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Risk Factors for Solid Organ Graft Failure and Death in Hematopoietic Cell Transplant Recipients Undergoing Solid Organ Transplantation- A Retrospective Center for International Blood and Marrow Transplant Research (CIBMTR) and Organ Procurement & Transplantation Network Study

Meera Gupta, MD, MSCE[1], **Michelle L. Schoettler, MD, MS**[2], **Ruta Brazauskas, PhD**[3,4], **Stephanie Bo-Subait, MPH**[5], **Gabriel Orozco, MD**[6], **Minoo Battiwalla, MD, MS**[7], **David Buchbinder, MD, MSHS**[8], **Betty K. Hamilton, MD**[9], **Bipin N. Savani, MD**[10], **Hélène Schoemans, MD, PhD**[11], **Mohamed L. Sorror, MD, MSc**[12], **Sairah Ahmed, MD**[13], **Sherif M. Badawy, MD, MS, MBA**[14], **Vikas Bhushan, MD**[15], **Kelly Birdsey, BA**[16], **Daniel Couriel, MD MS**[17], **Erin E. Doherty, MD**[18], **Michelle Donato, MD, MBA**[19], **Sherif S. Farag, MD, PhD**[20], **Jonathan Gutman, MD**[21], **Mitchell Horwitz, MD**[22], **Najla El Jurdi, MD**[23], **Joseph E. Maakaron, MD**[24], **Richard T. Maziarz, MD**[25], **Luis Pineiro, MD**[26], **Gary Schiller, MD**[27], **Daniel J. Weisdorf,**

Corresponding Author: Rachel Phelan, MD, MPH, 8701 Watertown Plank Rd, MFRC 3018, Milwaukee, WI 53226, rphelan@mcw.edu.

*Authors contributed equally

AUTHORSHIP:

MG, RB, DP, PLA and MHL participated in the initial research design, acquisition of the data, the data analysis and in the writing of the paper. MG, MLS, SBS, BS, and RP were responsible for study design updates, analyzing data and interpreting results, and writing and editing the manuscript. GO, MB, DB, BKH, BS, HS, and MS assisted in study design updates and critically reviewed analysis and the manuscript and provided formative commentary.

SA, SMB, VB, KB, DC, ED, MD, SF, JG, MH, NEJ, JM, RM, LP, GS, DW, and BMW critically reviewed the manuscript and provided formative commentary.

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MD[28], **Basem M. William, MD**[29], **Bronwen E. Shaw, MD, PhD**[4], **Rachel Phelan, MD, MPH**[4,30], **David L. Porter, MD**[31], **Peter L. Abt, MD**[32,*], **Matthew Levine, MD PhD**[33,*]

[1]Division of Transplantation, Department of Surgery, University of Kentucky, College of Medicine, Lexington, KY, USA

[2]Children's Healthcare of Atlanta, Aflac Blood and Cancer Disorder Center, Emory University, Atlanta, GA

[3]Division of Biostatistics, Institute for Health and Equity, Medical College of Wisconsin, Milwaukee, WI

[4]CIBMTR® (Center for International Blood and Marrow Transplant Research), Medical College of Wisconsin, Milwaukee, WI

[5]CIBMTR® (Center for International Blood and Marrow Transplant Research), NMDP, Minneapolis, MN

[6]Oregon Health and Science University, Portland, OR

[7]Sarah Cannon Transplant and Cell Therapy Network, Nashville, TN

[8]Division of Pediatric Hematology, Children's Hospital of Orange County, Orange, CA

[9]Blood & Marrow Transplant Program, Cleveland Clinic Taussig Cancer Institute, Cleveland, OH

[10]Division of Hematology/Oncology, Department of Medicine, Vanderbilt University Medical Center, Nashville, TN

[11]Department of Hematology, University Hospitals Leuven, Leuven, Belgium and Department of Public Health and Primary Care, ACCENT VV, KU Leuven – University of Leuven, Leuven, Belgium

[12]Clinical Research Division, Fred Hutchinson Cancer Center and Department of Medicine, University of Washington School of Medicine, Seattle, WA

[13]Department of Lymphoma/Myeloma and Stem Cell Transplantation, University of Texas, MD Anderson Cancer Center, Houston, TX

[14]Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL and Division of Hematology, Oncology, and Stem Cell Transplantation, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL

[15]Medical City Dallas Hospital, Dallas, TX

[16]The Colorado Blood Cancer Institute, a part of Sarah Cannon Cancer Institute at Presbyterian/St Luke's Medical Center, Denver CO;HCA Healthcare, Nashville, TN

[17]Transplant and Cellular Therapy Program, Huntsman Cancer Center Institute, University of Utah, Salt Lake City, Utah

[18]Baylor College of Medicine/Texas Children's Hospital, Houston TX

[19]Hackensack University Medical Center, Hackensack, NJ

[20]Stem Cell Transplant and Cellular Therapy Institute, Community Health Network MD Anderson cancer Center, Indianapolis, IN

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[21]Division of Hematology, University of Colorado, Aurora, CO

[22]Duke University Medical Center, Durham, NC

[23]Division of Hematology, Oncology and Transplantation, Department of Medicine, University of Minnesota, Minneapolis, MN

[24]Division of Hematology, Oncology and Transplantation, Department of Medicine, University of Minnesota, Minneapolis, MN;

[25]Knight Cancer Institute, Oregon Health and Science University, Portland, OR

[26]Baylor University Medical Center, Dallas, TX

[27]Hematological Malignancy/Stem Cell Transplant Program, David Geffen School of Medicine at UCLA, Los Angeles, CA

[28]Division of Hematology, Oncology and Transplantation, Department of Medicine, University of Minnesota, Minneapolis, MN

[29]Ohio Health Blood and Marrow Transplant and Cell Therapy program, Columbus, Ohio

[30]Division of Pediatric Hematology/Oncology/Blood and Marrow Transplant, Department of Pediatrics, Medical College of Wisconsin, Milwaukee, WI

[31]Center for Cell Therapy and Transplant, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA

[32]Hospital of the University of Pennsylvania, Department of Surgery, Division of Transplantation, Philadelphia, PA

[33]Perelman School of Medicine University of Pennsylvania and Children's Hospital of Philadelphia, Philadelphia, PA

Abstract

Background: There is a growing population of hematopoietic cell transplantation (HCT) survivors who later require a solid organ transplant (SOT). However, there are limited data on survival, risk factors for SOT graft loss, and death.

Methods: This is a retrospective Center for International Blood and Marrow Transplant Research study including recipients of HCT followed by SOT between 2001 and 2017. HCT data were merged with data from the Organ Procurement & Transplantation Network.

Results: Eighty patients underwent autologous (45%) or allogeneic (55%) HCT followed by single SOT. Common indications for HCT included leukemia/myelodysplastic syndrome (45%) and plasma cell disorders (38.8%). The median time from HCT to SOT was 47.7 months. There were 49 kidney, 26 thoracic, and 5 liver transplants. Overall survival from SOT was significantly different by organ (p=0.01). Three-year OS by organ type was 85% among kidney, 70.7% thoracic, and 30% liver SOT recipients. Significant risk factors (RF) for death included lymphoma versus plasma cell disorders, and SOT type; thoracic and liver SOT carried greater risk of death than kidney SOT. There was no significant difference in SOT failure incidence by SOT type; 3-year

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overall incidence was 27.8%. RF for SOT graft loss included lymphoma, liver SOT, and positive recipient cytomegalovirus status at SOT.

Discussion: In this study, liver SOT recipients had inferior outcomes. However, renal and thoracic SOT recipients after HCT have acceptable outcomes compared to the general SOT population, and thus SOT should be considered a viable treatment option in these patients.

INTRODUCTION

Hematopoietic cell transplantation (HCT) is the only curative therapy for many patients with malignant and non-malignant disorders[1, 2]. Over 20,000 HCTs are performed in the United States (US) every year[3, 4], and survival among HCT recipients continues to increase [5–7]. Despite increases in survival, HCT remains associated with significant morbidity and mortality. Toxicities from chemotherapy, medications, complications such as infection and graft-versus-host disease, and the exacerbation of underlying co-morbidities may result in the development of end-organ damage [3, 8–14]. Organ failure accounts for up to 14% of deaths 100 days post matched donor allogeneic HCT [15] and up to 9% among longer-term (>15 years) disease-free survivors of HCT [16].

For many patients with terminal organ damage after HCT, solid organ transplantation (SOT) may be the only effective treatment option. Given the significant short- and long-term toxicities related to HCT, these patients may be at increased risk of mortality. Some studies have reported lower survival rates after SOT among patients with prior history of HCT compared to the overall SOT population[13,14]. Data are limited and outcomes after SOT remain poorly defined. The aim of this study was to assess overall survival and solid organ graft failure among patients with a history of HCT who subsequently received a SOT in a large cohort of patients using data from the Center for International Blood & Marrow Transplant Research (CIBMTR) and Organ Procurement and Transplantation Network (OPTN).

METHODS

Data Source

The CIBMTR® (Center for International Blood and Marrow Transplant Research®) is a research collaboration between the Medical College of Wisconsin and NMDP. It comprises a voluntary working group of more than 380 participating centers worldwide that contribute detailed data on cellular and gene therapies. Participating centers are required to report all HCTs consecutively and data audits of participating centers ensure data quality. Studies conducted by the CIBMTR are performed in compliance with all applicable US federal regulations pertaining to the protection of human research participants. Protected Health Information used in the performance of such research is collected and maintained in CIBMTR's capacity as a Public Health Authority under the HIPAA Privacy Rule.

Globally, as required by that country's laws and regulations governing human subjects and privacy protection, the center is responsible for obtaining any necessary institutional review and approval of protocols. The center obtains consent of each patient participating in the research protocol.

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The Organ Procurement and Transplantation Network (OPTN) is a public-private partnership that links all professionals involved in the U.S. solid organ donation and transplantation system. The United Network for Organ Sharing (UNOS) is an independent contractor employed by the United States Congress to run the OPTN, which collects data on every solid organ donation and transplant event occurring in the U.S. since October 1, 1987. The registry is a secure internet-based transplant information database created to enable the nation's organ transplant institutions to register patients for transplants, match donated organs to waiting patients, and manage the data of all patients, before and after solid organ transplantation. This system is being used by all United States organ transplant programs, organ procurement organizations, and histocompatibility (tissue typing) laboratories.

Study Design/Data Acquisition

This is a retrospective cohort study of patients undergoing HCT followed by SOT registered in the CIBMTR and OPTN/UNOS between 2001 and 2017. Subjects registered in CIBMTR and OPTN/UNOS were identified and confirmed using name, social security number and date of birth. Data from both registries were merged and de-identified by the National Marrow Donor Program (NMDP). The principal investigators of the study received separate de-identified datasets from each source and merged them for analysis using subject's unique UNOS ID as the identifier. Appropriate CIBMTR review committee study approval, HRSA agreements, and IRB approvals for this study were obtained prior to data merging. Figure S1 shows the schema for merging the data from OPTN and CIBMTR databases and data analysis.

Of the 1,312,249 total records available in the UNOS/OPTN registry (all entries for all candidates and/or recipients), 345 SOT records matched to HCT records in the CIBMTR. A total of 265 records were excluded: 71 duplicates, 6 never received HCT, 73 who were listed for but never received SOT, 21 who received more than 1 SOT or HCT, and 10 who did not consent to research. One additional record was excluded because the death dates did not match. Of the remaining 163 matching records, 83 were identified to have undergone initial SOT followed by HCT (outcomes reported in companion manuscript), leaving 80 subjects who underwent initial HCT followed by subsequent SOT (Figure 1).

Statistical Analysis

Variables from both CIBMTR and OPTN registries included donor and recipient characteristics, recipient disease and indication for HCT or SOT, graft-versus-host disease[17] (GVHD) prophylaxis prior to HCT[18], transplant date, serologies, Karnofsky/Lansky performance score (KPS) [19], and HCT-comorbidity index. Solid organ graft failure was defined by the OPTN if the organ is no longer functioning as determined by the transplant center (i.e. return to dialysis), patient death, or retransplantation.[20] The HCT-comorbidity index (HCT-CI) is comprised of 17 different categories of organ dysfunction. It is predictive of overall mortality as well as non-relapse mortality risk after HCT.[21]

Summary statistics were used to describe patient, disease, and treatment characteristics. Categorical variables were expressed as counts (n) and percentages (%), and continuous variables were expressed as medians and interquartile ranges (IQR). The primary outcomes

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analyzed were overall survival and solid organ graft failure. Gray's test was used to compare cumulative incidence by organ type. Survival probabilities were estimated using Kaplan-Meier product limit estimates. Log-rank test was used to compare survival experience between groups of patients. Survival was estimated from time of SOT and all surviving patients were censored at the last contact date. Univariable Cox proportional hazards regression model was used to identify variables associated with overall survival from the time of SOT and solid organ graft failure after SOT. Multivariable analysis was not performed due to limited sample size. This manuscript is largely descriptive given the small sample size and our inability to generate significant conclusions among those undergoing liver and thoracic transplants. To that end, we have provided 95% confidence intervals for all estimates instead of p-values. A significance level of 5% was used throughout ($p<0.05$).[22–23] All statistical analyses were performed using SAS 9.4 software. (SAS Institute, Cary, NC).

RESULTS

Patient, Disease, and HCT Characteristics:

From 2001 to 2017, 80 patients were identified who received an autologous or allogeneic HCT followed by SOT. Most patients were male (68.8%) and White (86.3%), with a median age of 45 years at the time of HCT (IQR: 26.1–57.7). There were 36 recipients of autologous HCT (45%) and 44 recipients of allogeneic HCT (55%). Most patients underwent HCT for malignancy (78/80 97.5%). Acute leukemia (myeloid or lymphoid)/myelodysplastic syndrome (45%) and plasma cell disorders (38.8%) were the most common indications. At the time of HCT, most patients had a Karnofsky/Lansky score of ≥90 at HCT (71.3%), however, over half (53.8%) of patients had an HCT-CI of 2 or more, indicating a co-morbid patient population with potential organ dysfunction at baseline prior to HCT. The majority (n= 69, 86.3%) of patients received myeloablative conditioning for HCT, while others received reduced-intensity conditioning or non-myeloablative conditioning (n=10, 12.5%; data not shown). Chemotherapy alone was the most frequent conditioning regimen (72.5% overall), versus a combination of total body irradiation plus chemotherapy (27.5%). Data not shown.

Patient HCT characteristics stratified by HCT type, allogeneic and autologous, are described in Tables 1A and 1B respectively. Among allogeneic HCT recipients, 18 (40.9%) received a related HCT, 21 (47.7%) an unrelated HCT, and 5 (11.4%) an umbilical cord HCT. Patient in the autologous HCT cohort were older [54.3(45.8–63.1) vs 31.0(19.7–48.6)years, respectively] and more likely to a higher 3+ HCT-CI [16(44.4%) vs 9(20.5%)], compared to patients undergoing allogeneic HCT. Among allogeneic HCT recipients, the most common stem cell source was peripheral blood stem cells (PBSC, n=23, 52.3%). Graft-versus-host disease (GVHD) prophylaxis included a calcineurin inhibitor, most commonly tacrolimus (n=30, 68.2%), and either mycophenolate mofetil (n=13, 29.5%) or methotrexate (n=23, 52.3%), with or without other agents. Grade 2–4 acute and chronic GVHD occurred prior to SOT in 47.7% (n=21) and 84.1% (n=37) of patients, respectively.

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SOT Characteristics:

The most common SOT was a kidney transplant (n=49, 61.3%), followed by thoracic transplant (n=26, 32.5%) (heart [n=2] or lung [n=24]), and liver transplant (n=5, 6.3%). Of the 44 patients undergoing kidney transplant with HCT-CI data available, 26 (59.1%) patients had moderate or severe renal impairment and 4 patients (9.1%) had a diagnosis of diabetes prior to HCT. Of the 21 patients who received a heart or lung transplant and had HCT-CI data available, 9 (42.9%) had evidence of moderate or severe pulmonary dysfunction and 2 (9.5%) had evidence of cardiac disease prior to HCT. Both recipients of heart transplants had pre-HCT comorbidity of cardiac disease (any history of coronary artery disease, congenital heart failure, or low ejection fraction).

Among each organ group, those who received a thoracic transplant or liver transplant were notably younger at the time of HCT (median age at HCT was 29.2 years and 25.3 years, respectively) than those requiring kidney transplant (median age at HCT was 51.7 years). The overall median time interval between HCT and SOT was 47.7 months (IQR 25.7–66.1). By SOT type, median time interval was 53.2 months in thoracic, 46.8 months in kidney, and 10.1 months in liver. The time from listing to SOT was 2.1 months for thoracic transplant (IQR: 0.6–5.2), 17.5 months for kidney transplant (IQR: 4.7–31.7), and 1.3 months for liver transplant (IQR: 0.3–3.9).While 60% of liver transplant occurred within one year, most kidney and thoracic transplants occurred 1–5 years after HCT.

Among patients who underwent an autologous HCT, 91.7% subsequently received a kidney transplant (n=33), and 8.3% received a thoracic transplant (n=3). Among patients who underwent allogeneic HCT, 52.3% received a thoracic transplant (n=23), 36.4% a kidney transplant (n=16), and 11.4% a liver transplant (n=5). All 5 patients who received a liver transplant had leukemia/myelodysplastic syndrome, while most patients who underwent kidney transplant had plasma cell disorders/multiple myeloma (57.1%).

The most common indications for solid organ transplantation included GVHD (n=8 thoracic and 1 liver transplant), bronchiolitis obliterans (n=9 lung transplants), interstitial pulmonary fibrosis (n=6 lung transplants), Focal Segmental Glomerulosclerosis (FSGS)/Systemic Lupus Erythematosus(SLE)/Hemolytic Uremic Syndrome(HUS) (n=6 kidney transplants), hypertensive nephropathy (n=5 kidney transplants), disease related [myeloma/lymphoma (n=6 kidney transplants)] and restrictive cardiomyopathy (n=2 heart transplants).

Living Donor Solid Organ Transplantation:

Of the 49 kidney recipients, 27 (55.1%) received a living donor kidney transplant, of which 10 were from blood-related donors. Two of the 5 liver recipients (40%) received a living donor liver transplant. The median time from HCT to SOT among those who received a living donor organ transplant (n=29) was 38.1 months, compared to 53.6 months for patients receiving organs from deceased donors. The median time from SOT listing to date of living donor kidney or liver transplant was 7.2 months compared to 5.7 months for the whole cohort. There was one living donor liver transplant that was performed within 3 months of the HCT. The identity of the allogeneic HCT donors and their living organ donors were not available to determine if both transplanted HCT and SOT grafts were from the same donor.

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Univariable analysis of overall survival (HR 2.06, CI 0.73–5.83] and graft failure [HR 1.80, CI 0.68–4.77] showed no significant difference in outcomes between deceased vs living donor transplant after HCT. (Table 2).

Overall Survival after HCT-SOT:

The median time of follow-up after SOT was 27.6 months. Overall 1-, 3-, and 5-year survival was 93.6%, 75.7%, and 69.6%, respectively. Overall survival (OS) was significantly different by SOT type; liver SOT had the lowest OS and kidney SOT had the greatest (p= 0.01, Figure 2). Three-year OS after SOT was 85% (95% CI 70.1–95.4%) for kidney, 70.7% (95% CI 48.7–88.5%) for thoracic, and 30% (95% CI 0.5 −78.6%) for liver SOT. Cause of death included primary hematologic malignancy (n=5), organ failure (n=4), infection (n=2), GVHD (n=1), secondary malignancy (n=1), other cause (n=4), and unknown (n=2). Notably, cancer relapse was the cause of death in only 27.8% of patients who received an HCT for malignancy and subsequently died.

There were no significant differences in overall survival among those who received an allogeneic HCT stratified by organ type (p=0.08, Figure 3). However, overall survival appeared lower among thoracic transplant recipients who had received a prior allogeneic HCT (3-year OS, 66.3% 95% CI 42.3–86.6%) compared to autologous HCT (100% 3-year survival). In contrast, there were no discernable differences in OS among kidney transplant recipients who had a prior allogeneic HCT (84% 3-yr survival, 95% CI 59–98.4%) versus autologous HCT (84% 3-yr survival, 95% CI 62.8–97.2%).

In a univariable analysis, risk factors for mortality included indication for HCT and the type of SOT. Patients diagnosed with lymphoma had a higher risk of mortality compared to those with plasma cell disorders/multiple myeloma (HR=8.7, 95% CI=1.66–45.69). Receiving a thoracic (HR=2.97, 95% CI 1.07–8.17) or liver transplant (HR=6.39, 95% CI 1.57–25.96) was associated with increased mortality compared to a kidney transplant. Age, HCT-CI, transplant type, and other donor/recipient characteristics were not significantly associated with overall survival (Table 3). Although allogeneic HCT recipients appeared to have an increased risk of death (HR= 2.94, 95% CI 0.97–8.92) compared to autologous HCT, this difference was not statistically significant.

SOT Graft Failure:

Solid organ transplant graft failure occurred in 22 patients; the estimated incidences of 1-, 3- and 5-year overall graft failure were 11.3%, 27.8% and 35.2% respectively. While there were no significant differences in graft failure incidence by SOT type (p=0.15), liver transplant recipients appeared to have a higher incidence of early SOT graft failure (40% one-year graft loss). The estimated 5-yr cumulative incidence of SOT graft failure by organ type was 46.2% (95% CI 19.1–74.6%) in thoracic, 21.5% (95% CI 8.4–38.7%) in kidney, and 70% (95% CI 8.5–100%) in liver SOT recipients. Two of the 5 liver transplant grafts were lost due to infection, one of which was also due to graft thrombosis. Kidney losses were attributed to graft thrombosis (n=1), recurrent primary kidney disease (n=1), thrombotic microangiopathy (n=1), hepato-renal syndrome (n=1), BK polyomavirus (n=1), and others/missing (n=5). Of the 9 thoracic organ losses, 3 were due to rejection.

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Univariable risk factor analysis for SOT organ failure demonstrated that patients with lymphoma as compared to plasma cell disorders (HR=4.48, 95% CI 1.06–18.84), positive cytomegalovirus serostatus at the time of SOT (HR=2.59, 95% CI 1.02–6.59), and liver transplantation as compared to kidney transplantation (HR=3.83, 95% CI 1.01–14.49) had significantly higher risk of SOT graft failure (Table 4). Those with prior allogeneic HCT had higher risk of SOT graft failure (HR=1.37, 95% CI 0.55–3.40), but this was not significant.

We explored overall patient and graft outcomes stratified by those with kidney disease prior to HCT (53%) vs those with de novo kidney disease following HCT. Of the 26 patients with preexisting kidney disease, there was only one (3.8%) that died and 4 (15.4%) experienced SOT graft failure after SOT. Among those with de novo kidney disease after HCT, there were 5 deaths (27.8%) and 5 (27.8%) graft losses after SOT during the follow up period. HCT-CI was not associated with graft or patient outcomes.

DISCUSSION

Patients undergoing HCT are at increased risk of developing solid organ failure due to conditioning chemotherapy/radiation, drug toxicities, and GVHD. However, outcomes including SOT graft loss and OS in those who require a SOT after HCT are unclear, and there is little data in the literature to guide practice. Here, we report outcomes of 80 patients who underwent kidney, liver, heart, or lung transplants following allogeneic or autologous HCT. Kidney transplant recipients represented most of the cohort (61.3%), followed by thoracic (lungs and heart, 32.5%) and liver transplant recipients (6.3%).

Chronic kidney disease (CKD) is common after HCT and has been reported in 60–70%[24,25] of HCT survivors. Patients with multiple myeloma/plasma cell disorders commonly have underlying renal dysfunction before HCT through different mechanisms including cast nephropathy, amyloidosis, and monoclonal Ig deposition disease.[26] Among patients who required a kidney transplant in this cohort, we found that at least 53% had a moderate or severe decrease in renal function before HCT; and of those with decreased renal function, plasma cell disorders and multiple myeloma were the main indications for HCT (84.6%).

Glomerular pathologies, immune- mediated nephropathies[27], and treatment-associated nephrotoxicity were also a significant indication for kidney transplant in this cohort. Treatment-associated nephrotoxicity has been associated with drugs commonly used by HCT recipients (e.g., calcineurin inhibitors, antifungals) and are known to accelerate the development of chronic kidney disease in this cohort leading to the need for SOT.[28] Among the 45 allogeneic HCT patients, 88.9% (n=40) were on CNI regimens after HCT for graft versus host disease prophylaxis. Regarding immune-mediated pathologies, whether the donor's immune cells recognize host antigens (alloimmunity, GVHD) or an unbalanced immune system favors the recognition of common antigens to the host and donor (autoimmunity) is a matter of debate[18,25]. Furthermore, case reports of glomerulopathies occurring after autologous HCT reveal a unique and complex immune balance where both, alloimmunity and autoimmunity, can lead to kidney injury[25, 29–31]. Kidney SOT was the only group where a greater proportion of patients underwent autologous HCT (67.3%) and living donor kidney SOT (55.1%).

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In this cohort, solid organ graft failure and patient survival 3 years after SOT among kidney recipients was estimated to be 21.5% and 85%, respectively, which compared to the 3-year SOT only renal graft failure and patient survival reported by UNOS as of July 2022 (4.8% and 86.5%, respectively) reveals worse graft failure, although comparable overall survival.[32] In a systematic review of the literature of outcomes in patients who receive an allogeneic HCT and then SOT, Brockman et al. found similar outcomes reporting 85% patient survival and 12% incidence of graft rejection among 53 kidney transplant recipients [24]. Other authors have reported 3-year survival as high as 100%, however these studies excluded patients with active malignancies or severe infections at the time of SOT[13]. Thus, given relatively acceptable survival outcomes of those who undergo allogeneic and autologous HCT followed by kidney transplant, prior HCT alone should not be a contraindication to renal SOT, but knowledge of risk factors and management of the allograft should be considered and used when counseling the patient.

Pulmonary complications are frequent after HCT and can account for up to 50% of transplant-related deaths[33–36]. Most patients who received a thoracic transplant previously underwent an allogeneic HCT (88.5%) with the most common indications for SOT including interstitial obliterative bronchiolitis, GVHD, and pulmonary fibrosis. The estimated OS and graft failure in this cohort (3-yr 70.7% and 27.8%, respectively) is improved compared to UNOS data on the general population who receive a lung transplant (3-yr OS 58.3% and graft failure 41.7%). Bronchiolitis obliterans syndrome (BOS) has been reported as a main indication for lung transplantation following HCT[37]. Low pre-transplant FEV1/FVC is a known risk factor for BOS[38,39], and 34.6% of patients who received a thoracic transplant in this cohort had previous moderate to severe pulmonary disease. BOS is strongly associated with GVHD, but non-allogeneic factors such as conditioning chemotherapy and infections contribute to its development[36,38–40]. The estimated five-year survival among thoracic recipients was 53%, almost comparable to the 65% reported by Brockmann et al. for lung transplant recipients[24]. In our study, the most common cause of graft failure was chronic rejection (33%) and the most common cause of death was related to complications of the SOT or HCT including GVHD, infection, and organ failure (63%), while death due to recurrence of primary disease occurred in one patient. Only two patients in our cohort required heart transplantation for amyloid restrictive cardiomyopathy. After HCT, use of cyclophosphamide, proteasome inhibitors, or radiation has been associated with restrictive cardiomyopathy requiring heart transplantation [13,24,41]. Together, these data suggest that prior HCT should not be an absolute contraindication to thoracic HCT, although careful patient selection and management is advised.

In line with other HCT followed by SOT data, liver SOT patients had the lowest overall survival in this cohort[24]. Veno-occlusive disease and GVHD have been reported as the most common causes of liver failure requiring liver transplant in HCT recipients[24,42–50]. In our cohort, GVHD was identified as the indication for liver transplant in only one of the five patients. The survival estimates in this study (3-year OS 30%) are notably lower than survival for liver transplant in the general population of 83% 3 years after SOT. Estimated liver SOT graft failure in this was quite high, 70% 3 years after SOT; much higher than the expected 14.2% liver graft loss in the general population. We observed a 30% 3-year OS (95% CI 0.5–78.6) in comparison to that reported by Brockmann et al. who found a

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mortality of 55% at 29 months follow-up among 47 patients; these authors also identified infections as the main cause of death.[24]

When compared to deceased donors, the proportion of living kidney (55%) and living liver (40%) donation was notably higher than for the general transplant population, which based on OPTN data for 2022, represented 23% and 6% of all kidney and liver transplants, respectively.[32] Contrary to the general solid organ transplant population and despite higher mortality and graft failure risk s among deceased donor recipients, we found no significant difference in overall survival and graft failure outcomes between deceased donor and living donor transplants after HCT.[51,52]

Risk factors for death in the whole cohort included an HCT indication of lymphoma compared to those with plasma cell disorders. Despite great heterogeneity in the survival trends after HCT according to the lymphoma subtype, sensitivity to chemotherapy, and HCT type (autologous vs. allogeneic), most subgroups of patients with lymphoma tend to have inferior survival than those with plasma cell disorders. Some exceptions include those with chemosensitive Hodgkin or follicular lymphoma undergoing autologous HCT (89% and 82% 3-year survival, respectively) compared to patients with plasma cell leukemia (48% 3-year survival)[3,53]. Also, our data shows that recipients of liver and thoracic transplantation had approximately 3- and 6-fold decreased survival compared to kidney recipients, respectively. This is similar to the general SOT population where kidney transplantation has better survival than liver and thoracic transplantation; 5-year OS 86–88%, 75–77%, and 32–62%, respectively.[32]

Risk factors for SOT graft failure included a positive CMV serostatus, lymphoma as an HCT indication, and SOT type, with liver at increased risk compared to kidney. Similar to other reports on transplant-recipient populations HCT-SOT patients with positive CMV serostatus had increased risk of graft loss (HR=2.59, p=0.05), with 10(12.5%) of the cohort being donor CMV positive to recipient CMV negative SOT. CMV reactivation can present as a generalized syndrome (fever, arthralgia, cytopenias) or as invasive disease affecting the organs[54,55]. Both clinical presentations have been associated with worse outcomes in transplant recipients[56,57], suggesting a lower threshold for aggressive intervention using current therapeutic strategies to decrease the negative impact of CMV infection on SOT outcomes[,55,58]. There was no significant difference in death and organ loss when comparing allogeneic and autologous recipients.

We acknowledge several limitations to this analysis. As a retrospective and largely descriptive analysis of large databases, some key variables relevant for the HCT-SOT patients were not captured, including the origin of HCT and SOT donors, donor chimerism at the time of SOT, and details of pre-and post-transplant treatments. This study spans over 17 years and we do not have data on adjunct agents used for these patients pre- and post-HCT. Despite the long study period, there were 73 patients who had prior HCT and were listed for SOT, but did not receive the organ. We could not include the outcomes of these 73 patients who did not receive a solid organ, because we do not have detailed data, which are subject to speculation, to determine the few or many reasons for inability to perform solid organ transplant. This study noted that the median time from SOT listing

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to date of living donor kidney or liver transplant was 7.2 months compared to 5.7 months for the whole cohort. The average waiting time for a kidney transplant in the United States is 5–7 years depending on location[32]. The National Kidney Registry reports a 4.9-month average waiting time from enrollment to transplant for living donor kidney transplant. We suspect that given the immunologic complexity, need for closer follow-up and management of HCT, and likely higher antibody profile of the recipient, coordinating and clearing a patient for SOT after HCT may take a little longer. But we do not have this granular data. Additionally, the ability to match patients is limited by the identifiers available and completeness in each registry. The limited number of patients identified also precluded more detailed multivariable analyses, deeming only univariable analysis appropriate for determining factors associated with higher risk of graft failure and survival. That being said, describing the effect size of each predictor is informative regardless of statistical significance. Despite these limitations, we describe outcomes of one of the largest cohort of patients undergoing HCT followed by SOT using 2 large registry databases (OPTN and CIBMTR), offering a unique evaluation of patients that have received sequential transplants in the United States.

In conclusion, we demonstrate that SOT, particularly kidney and thoracic transplants, after HCT are feasible with acceptable organ and patient survival, comparable to the general population. SOT thus offers a valuable therapeutic option for select patients with renal or thoracic failure after HCT. Additional studies and larger patient cohorts are needed to understand why outcomes in liver SOT after HCT differ from other organs and the general population and develop strategies to mitigate complications and improve outcomes. The findings of this study offer clinical utility for clinicians who are faced with selecting patients with prior HCT for SOT, and may be used in counseling such potential candidates with unique challenges they may face compared to the general SOT population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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DATA USE STATEMENT:

CIBMTR supports accessibility of research in accord with the National Institutes of Health (NIH) Data Sharing Policy and the National Cancer Institute (NCI) Cancer Moonshot Public Access and Data Sharing Policy. The CIBMTR only releases de-identified datasets that comply with all relevant global regulations regarding privacy and confidentiality.

ABBREVIATIONS:

CIBMTR	Center for International Blood and Marrow Research
CRF	Comprehensive Report Form
CI	Confidence Interval
CMV	Cytomegalovirus
EBV	Epstein Barr Virus
FSGS	Focal Segmental Glomerulosclerosis
GVHD	Graft-Versus-Host Disease
HR	Hazard Ratios
HRSA	Health Resources and Services Administration
HCT	Hematopoietic Cell Transplantation
HCT-CI	Hematopoietic Cell Transplant-Comorbidity Index
HUS	Hemolytic Uremic Syndrome
HLA	Human Leukocyte Antigen
IRB	Institutional Review Board
MDS	Myelodysplastic Syndrome
NMDP	National Marrow Donor Program
OPTN	Organ Procurement & Transplantation Network
OS	Overall survival
PBSC	Peripheral Blood Stem Cells
RF	Risk Factors
SOT	Solid Organ Transplant
TED	Transplant Essential Data

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UNOS United Network for Organ Sharing

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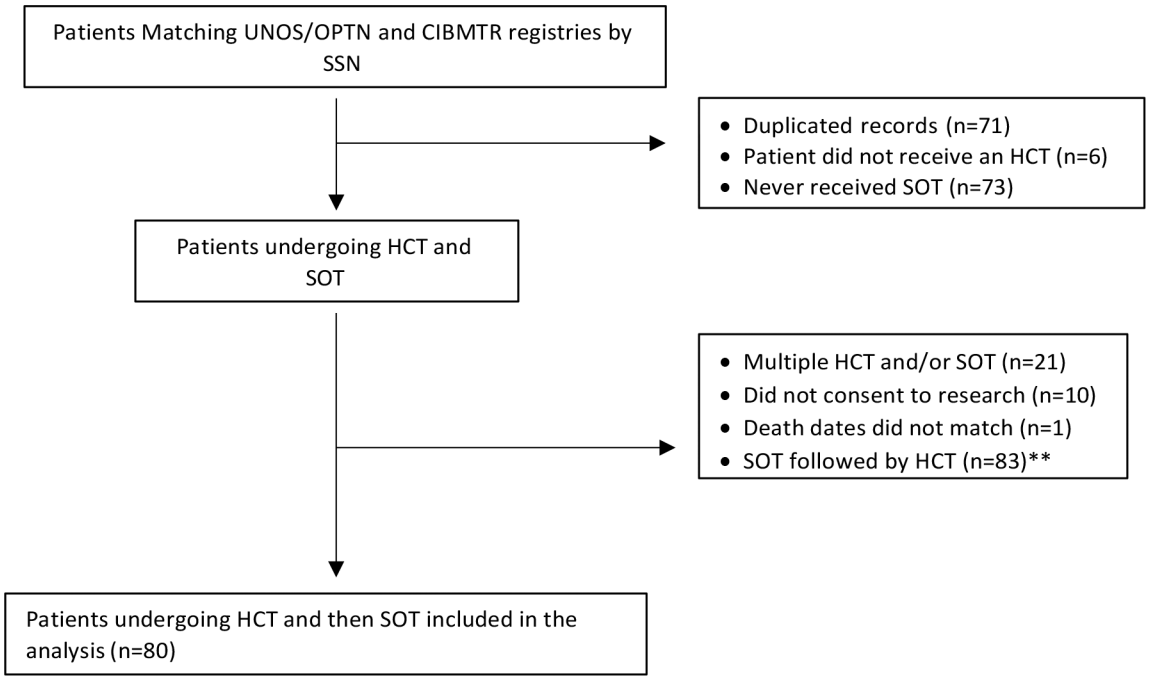


Figure 1: Study Design Diagram

Patients were matched from the United Network for Organ Sharing (UNOS) and Organ Procurement & Transplantation Network (OPTN) and Center for International Blood and Marrow Transplant Registry (CIBMTR) using social security numbers (SSN). There were 71 duplicate records, 6 patients who never received a hematopoietic cell transplant (HCT), and 73 who never received a solid organ transplant (SOT) who were excluded. Of the 195 patients who received both transplant types, an additional 112 were excluded, including 83 patients who received a SOT and then HCT. **Outcomes for these 83 patients are reported in a companion manuscript

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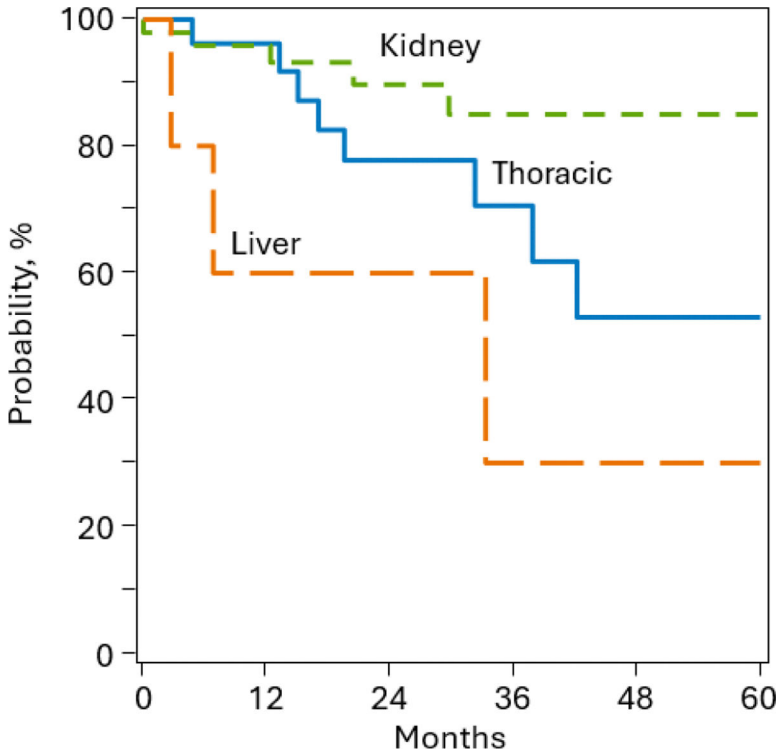


Figure 2: Overall Survival after HCT and SOT by SOT type (n=80)

Overall survival was significantly different by organ type (p=0.01). Estimated 1-year OS by organ type was: 96.2% thoracic, 95.9% kidney, and 60% liver. However, OS declined overtime and estimated 3-yr survival by organ type was: 70.7% thoracic, 85% kidney, and 30% liver.

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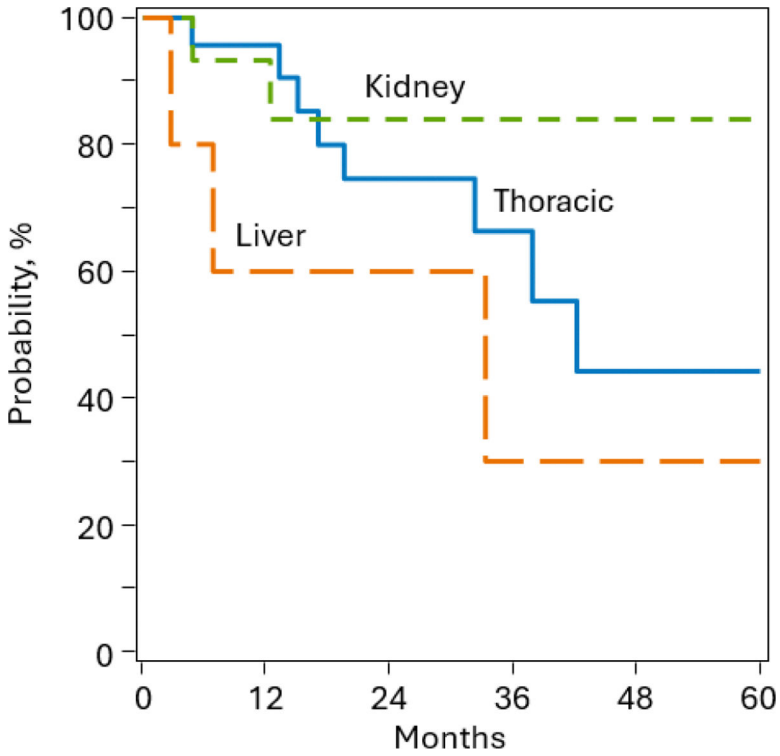


Figure 3: Overall Survival after Allogeneic HCT and SOT by SOT type (n=44)

Overall survival was not significantly different by organ type among allogeneic HCT recipients (p=0.08). Estimated 1-year OS by organ type was: 95.7% thoracic, 93.3% kidney, and 60% liver. OS declined overtime and estimated 3-yr survival by organ type was: 66.3% thoracic, 84% kidney, and 30% liver.

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Table 1.

Baseline and Allogeneic HCT Characteristics of Cohort

Characteristic	Total	Thoracic[a]	Kidney	Liver
No. of patients	44	23	16	5
Recipient race - no. (%)				
Caucasian	40 (90.9)	21 (91.3)	14 (87.5)	5 (100.0)
African-American	1 (2.3)	1 (4.3)	0 (0.0)	0 (0.0)
Other	1 (2.3)	1 (4.3)	0 (0.0)	0 (0.0)
Not reported	2 (4.5)	0 (0.0)	2 (12.5)	0 (0.0)
Recipient sex - no. (%)				
Male	33 (75.0)	17 (73.9)	12 (75.0)	4 (80.0)
Female	11 (25.0)	6 (26.1)	4 (25.0)	1 (20.0)
Recipient age at HCT, years				
Median (25th-75th pctl)	31.0 (19.7–48.6)	28.1 (21.2–50.1)	33.5 (18.8–48.0)	25.3 (3.8–31.5)
HCT Karnofsky/Lansky score - no. (%)				
90–100	36 (81.8)	21 (91.3)	11 (68.8)	4 (80.0)
< 90	5 (11.4)	1 (4.3)	3 (18.8)	1 (20.0)
Not reported	3 (6.8)	1 (4.3)	2 (12.5)	0 (0.0)
HCT-Comorbidity Index - no. (%)				
0	16 (36.4)	10 (43.5)	3 (18.8)	3 (60.0)
2	8 (18.2)	3 (13.0)	4 (25.0)	1 (20.0)
3+	9 (20.5)	5 (21.7)	4 (25.0)	0 (0.0)
Not reported	11 (25.0)	5 (21.7)	5 (31.3)	1 (20.0)
HCT primary disease - no. (%)				
Leukemia/MDS	36 (81.8)	16 (69.6)	15 (93.8)	5 (100.0)
Lymphoma/non-Hodgkin’s disease	4 (9.1)	4 (17.4)	0 (0.0)	0 (0.0)
Plasma cell disorder/multiple myeloma	2 (4.5)	1 (4.3)	1 (6.3)	0 (0.0)
Non-malignant diseases	2 (4.5)	2 (8.7)	0 (0.0)	0 (0.0)
GVHD Prophylaxis prior to HCT - no. (%)				
Ex-vivo T-cell depletion and CD34 selection	2 (4.5)	1 (4.3)	1 (6.3)	0 (0.0)
TAC + MMF ± other(s) (except post-CY)	7 (15.9)	2 (8.7)	5 (31.3)	0 (0.0)
TAC + MTX ± other(s) (except MMF, post-CY)	19 (43.2)	12 (52.2)	5 (31.3)	2 (40.0)
TAC ± other(s) (except MMF, MTX, post-CY)	4 (9.1)	2 (8.7)	1 (6.3)	1 (20.0)
CSA + MMF ± other(s) (except post-CY)	6 (13.6)	2 (8.7)	3 (18.8)	1 (20.0)
CSA + MTX ± other(s) (except MMF, post-CY)	4 (9.1)	3 (13.0)	1 (6.3)	0 (0.0)
Other(s)	1 (2.3)	1 (4.3)	0 (0.0)	0 (0.0)
Not reported	1 (2.3)	0 (0.0)	0 (0.0)	1 (20.0)
HCT graft type - no. (%)				
Bone marrow	16 (36.4)	8 (34.8)	5 (31.3)	3 (60.0)
Peripheral blood	23 (52.3)	15 (65.2)	7 (43.8)	1 (20.0)

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Characteristic	Total	Thoracic[a]	Kidney	Liver
Umbilical cord blood	5 (11.4)	0 (0.0)	4 (25.0)	1 (20.0)
HCT donor type - no. (%)				
HLA-identical sibling	17 (38.6)	13 (56.5)	1 (6.3)	3 (60.0)
Other related	1 (2.3)	0 (0.0)	1 (6.3)	0 (0.0)
Unrelated	21 (47.7)	10 (43.5)	10 (62.5)	1 (20.0)
Cord blood	5 (11.4)	0 (0.0)	4 (25.0)	1 (20.0)
Year of HCT - no. (%)				
2001–2005	9 (20.5)	4 (17.4)	4 (25.0)	1 (20.0)
2006–2010	24 (54.5)	13 (56.5)	7 (43.8)	4 (80.0)
2011–2013	11 (25.0)	6 (26.1)	5 (31.3)	0 (0.0)

[a]Thoracic includes lung (n=23) ; HCT-Hematopoietic Cell Transplant

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Table 2.

Baseline and Autologous HCT Characteristics of Cohort

Characteristic	Total	Thoracic[a]	Kidney
No. of patients	36	3	33
Recipient race - no. (%)			
Caucasian	29 (80.6)	3 (100.0)	26 (78.8)
African-American	7 (19.4)	0 (0.0)	7 (21.2)
Recipient sex - no. (%)			
Male	22 (61.1)	3 (100.0)	19 (57.6)
Female	14 (38.9)	0 (0.0)	14 (42.4)
Recipient age at HCT, years			
Median (25th-75th pctl)	54.3 (45.8–63.1)	37.7 (0.9–54.5)	56.6 (48.3–63.3)
HCT Karnofsky/Lansky score - no. (%)			
90–100	21 (58.3)	1 (33.3)	20 (60.6)
< 90	13 (36.1)	2 (66.7)	11 (33.3)
Not reported	2 (5.6)	0 (0.0)	2 (6.1)
HCT-Comorbidity Index - no. (%)			
0	6 (16.7)	1 (33.3)	5 (15.2)
1	4 (11.1)	1 (33.3)	3 (9.1)
2	10 (27.8)	0 (0.0)	10 (30.3)
3+	16 (44.4)	1 (33.3)	15 (45.5)
HCT primary disease - no. (%)			
Lymphoma/non-Hodgkin’s disease	6 (16.7)	0 (0.0)	6 (18.2)
Plasma cell disorder/multiple myeloma	29 (80.6)	2 (66.7)	27 (81.8)
Other malignancies	1 (2.8)	1 (33.3)	0 (0.0)
Year of HCT - no. (%)			
2006–2010	21 (58.3)	2 (66.7)	19 (57.6)
2011–2013	15 (41.7)	1 (33.3)	14 (42.4)

[a]Thoracic includes heart (n=2) and lung (n=1); HCT-Hematopoietic Cell Transplant

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Table 3:

Solid Organ Transplant (SOT) Characteristics of Cohort

	Total (n=80)	Thoracic[a] (n=26)	Kidney (n=49)	Liver (n=5)
Time from HCT to SOT, months (Median [IQR])	47.7 (25.7–66.1)	53.2 (33.2–66.3)	46.8 (26.6–67.2)	10.1 (2.0–32.8)
Recipient age at SOT, years (Median [IQR])	51.5 (32.0–61.5)	34.5 (26.0–59.0)	55.0 (40.0–65.0)	25.0 (5.0–32.0)
Indication for SOT at time of listing - N (%)				
Thoracic				
Amyloid Restrictive Cardiomyopathy	2 (2.5)	2 (7.7)	0 (0.0)	0 (0.0)
Obstructive Lung Disease	1 (1.3)	1 (3.8)	0 (0.0)	0 (0.0)
Interstitial Pulmonary Fibrosis	6 (7.5)	6 (23.1)	0 (0.0)	0 (0.0)
Bronchiolitis Obliterans	9 (11.3)	9 (34.6)	0 (0.0)	0 (0.0)
GVHD	8 (10.0)	8 (30.8)	0 (0.0)	0 (0.0)
Kidney				
Hypertension	5 (6.3)	0 (0.0)	5 (10.2)	0 (0.0)
Glomerular Disease	1 (1.3)	0 (0.0)	1 (2.0)	0 (0.0)
Diabetes	1 (1.3)	0 (0.0)	1 (2.0)	0 (0.0)
FSGS/SLE/HUS	6 (7.5)	0 (0.0)	6 (12.2)	0 (0.0)
Myeloma/Lymphoma	6 (7.5)	0 (0.0)	6 (12.2)	0 (0.0)
Treatment Induced Disease	2 (2.5)	0 (0.0)	2 (4.1)	0 (0.0)
Other (Wegener's, Amyloid, Other)[b]	28 (35.0)	0 (0.0)	28 (57.1)	0 (0.0)
Liver				
GVHD	1 (1.3)	0 (0.0)	0 (0.0)	1 (20.0)
Other (Drug, NASH, BA, Infiltrative)	4 (5.0)	0 (0.0)	0 (0.0)	4 (80.0)
SOT donor status - N (%)				
Living	29 (36.3)	0 (0.0)	27 (55.1)	2 (40.0)
Deceased	51 (63.8)	26 (100.0)	22 (44.9)	3 (60.0)
Follow-up from SOT, months (median [IQR])	27.6 (15.6–67.4)	35.8 (23.2–72.1)	25.4 (14.0–60.1)	62.4 (19.1–62.4)
Donor/Recipient CMV Status at SOT				
+/+	28(35)	8(30.8)	19(38.8)	1(20)
+/−	10(12.5)	3(11.5)	6(12.2)	1(20)
−/+	15(18.8)	7(26.9)	7(14.3)	1(20)
−/−	23(28.8)	8(30.8)	14(28.6)	1(20)
Unknown/+	2(2.5)	0(0)	1(2)	1(20)
Unknown/+	2(2.5)	0(0)	2(4.1)	0(0)

CMV – Cytomegalovirus, HCT- hematopoietic cell transplant, SOT- solid organ transplant, IQR- interquartile range; FSGS- Focal segmental glomerulosclerosis; SLE- systemic lupus erythematosus; HUS- hemolytic uremic syndrome; NASH- non-alcoholic steatohepatitis; BA- biliary atresia

[a] Thoracic includes heart (n=2) and lung (n=24)

[b] includes amyloidosis (n=15); acute tubular necrosis (n=1); chronic nephrosclerosis-unspecified (n=1); Wegener's granulomatosis (n=1); and other specify: "atypical HUS" (n=1), "BK nephropathy" (n=1), "cast nephropathy-treating myelomas" (n=1), "drug related nephrotoxicity post-BMT"

(n=1), “interstitial fibrosis” (n=1), “multiple myeloma” (n=1), “nephrotoxic medications” (n=1), “post BMT acute kidney injury” (n=1), “sepsis after chemotherapy” (n=1), “thrombotic microangiopathy/radiation nephritis” (n=1)

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Table 4:

Univariable Analysis of Overall Survival of patients receiving HCT followed by SOT

Variable	Events/N	HR (95% CI)	P-value
Recipient age at HCT (years)			
0–17	2/12	1.00	
18–49	9/33	1.93 (0.42–8.99)	0.40
≥50	8/35	1.67 (0.35–7.97)	0.52
Recipient sex			
Male	16/55	1.00	
Female	3/25	0.37 (0.11–1.28)	0.12
Recipient race			
White	18/69	1.00	
Black	1/8	0.60 (0.08–4.52)	0.62
Other	0/1	--	--
Not reported	0/2	--	--
KPS			
90–100	16/57	1.00	
<90	3/18	0.56 (0.16=1.91)	0.35
Not reported	0/5	--	--
HCT-CI			
0–1	8/26	1.00	
2	4/18	0.50 (0.15–1.69)	0.26
≥3	3/25	0.39 (0.10–1.46)	0.16
Not reported	4/11	0.56 (0.15–2.07)	0.38
Disease			
Plasma cell disorder	3/31	1.00	
Leukemia/MDS	12/36	3.20 (0.90–11.44)	0.07
Lymphoma	3/10	**8.70 (1.66–45.69)**	**0.01**
Other	0/1	--	--
Non-malignant	1/2	5.21 (0.53–50.76)	0.16
Conditioning			
Reduced intensity	4/10	1.00	
Myeloablative	15/69	0.69 (0.23–2.12)	0.52
Not reported	0/1	--	--
Disease status			
High risk	5/19	1.00	
Intermediate	10/46	0.72 (0.25–2.11)	0.55
Low risk	2/4	2.13 (0.40–11.22)	0.37
Other	1/3	0.92 (0.11–7.97)	0.94

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Variable	Events/N	HR (95% CI)	P-value
Not reported	1/8	0.30 (0.03–2.55)	0.27
Transplant type			
Autologous	4/36	1.00	
Allogeneic	15/44	2.94 (0.97–8.92)	0.06
Donor			
Auto	4/36	--	--
HLA identical sibling	7/17	1.00	
Other related	0/1	--	0.29
Unrelated	7/21	0.57 (0.19–1.65)	0.35
Cord Blood	1/5	0.37 (0.04–3.00)	
HCT Donor Sex			
Male	7/23	1.00	
Female	8/21	1.38 (0.50–3.82)	0.54
Graft type			
Bone marrow	4/16	1.00	
Peripheral blood	10/23	2.11 (0.65–6.84)	0.21
Cord blood	1/5	0.83 (0.09–7.48)	0.87
Auto transplant	4/36	--	--
Recipient CMV status			
Negative	10/41	1.00	
Positive	9/37	1.34 (0.54–3.36)	0.53
Not reported	0/2	--	--
Donor CMV status		1.00	
Negative	5/18	1.10 (0.36–3.36)	
Positive	10/24	--	0.87
Not reported	0/2		--
Chronic GVHD (allo only)			
No	2/6	1.00	
Yes	12/34	0.48 (0.10–2.32)	0.36
Year of HCT			
2001–2007	5/13	1.00	
2008–2013	14/67	0.97 (0.32–2.88)	0.95
Recipient age at SOT (years)			
0–17	2/7	1.00	
18–49	8/31	1.18 (0.25–5.58)	0.83
≥50	9/42	1.07 (0.23–4.97)	0.93
Solid organ			

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Variable	Events/N	HR (95% CI)	P-value
Kidney	6/49	1.00	
Thoracic[a]	10/26	**2.97 (1.07–8.17)**	**0.04**
Liver	3/5	**6.39 (1.57–25.96)**	**0.01**
SOT donor status			
Living	5/29	1.00	
Deceased	14/51	2.06 (0.73–5.83)	0.17
SOT donor gender			
Male	7/44	1.00	
Female	12/36	1.96 (0.77–5.00)	0.16
SOT donor race			
White	14/58	1.00	
Black	2/13	0.60 (0.14–2.63)	0.49
Other	3/9	1.41 (0.40–4.96)	0.59
Recipient CMV at SOT			
Negative	6/35	1.00	
Positive	13/45	2.59 (0.97–6.92)	0.06
Recipient EBV at SOT			
Negative	6/19	1.00	
Positive	12/53	1.13 (0.41–3.12)	0.81
Not reported	1/8	0.34 (0.04–2.88)	0.32
Donor CMV at SOT			
Negative	8/38	1.00	
Positive	9/38	1.58 (0.61–4.13)	0.35
Not reported	2/4	1.59 (0.32–7.82)	0.57
Donor EBV at SOT			
Negative	0/4		
Positive	16/64	1.00	
Not reported	3/12	0.57 (0.15–2.05)	0.39
Time from HCT to SOT (years)			
0–0.9	2/5	1.00	
1–1.9	2/12	0.33 (0.05–2.33)	0.26
2–4.9	10/38	0.93 (0.20–4.38)	0.93
≥ 5	5/25	1.31 (0.24–7.09)	0.76
Time from HCT to wait list (years)			
0–0.9	3/9	1.00	
1–1.9	1/18	0.16 (0.02–1.56)	0.11

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Variable	Events/N	HR (95% CI)	P-value
2–4.9	9/32	1.42 (0.37–5.40)	0.61
≥ 5	5/15	2.84 (0.62–13.12)	0.18
Pre-HCT	1/5	0.58 (0.06–5.64)	0.64
Time from wait list to SOT (years)			
0–0.9	16/53	1.00	
1–1.9	1/8	0.46 (0.06–3.45)	0.45
2–5	2/18	0.73 (0.16–3.27)	0.68
Not reported	0/1	--	--
SOT donor age			
0–17	1/7	1.00	
18–49	12/54	2.06 (0.27–15.84)	0.49
≥ 50	6/19	3.90 (0.47–32.63)	0.21
Cause of SOT donor death			
Anoxia	1/13	1.00	
Cerebrovascular event	6/14	4.97 (0.60–41.38)	0.14
Head trauma	5/18	2.63 (0.31–22.60)	0.38
C tumor	0/1	--	--
Other	2/5	10.47 (0.91–120.71)	0.06

CMV - Cytomegalovirus, CNS – Central Nervous System, EBV – Epstein Barr Virus, GVHD – Graft Versus Host Disease, HCT- Hematopoietic Cell Transplant, HCT-CI – HCT Ccomorbidity Index, HR-Hazard Ratio; KPS – Karnofsky Performance Scale, MDS – Myelodysplastic Syndrome, SOT- Solid Organ Transplant

[a]Thoracic includes heart and lung

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Table 5:

Univariable Analysis of Solid Organ Failure of patients receiving HCT followed by SOT.

Variable	Events/N	HR (95% CI)	P-value
Recipient age at HCT (years)			
0–17	4/12	1.00	
18–49	10/33	1.21 (0.38–3.88)	0.75
≥50	8/35	0.96 (0.28–3.29)	0.95
Recipient sex			
Male	17/55	1.00	
Female	5/25	0.75 (0.27–2.05)	0.57
Recipient race			
White	20/69	1.00	
Black	2/8	1.47 (0.33–6.49)	0.61
Other	0/1	--	--
Not reported	0/2	--	--
KPS			
90–100	18/57	1.00	
<90	3/18	0.48 (0.14–1.66)	0.25
Not reported	1/5	0.34 (0.05–2.58)	0.30
HCT-CI			
0–1	8/26	1.00	
2	4/18	0.54 (0.16–1.83)	0.32
≥3	4/25	0.55 (0.16–1.82)	0.32
Not reported	6/11	0.58 (0.17–1.96)	0.38
Disease			
Plasma cell disorder	6/31	1.00	
Leukemia/MDS	12/36	1.24 (0.46–3.38	0.67
Lymphoma	3/10	**4.48 (1.06–18.84)**	**0.04**
Other	0/1	--	--
Non-malignant	1/2	2.71 (0.32–22.89)	0.36
Conditioning			
Reduced intensity	2/10	1.00	
Myeloablative	20/69	1.26 (0.29–5.51)	0.76
Not reported	0/1	--	--
Disease status			
High risk	7/19	1.00	
Intermediate	11/46	0.66 (0.25–1.71)	0.39
Low risk	2/4	2.45 (0.49–12.16)	0.27
Other	1/3	0.87 (0.10–7.25)	0.90

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Variable	Events/N	HR (95% CI)	P-value
Not reported	1/8	0.21 (0.03–1.79)	0.15
Transplant type			
Autologous	7/36	1.00	
Allogeneic	15/44	1.37 (0.55–3.40)	0.58
Donor			
Auto	7/36	--	--
HLA identical sibling	6/17	1.00	
Other related	0/1	--	--
Unrelated	7/21	0.65 (0.21–1.98)	0.45
Cord Blood	2/5	0.62 (0.11–3.38)	0.58
HCT Donor Sex			
Male	8/23	1.00	
Female	7/21	0.99 (0.35–2.75)	0.98
Graft type			
Bone marrow	5/16	1.00	
Peripheral blood	8/23	1.60 (0.50–5.13)	0.43
Cord blood	2/5	1.04 (0.19–5.58)	0.96
Auto transplant	7/36	--	--
Recipient CMV status			
Negative	12/41	1.00	
Positive	10/37	1.30 (0.55–3.08)	0.56
Not reported	0/2	--	--
Donor CMV status			
Negative	5/18	1.00	
Positive	9/24	0.74 (0.22–2.47)	0.62
Not reported	1/2	0.27 (0.02–2.80)	0.27
Chronic GVHD (allo only)			
No	2/6	1.00	
Yes	12/34	0.37 (0.07–2.05)	0.25
Year of HCT			
2001–2007	7/13	1.00	
2008–2013	15/67	1.06 (0.39–2.90)	0.91
Recipient age at SOT (years)			
0–17	3/7	1.00	
18–49	9/31	1.18 (0.31–4.45)	0.81
≥50	10/42	1.16 (0.30–4.46)	0.83
Solid organ			

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Variable	Events/N	HR (95% CI)	P-value
Kidney	10/49	1.00	
Thoracic[a]	9/26	1.64 (0.64–4.14)	0.30
Liver	3/5	**3.83 (1.01–14.49)**	**0.05**
SOT donor status			
Living	7/29	1.00	
Deceased	15/51	1.80 (0.68–4.77)	0.24
SOT donor gender			
Male	8/44	1.00	
Female	14/36	1.70 (0.70–4.12)	0.24
SOT donor race			
White	18/58	1.00	
Black	2/13	0.49 (0.11–2.11)	0.33
Other	2/9	0.74 (0.17–3.20)	0.68
Recipient CMV at SOT			
Negative	8/35	1.00	
Positive	14/45	**2.59 (1.02–6.59)**	**0.05**
Recipient EBV at SOT			
Negative	8/19	1.00	
Positive	13/53	1.22 (0.46–3.26)	0.69
Not reported	1/8	0.30 (0.04–2.48)	0.27
Donor CMV at SOT			
Negative	11/38	1.00	
Positive	9/38	1.29 (0.53–3.17)	0.57
Not reported	2/4	0.71 (0.14–3.52)	0.67
Donor EBV at SOT			
Negative	0/4		
Positive	17/64	1.00	
Not reported	5/12	0.80 (0.29–2.23)	0.66
Time from HCT to SOT (years)			
0–0.9	3/5	1.00	
1–1.9	4/12	0.25 (0.05–1.21)	0.09
2–4.9	11/38	0.55 (015–2.00)	0.36
≥ 5	4/25	0.41 (0.08–2.00)	0.27
Time from HCT to wait list (years)			
0–0.9	3/9	1.00	
1–1.9	3/18	0.53 (0.11–2.68)	0.44

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Variable	Events/N	HR (95% CI)	P-value
2–4.9	10/32	1.49 (0.40–5.60)	0.55
≥ 5	3/15	1.73 (0.32–9.37)	0.53
Pre-HCT	2/5	1.81 (0.29–11.35)	0.53
Not reported	1/1	1.70 (0.17–16.9)	0.65
Time from wait list to SOT (years)			
0–0.9	16/53	1.00	
1–1.9	1/8	0.75 (0.10–5.81)	0.78
2–5	4/18	2.09 (0.65–6.75)	0.22
Not reported	1/1	1.65 (0.21–13.05)	0.63
SOT donor age			
0–17	1/7	1.00	
18–49	15/54	3.03 (0.39–23.24)	0.29
≥ 50	6/19	4.96 (0.59–41.56)	0.14
Cause of SOT donor death			
Anoxia	2/13	1.00	
Cerebrovascular event	7/14	3.82 (0.76–19.21)	0.10
Head trauma	4/18	1.00 (0.18–5.47)	0.99
CNS tumor	0/1	--	--
Other	2/5	6.26 (0.82–48.06)	0.08

CMV - Cytomegalovirus, CNS – Central Nervous System, EBV – Epstein Barr Virus, GVHD – Graft Versus Host Disease, HCT- Hematopoietic Cell Transplant, HCT-CI – HCT Ccomorbidity Index, HR-Hazard Ratio; KPS – Karnofsky Performance Scale, MDS – Myelodysplastic Syndrome, SOT- Solid Organ Transplant

[a]Thoracic includes heart and lung