to graft-versus-host disease (GVHD) (n = 1), and primary pulmonary hypertension (n = 1). Median survival was 49 months (range, 2 weeks to 87 months), and 1 patient remains alive at more than 3 years after LT. Survival at 1 year and 5 years after LT was 89% and 37%, respectively. In the medical literature between 1992 and July 2013, we identified 20 articles describing 61 cases of LT after HCT from various centers in the United States, Europe, and Asia. Twenty-six of the 61 cases (43%) involved patients age <18 years at the time of LT. BOS and GVHD of the lung were cited as the indication for LT in the majority of cases (80%; n = 49), followed by pulmonary fibrosis and interstitial lung disease (20%; n = 12). In publications reporting 3 or more cases with a follow-up interval ranging from the immediate postoperative period to 16 years, the survival rate was 71% (39 of 55). Most deaths were attributed to long-term complications of the lung allograft, including infections and BOS. Two deaths were related to recurrent or relapsed hematologic malignancy. LT can prolong survival in some patients who suffer from end-stage pulmonary complications after HCT. Patient factors that likely improve the chances of a good long-term outcome include young age, at least 2 years post-HCT free of relapse from the original hematologic malignancy, and lack of other end-organ dysfunction or manifestations of chronic GVHD that require treatment with immunosuppressive agents.

INTRODUCTION

Survival after allogeneic hematopoietic stem cell transplantation (HCT) has improved over the course of several decades, owing to the development of less-toxic pretransplantation conditioning regimens, more effective prophylaxis of acute graft-versus-host disease (GVHD), improved infection control, and advances in supportive care in the posttransplantation period [1]. Accordingly, more individuals are living longer after HCT.

Long-term survival still comes at a cost, however. Up to 26% of allogeneic transplant recipients develop late-onset noninfectious pulmonary complications, including bronchiolitis obliterans syndrome (BOS). BOS, considered part of the spectrum of chronic GVHD (cGVHD) manifestations [2], affects 5.5% of allogeneic transplant recipients and 14% of those who develop cGVHD [3]. In addition to BOS, allogeneic HCT recipients may suffer from other manifestations of pulmonary GVHD, such as cryptogenic organizing pneumonia, or from pulmonary fibrosis resulting from treatment for the underlying malignancy or the pretransplantation regimen. These noninfectious pulmonary complications of allogeneic HCT significantly compromise quality of life and contribute to nonrelapse mortality after cure of the patient's original hematologic disease.

Lung transplantation (LT) is now a well-established therapy for many pulmonary conditions—chronic obstructive pulmonary disease, cystic fibrosis, idiopathic pulmonary fibrosis—when all other forms of medical and surgical therapy have failed. Through June 2012, 45,000 LTs have been reported worldwide [4]. Similar to some of these pulmonary conditions, no specific disease-modifying therapies exist for BOS related to cGVHD or toxicity-related interstitial lung disease. Thus, it seems reasonable to consider LT as an option for BOS or other pulmonary complications when end-organ damage has resulted in severe compromise of activities of daily living and appears to be inexorably leading to the patient's early demise.

The first case of LT after bone marrow transplantation was reported in 1992 [5], and since then, sporadic case reports and case series have been published documenting the use of

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this procedure to treat life-threatening pulmonary complications of HCT. Even so, LT after HCT is rare, and the outcomes of LT in this population have not been well described.

In this report, we present our institutional experience with outcomes of LT after HCT and review the experience reported in the literature. We also review the current considerations of LT and propose recommendations for the selection of appropriate candidates for LT from this population of patients.

METHODS

Case Series

We performed a retrospective chart review of cases of LT performed after HCT at Fred Hutchinson Cancer Research Center (FHCRC). Cases of LT after HCT were identified by physicians of the Long-Term Follow-Up (LTFU) program and pulmonary consultative services. The data used in this study rely on documentation in the medical record generated by the LTFU, which provides lifelong telemedicine to all patients undergoing transplantation at FHCRC and to their physicians in addition to onsite consultation, as described previously [6]. All patients who underwent allogeneic HCT at FHCRC between January 1971 and December 2011 with proven documentation of LT from the LTFU database are included in this report. This time frame for the cohort was selected to ensure adequate follow-up time. Follow-up for identified LT cases was date of recorded death or December 31, 2013, whichever came first. Clinical information was extracted by chart and database review. Written consent for the use of medical records for research was obtained from patients before transplantation. This study was approved by the FHCRC Institutional Review Board.

Literature Review

We performed a computerized search of the MEDLINE and Scopus databases using the key terms "lung transplantation," "after," "bone marrow transplantation," "hematopoietic cell transplantation," and "bronchiolitis obliterans" between January 1991 and July 31, 2013. We also reviewed reference lists of included studies for additional publications. All English language publications describing a case of LT after HCT were included. Publications were reviewed individually, and specific parameters and outcomes were collated.

Statistical Analysis

Survival analysis was performed with the Kaplan-Meier method.

RESULTS

Patient Characteristics and Outcomes after LT

We identified 9 individuals out of 10,548 recipients of allogeneic HCT performed in Seattle between 1971 and 2011 who subsequently underwent LT between 1990 and 2010 (Table 1). The median age at HCT was 16 years (range, 10 to 35 years). Indications for HCT included acute leukemia (n = 7), chronic myelogenous leukemia (n = 1), and aplastic anemia (n = 1). Six patients underwent HCT from an HLA-matched related donor, and the other 3 did so from an HLA-matched unrelated donor. The median age at LT was 34 years (range, 17 to 44 years), with a median interval of 10 years (range, 2.9 to 27 years) from HCT to LT. Indications for LT included interstitial lung disease (ie, interstitial fibrosis, pulmonary fibrosis, interstitial pneumonitis) in 5 patients, BOS in 3 patients, and primary pulmonary arterial hypertension in 1 patient. Four patients underwent single LT, and 5 underwent bilateral LT; all transplanted lungs were from cadaver donors. Owing to a wide geographic distribution as well as variability in LT selection criteria, the patients underwent LT at several institutions. Data regarding pulmonary function tests, immunosuppressive medications, and the presence of active cGVHD were limited.

Of the 9 patients who underwent LT over a period of >20 years, 1 patient remains alive more than 3 years after his bilateral LT and 7 years after his HCT. Median survival after LT was 49 months in the remaining patients (Figure 1). One-year survival of this cohort was 89%, and 5-year survival was 37%. Most of the deaths were related to lung allograft rejection or infectious complications (Table 1). One patient died at 2 weeks after LT; the cause was not reported.

Literature Review

Excluding our present cohort, a total of 61 cases of LT after HCT were reported in 20 published manuscripts in the English language medical literature between 1992 and 2013

Table 1
Characteristics of the Case Series Cohort, FHCRC

Case	Sex	Year of LT	Age at HCT, yr	Age at LT, yr	Indication for HCT	HCT Source	Time from HCT to LT, mo	Indication for LT	Type of LT	Survival after LT	Cause of Death
1	Female	1990	19/23	25	ALL	BM (2), related	35	Pulmonary fibrosis due to chemotherapy	Single	6 yr, 2 mo	Chronic rejection/CMV pneumonitis
2	Female	1991	11	17	AML	BM, related	66	Interstitial fibrosis due to radiation therapy, versus interstitial pneumonitis due to GVHD	Single	4 yr, 6 mo	Respiratory failure/ progressive pneumonia due to stenotic complication of LT
3	Male	1995	16	40	Aplastic anemia	BM, related	292	BOS	Bilateral	3 yr, 8 mo	Chronic graft rejection (bronchiolitis obliterans), bilateral bronchial stenosis, pseudomonas infection
4	Female	1997	10	24	ALL	BM, related	174	BOS	Bilateral	2 yr, 7 mo	Brain damage due to cardiac/respiratory arrest
5	Male	2000	35	44	AML	BM, related	123*	Interstitial pneumonitis/ interstitial fibrosis	Single	2 wk	Immediate post-LT; immediate cause unknown
6	Female	2002	32	41	CML	BM, unrelated	113	Primary pulmonary hypertension not related to malignancy or HCT	Single	7 yr, 3 mo	Respiratory failure/viral pneumonia in transplanted lung; recurrence of CML
7	Female	2004	10	37	AML	BM, related	326	Pulmonary fibrosis due to chemotherapy and radiation therapy	Bilateral	6 yr, 1 mo	Septic shock, pulmonary fungal infection
8	Male	2009	16	34	ALL	PBSC, unrelated	204	Pulmonary fibrosis due to chemotherapy and radiation therapy	Bilateral	2 yr, 6 mo	Chronic graft rejection/ primary graft dysfunction
9	Male	2010	28	32	ALL	PBSC, unrelated	45	BOS	Bilateral	>3 yr	NA

LT, lung transplantation; HCT, hematopoietic stem cell transplantation; BM, bone marrow; PBSC, peripheral blood stem cells; ALL, acute lymphoblastic leukemia; AML, acute myelogenous leukemia; CML, chronic myelogenous leukemia; GVHD, graft-versus-host disease; BOS, bronchiolitis obliterans syndrome; CMV, cytomegalovirus; NA, not applicable.

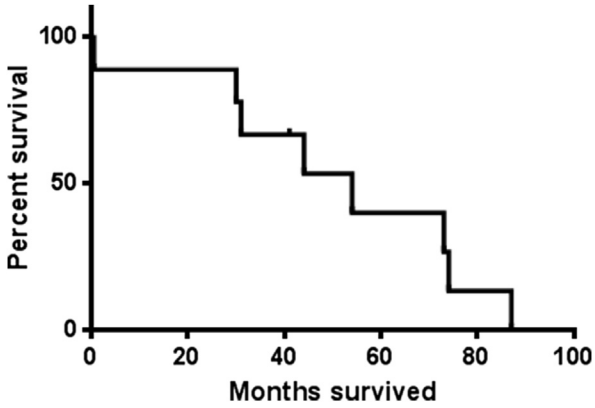

Figure 1. Survival of LT after HCT recipients from the FHCRC cohort (n = 9). The tick mark denotes a patient who was alive at 41 months post-LT as of last contact in December 2013.

[5,7-25] (Table 2). Twelve single case reports have been published, 1 of which was reported in 2 different publications [9,10]. Five cases were reported twice as part of a larger case series [8,11,12,14,19]. These cases originated from multiple centers in the United States, Europe (United Kingdom, Austria, Denmark, and the Nordic nations), and Asia (Japan, Hong Kong, and Korea).

Of note, the first known case of LT after HCT reported in *Chest* in 1992 was a 25-year-old woman who underwent her first related-donor allogeneic bone marrow transplantation at Fred Hutchinson Cancer Research Center in 1984 for acute lymphocytic leukemia [5]. She underwent a second bone marrow transplantation 4 years later for disease relapse. She developed progressive pulmonary fibrosis leading to respiratory failure, and underwent a single LT at another institution in 1990, 2 years after her second bone marrow transplantation. This patient is included in our analysis of outcomes.

Twenty-six of the 61 patients in the literature cohort (43%) were age <18 years at the time of LT. The cohort included 12 living-donor lobar LT (LDLLT) recipients, 6 of whom were age ≥18 years at the time of transplantation. Most of the LDLLTs were performed in Japan. At least 33 patients underwent bilateral cadaveric LT, and 6 patients underwent single cadaveric LT. Yousef et al. [23] did not report the types of LTs performed in their multicenter series of 11 pediatric HCT recipients.

The median interval between HCT and LT was 5 years (range, 0.67 to 25 years) in 15 publications reporting this information, and the median age at the time of LT was 24.5 years (range, 4 to 59 years) in 18 publications. The youngest patient was a 4-year-old child who underwent LDLLT from his mother at 3 years after undergoing peripheral blood stem cell transplantation for myelomonocytic leukemia, for which the mother was the donor as well [16].

For the 11 single case reports, the median length of follow-up was 14 months (range, 1 to 38 months) at the time of this writing, which included 1 death at 9 months. Among the remaining publications that analyzed 3 or more cases, for a total of 55 cases, the aggregate survival rate at the time of publication was 71% (n = 39), with the majority of cases followed for ≥2 years (range, immediate postoperative period to 16 years) (Table 2). Most deaths were attributed to long-term complications of the lung allograft, specifically infectious complications from chronic immunosuppression or BOS. Only 1 reported death was due to recurrent hematologic malignancy.

DISCUSSION

Chronic pulmonary disease that arises as a complication of HCT presents a challenging and frustrating problem, particularly when the patient is young and essentially cured of a previously life-threatening condition. Prognosis after a diagnosis of BOS is associated with a 1.6-fold increase in the risk of mortality compared with HCT recipients without BOS [3], and the reported 5-year survival rate is only 13% [26]. As with end-stage lung disease from other causes, therapeutic options for pulmonary GVHD and regimen-related pulmonary fibrosis are limited to palliation once chronic respiratory failure ensues. LT improves quality of life and survival in patients with various pulmonary conditions refractory to maximal medical therapy; however, limited information is available regarding the indications and outcomes of LT after HCT to help guide clinicians in exploring this therapeutic option.

Here we report 9 recipients of allogeneic HCT performed at FHCRC who received LT for end-stage lung disease over a 20-year time frame, and summarize 61 cases published in the medical literature. This aggregate of 70 cases worldwide suggests that LT may be an increasingly acceptable option in select patients. The apparent increase in number of publications in the past 5 years describing LT after HCT likely reflect the rise in the number of HCT recipients who are living longer, the increasing number of LT programs worldwide, as well as cumulative accrual of these LT after HCT recipients over time.

Based on the growing list of indications for HCT, as well as the increasing number of long-term HCT survivors, we can expect to see more HCT recipients who experience late-onset pulmonary complications. The number of allogeneic HCTs performed worldwide increased from 2006 to 2008 to exceed 20,000 annually [27]. One-year survival approached 60% in 2010 [28] and continues to improve. Approximately 30% to 50% of these long-term survivors will develop cGVHD [29], and 14% will develop BOS [3]. Patients with BOS, along with patients with other treatment-related pulmonary complications, such as interstitial lung disease, yield a substantial population for whom LT could be considered. In 2011, 3747 LTs were performed worldwide (26% single and 74% bilateral); 97% of recipients were age >17 years [4]. The use of LT is limited by donor organ availability as well as recipient characteristics, which in the setting of HCT may include other morbidities related to the previous graft. Because of the scarcity of donor lungs, this life-saving procedure is necessarily limited to patients with the most urgent need for intervention with factors that confer a high likelihood of a good outcome.

Outcomes

Given the heterogeneity in age, transplant type, era of transplantation, and limited data available for the 70 patients identified in our study, a statistically meaningful comparison of long-term outcomes for LT after HCT with LT overall is not possible. However, we can conclude that long-term survival with a good quality of life is possible in some patients, as observed in our cohort as well as in the reviewed literature.

In our cohort, the 1-year survival after LT of 89% is comparable to the 2010 national 1-year survival of 87% reported by the Organ Procurement and Transplantation Network/Scientific Registry of Transplant Recipients (OPTN/SRTR) [30]. This organization administers the unified national waiting list for solid organ transplant candidates, and maintains data from every organ donation and transplant event occurring in the United States since 1987. Our cohort's 37% 5-year survival is comparable to the 39% survival rate of

Table 2
Publications Reporting Cases of LT after HCT

Reference	Year of Publication	First Author	Journal	Location of LT	n	Age at HCT, yr	Age at LT, yr	Indication for LT	Follow-Up	Outcome at Publication (n ≥3)
5	1992	Calhoon	Chest	San Antonio, Texas	1	19/23	25	PF	9 mo	
7	1994	Gascoigne	Chest	England	1	Unknown	27	BOS	9 mo	
8	1994	Boas	Chest	University of Pittsburgh Children's Hospital	1	5	14	GVHD of lung (BOS and fibrosis)	15 mo	
9	1995	Svendsen	Eur Resp J	Denmark	1	5	11	GVHD of lung	14 mo	
10	1999	Svendsen	J Heart Lung Transplant	Denmark	1[9]*	5	11	GVHD of lung	14 mo	
11	2001	Heath	Transplantation	Pittsburgh, Philadelphia	4†	3-16	30, 13.5, 6, 14.5	GVHD of lung (3), PF (1)	3-6 yr	2 deaths at 3 and 6 yr, 2 alive at 5.5-6 yr
12	2001	Rabitsch	Transplantation	Austria	1	37	38	BOS	23 mo	
13	2003	Pechet	J Heart Lung Transplant	St Louis Children's Hospital	6	Not reported	12.4 (mean)	BOS (3), PF (3)	>48 mo	2/3 (67%) survival
14	2005	Sano	Ann Thoracic Surg	Okayama, Japan	1	29	34	BOS	38 mo	
15	2007	Okumura	Int J Hematol	Kanazawa, Japan	1	17	24	BOS	30 mo	
16	2007	Shiraishi	J Thorac Cardiovasc Surg	Fukuoka City, Japan	1	1	4	BOS	Immediate	
17	2007	Au	J Heart Lung Transplant	Hong Kong	1	Not reported	29	BOS	6 mo	
18	2008	Yamane	Transplantation	Okayama, Japan	7[14]‡	Not reported	6, 13, 23, 24, 27, 29, 45	BOS (6), PF (1)	38 mo	5/7 (71%) survival
19	2009	Oshima	Int J Hematol	Okayama, Japan	1[18]§	8	13	BOS	30 mo	
20	2010	Redel-Montero	Transplant Proc	Cordoba, Spain	3	8-27	36, 36, 34	BOS	9 mo to 8 yr	100% survival
21	2012	Whitson	Clin Transplant	University of Minnesota	4	6-53	40, 20, 30, 59	GVHD of lung (2), PF (2)	19-119 mo	100% survival
22	2012	Kim	Yonsei Med J	Seoul, Korea	1	Not reported	21	BOS	10 mo	
23	2012	Yousef	Pediatr Transplant	Multicenter (US, Switzerland, Austria)	11[11]‖	1-12	15 (median)	BOS (5), GVHD (3), PF (3)	19 mo (median)	7/11 (64%) survival
24	2013	Vogl	Transplantation	Austria	7[12]¶	24 (median)	Not reported; all >18	BOS (7)	1 mo to 16 yr	3/7 (43%) survival
25	2013	Holm	Bone Marrow Transplant	Nordic countries (Finland, Norway, Sweden, Denmark)	13	24 (median)	34 (median)	BOS (13)	4.2 yr (median)	1-yr survival, 90%; 3-yr survival, 78%; 5-year survival, 75%

PF indicates pulmonary fibrosis.
* Reported in [9].
† Reported in [8].
‡ One case reported in [14].
§ Reported in [18].
‖ One case reported in [11].
¶ One case reported in [12].

LT recipients reported in 1990, but inferior to the 57% rate reported in 2006, the last year for which data are available (Figure 2) [30]. Our cohort underwent LT between 1990 and 2010, during which long-term outcomes for LT of all types of recipients steadily improved [31].

LT, like HCT, carries significant associated risks and complications. In our review series, BOS was the most common indication for LT as well as the most common post-LT complication and cause of death or indication for retransplantation. BOS is the leading cause of death beyond the first year post-LT, and nearly 50% of recipients develop BOS by year 5 post-LT [32]. As with BOS after HCT, few therapeutic options are available for progressive BOS after LT. Immunosuppression after LT is lifelong, conferring the risk of opportunistic infections, malignancy, and systemic side effects. Some 40% of deaths within the first year after LT, and 20% of deaths after the first year, are due to infection, and more than 10% of long-term deaths are due to malignancy [4].

Recipients of LT after HCT tend to be younger than LT recipients overall. More than one-third of the cases in this review were pediatric patients at the time of LT. In contrast, <3% of LT recipients are age <18 years; most of these are patients with cystic fibrosis age 12 to 17 years [33]. In addition to the pediatric cases reported, most adult cases were younger at the time of LT than the average LT candidate, which also reflects the younger age of HCT recipients historically. The median age at LT of our FHCRC cohort was 34 years; worldwide, it was 56 in 2011. In the most recent series reported by Holm et al. [34], the median age at HCT was 24 years, with a median time to LT of 8.2 years. In adult patients, older age has been associated with increased risk of mortality.

Twelve cases of LDLLT have been reported among HCT recipients, ranging in age from 4 to 45 years. All but 1 of these procedures were performed in Japan. LDLLT is an uncommon procedure. Obvious advantages of this technique include eliminating the time factor of waiting for a cadaveric donor. Whereas chronic immunosuppression could be avoided if the living lobar donor were also the donor of the previous HCT, functional outcome after a single LT likely would be suboptimal. In 3 cases, a pediatric patient received a lung allograft from the mother, who was also the donor of the previous HCT [9,10,16,19]. Chimerism from the HCT induced tolerance of the lung allograft, obviating the need for chronic immunosuppression. The tolerance induced by chimerism also has been reported in renal transplantation after HCT [35,36].

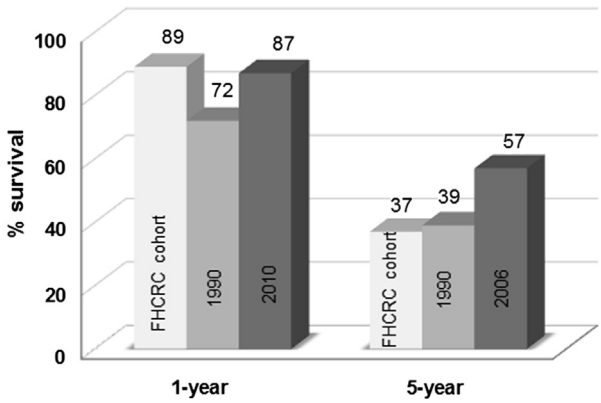

Figure 2. One-year and 5-year survival of the FHCRC cohort (n = 9) compared with national outcomes. Survival outcome is shown for all LTs performed in the United States for the year shown on the bar graph. Survival data obtained from the 2011 Annual Data Report published by OPTN/SRTR, accessed online January 31, 2014.

From a practical standpoint, LDLLT may be challenging because it requires more than 1 donor unless the recipient is a small child. Since the implementation of the Lung Allocation Score in the United States in 2005, which prioritizes the waiting list by need rather than by time of listing, the time to obtaining a suitable cadaveric allograft has declined significantly, thus obviating the need for LDLLT [31]. Only 12 LDLLT procedures have been performed in the United States since 2005 (based on OPTN data as of February 21, 2014 at http://optn.transplant.hrsa.gov).

Relapse of the original indication for HCT is a limitation that can adversely affect the outcome of LT, but a previous history of cancer does not automatically disqualify a patient for consideration of LT. In 2006, the International Society for Heart and Lung Transplantation (ISHLT) published guidelines for the selection of LT candidates, based on retrospective registry data and expert consensus opinion. These guidelines suggest that absolute contraindications include malignancy within the past 2 years, as well as any other end-organ failure (Table 3) [37]. The appropriate time frame in which one can be deemed free of recurrence is matter of expert consensus, although there are reports suggesting that in patients with a history of previous malignancy, the risk of recurrence is greatest within the first year and significantly lower after 5 years [38].

Nearly all of our cases conformed to the 2006 ISHLT guidelines proposing that LT is contraindicated in patients who have had malignancy within the past 2 years [37]. Most cases had much longer intervals between HCT and LT (median, 5 years), but in a few cases, the progression and severity of the lung disease prompted LT earlier than 2 years from HCT. In an Austrian series reported by Vogl et al. [24], the median time between HCT and LT was 18 months, with a range of 6 months to 120 months, likely reflecting the relatively early onset of pulmonary GVHD at a median of 8.2 months after HCT in this cohort. One patient died of a secondary malignancy (myxofibrosarcoma) at 24 months after LT.

In our series, only 1 patient experienced recurrence of the original hematologic disease after LT, which she underwent at 9.4 years after undergoing allogeneic HCT for chronic myelogenous leukemia. The indication for LT was primary pulmonary arterial hypertension thought to be unrelated to the HCT. This patient lived for 7.3 years after LT, and died of pulmonary infection and active chronic myelogenous leukemia. The only other reported malignant complication after LT was reported in a Scandinavian series, in which 1 of the 2 deaths was a patient who died with relapsed acute myelogenous leukemia at 2.1 years after allogeneic HCT and 1.1 years after bilateral LT [25].

Considerations in the Selection of LT Candidates after HCT

Specific recommendations for the selection of LT candidates after HCT must be extrapolated from our knowledge of

Table 3
Contraindications to LT (Summary of ISHLT 2006 Guidelines)

Absolute	Relative
• Malignancy within last 2 years	• Age >65 years
• Advanced dysfunction of other organ system	• Critical condition
• Noncurable chronic infection	• Poor functional status
• Chest wall deformity	• Colonization with resistant organisms
• Noncompliance	• Body mass index >30
• Lack of social support	• Severe osteoporosis
• Substance abuse	• Mechanical ventilation

common indications and the ISHLT generalized consensus guidelines, as well as considerations specific to HCT survivors. In addition to a history of malignancy or hematologic disease, the HCT population is distinguished from conventional LT candidates by late complications of GVHD and ongoing systemic immunosuppression. The evaluation of potential candidates for LT should include assessment and consideration of extrapulmonary morbidities. In the HCT population, hematologic cell populations, as well as cellular and humoral immune function, should be evaluated. The presence and activity of systemic GVHD manifestations and treatment complications must be considered as well. Malabsorption, nutritional compromise, hepatic dysfunction, renal dysfunction, and esophageal disease pose additional potential risks for LT. Significant immunosuppression requirements for control of GVHD suggest continued systemic disease activity and may preclude LT.

Patient factors that likely improve the chances of a good long-term outcome include young age, at least 2 years post-HCT free of relapse from original hematologic malignancy, and lack of other end-organ dysfunction or manifestations of severe active cGVHD that require treatment with immunosuppressive agents.

CONCLUSION

LT after HCT is a viable therapeutic option for patients cured of their hematologic disease and whose only significant post-HCT morbidity is end-stage lung disease. Our case series and review of the literature suggest that select patients with a history of hematologic malignancy or disease treated by HCT can have acceptable long-term outcomes after LT. Ideal candidates should have a prolonged period of malignancy-free survival after HCT, minimal extrathoracic disease with minimal chronic manifestations of GVHD, minimal immunosuppressive needs for GVHD treatment, and normal engraftment and immune function. As the HCT survivor population continues to grow, consensus guidelines and a prospective international registry are necessary to further refine selection criteria for LT.

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