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Solid organ transplantation after hematopoietic stem cell transplantation in childhood: A multicentric retrospective survey

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Abbreviations: a-GvHD, acute-Graft vs Host disease; allo-HSCT, allogeneic hematopoietic stem cell transplantation; auto-HSCT, autologous hematopoietic stem cell transplantation; BO, bronchiolitis obliterans; c-GvHD, chronic-Graft vs Host disease; EBMT, European Society for Blood and Marrow Transplantation; HTx, heart transplantation; IS, immunosuppressive; KTx, kidney transplantation; LTX, liver transplantation; LuTx, lung transplantation; OS, overall survival; PID, primary immunodeficiency; SCD, sickle cell disease; SOT, solid organ transplantation; TBI, total body irradiation.

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We report data obtained from a retrospective multicenter pediatric survey on behalf of the European Society for Blood and Marrow Transplantation (EBMT). Information on solid organ transplantation (SOT) performed in pediatric recipients of either autologous or allogeneic hematopoietic stem cell transplantation (HSCT) between 1984 and 2016 was collected in 20 pediatric EBMT Centers (25.6%). Overall, we evaluated data on 44 SOTs following HSCT including 20 liver (LTx), 12 lung (LuTx), 6 heart (HTx), and 6 kidney (KTx) transplantations. The indication for SOT was organ failure related to intractable graft-vs-host disease in 16 children (36.3%), acute or chronic HSCT-related toxicity in 18 (40.9%), and organ dysfunction related to the underlying disease in 10 (22.8%). The median follow-up was 10.9 years (95% confidence interval: 1.7-29.5). The overall survival rate at 1 and 5 years after SOT was 85.7% and 80.4%, respectively: it was 74% and 63.2% after LTx, 83.2% after HTx, and 100% equally after LuTx and KTx. This multicenter survey confirms that SOT represents a promising option in children with severe organ failure occurring after HSCT. Additional studies are needed to further establish the effectiveness of SOT after HSCT and to better understand the mechanism underlying this encouraging success.

KEYWORDS
bone marrow/hematopoietic stem cell transplantation, clinical research/practice, graft-vs-host disease (GVHD), heart failure/injury, kidney failure/injury, liver disease, lung (allograft) function/dysfunction, organ transplantation in general, pediatrics

1 | INTRODUCTION

Solid organ transplantation (SOT) represents a therapeutic opportunity for pediatric and adult patients affected by severe/intractable chronic or acute organ failure. Since the first report of a kidney transplant performed in 2 identical twins in 1956,[1] the number of SOTs in children has increased over time. More appropriate choice of donor, as well as improved surgical procedures and supportive care, dramatically reduced SOT mortality.[2] Table 1 shows the most frequent indications for SOT in children that differ according to organ dysfunction.[3-6] Considering the spectrum of severe acute and chronic complications that may occur after hematopoietic stem cell transplantation (HSCT), HSCT-related potential SOT indications include the following: (1) severe acute or chronic Graft-vs-Host disease (GvHD); (2) acute and chronic toxicity related to chemo-radiotherapy and immunosuppressive therapies administered before, during, and after HSCT; and (3) organ dysfunction related to the underlying disease. In particular, the most frequent determinants of organ failure requiring SOT after HSCT are the following: acute or chronic GvHD involving liver or lung (vanishing bile duct syndrome and bronchiolitis obliterans [BO], severe veno-occlusive disease, acute or chronic nephrotoxicity due to total body irradiation [TBI] or chemotherapy [ie, carboplatin or ifosfamide], severe restrictive pulmonary insufficiency secondary to TBI or chemotherapy [ie, busulfan], severe hypertrophic cardiomyopathy due to high doses of anthracycline [>360 mg m^2] or cyclophosphamide [>240 mg kg] and/or TBI).[7-9]

The use of SOT after HSCT has been recently described by the Leukemia Working Party group of the European Society for Blood and Marrow Transplantation (EBMT) in a retrospective survey including both children and adults.[10] However, little is known about the use of SOT after HSCT in pediatric patients. Indeed, it has only been discussed in single case reports[11-16] and in a multicenter study of children who underwent exclusively lung transplantation after HSCT.[17]

The present study represents the first multicenter survey on pediatric patients receiving SOT after HSCT. The main aim is to analyze indications and outcome of SOTs performed after HSCT, as well as patient- and disease-related variables affecting the outcome.

2 | MATERIAL AND METHODS

Patients' eligibility criteria for this retrospective survey included a previous allogeneic (allo-HSCT) or autologous HSCT (auto-HSCT) in a pediatric EBMT center between 1984 and 2016 and age <18 years at the time of HSCT. Data were collected through a questionnaire that was sent to all EBMT pediatric centers, and included demographic data, type of primary diagnosis, date and type of HSCT, conditioning regimens, occurrence of acute and chronic GvHD, grade of GvHD, date of SOT, type of SOT, indication for SOT, presence of GvHD at the time of SOT, type of donor SOT (living or deceased donor), immunosuppressive (IS) therapy, major complications after

TABLE 1 Indications for SOT in pediatric age

Liver transplantation	Kidney transplantation	Heart transplantation	Lung transplantation
Extrahepatic and intrahepatic cholestasis	Renal aplasia/hypoplasia/dysplasia	Congenital heart disease	Cystic fibrosis
Metabolic disorders	Obstructive uropathy	Coronary artery disease	Interstitial lung disease
Acute liver failure	Focal renal glomerulosclerosis	Dilated left ventricular cardiomyopathy	Pulmonary hypertension
Primary liver malignancies	Chronic glomerulonephritis	Restrictive cardiomyopathy	Bronchiolitis obliterans
		Cardiac tumor	

SOT, solid organ transplantation.

SOT, and outcome. Two hundred forty-nine EBMT centers were contacted: 78 centers (31%) filled in the questionnaire and 20 of them (25.6%) reported data of at least 1 child who received SOT after HSCT.

Overall, SOT was performed in patients affected by severe organ failure that occurred after HSCT as a consequence of: (1) acute and chronic GvHD (a-GvHD and c-GvHD); (2) acute and late toxicity related to chemotherapy and/or radiotherapy and/or immunosuppressive drugs; (3) organ dysfunction related to the underlying disease (ie, congenital kidney or liver abnormalities, organ insufficiency related to surgical procedure).

2.1 | Statistical analyses

Standard demographic and baseline characteristics were summarized using the number of available data, median and range (minimum, maximum) for continuous data, and using the number and percentage of patients for categorical and ordinal data. *P* values on demographic and baseline characteristic data were calculated using Fisher exact test or χ^2 test or Mann-Whitney test, as appropriate.

Overall survival (OS) was defined as the time elapsing between the SOT and the date of death due to any cause. Univariate Cox proportional hazards (PH) models were developed in order to determine potential risk factors. Results of Cox-PH models were summarized using hazard ratio and 95% confidence interval (CI). A *P* value <.05 was considered statistically significant, and all *P* values were based upon 2-tailed tests. Statistical analysis was performed using R version 3.2.3 (2015-12-10).

3 | RESULTS

3.1 | Patient and transplant characteristics of SOT recipients

A total of 44 SOTs following HSCT in childhood has been reported by 20 EBMT pediatric centers (25.6%) between 1986 and 2014. This number represents 0.062% of the total HSCT number reported in the same time period to the EBMT registry from the centers participating in this survey (allo-HSCT n = 44 764 and auto-HSCT n = 26 007; 73% for malignant and 27% for nonmalignant diseases). Thirty-five SOTs were performed after allo-HSCT (0.078%) and 9 after auto-HSCT (0.034%). Twenty patients received liver transplantation (LTx) (45%), 12 lung transplantation (LuTx) (27%), 6 heart transplantation (HTx) (14%), and 6 kidney transplantation (KTx) (14%).

The median age at HSCT of these 44 patients was 7.2 years (range 1.8-15.8 years), whereas it was 12.1 years (range 5.9-22.7 years) at time of SOT (see also Table 2 for patient's characteristics). First, we stratified the patients based on age at the time of SOT: within children aged (1) 1-4 years, 7 children received LTx (100%); (2) 4-12 years, 8 received LTx (53.3%), 4 received LuTx (26.7%), and 3 underwent KTx (20%); (3) 12-18 years, 6 received LuTx (46.8%), 5 LTx (38.5%), and 2 HTx (15.4%); and (4) >18 years, 2 received HTx (50%), 2 KTx (25%), and 2 LuTx (25%).

The median time elapsing between HSCT and SOT was 5.2 years (range 4.08-8.4 years), specifically 0.83 years for KTx, 1.8 years for LTx, 5.9 years for LuTx, and 12.4 years for HTx.

Second, we analyzed our cohort by the underlying disease requiring HSCT. Twenty-six patients (59%) received HSCT for a malignant disease: it was an acute leukemia in 14 (31.8%), a solid tumor in 7 (15.9%), a lymphoma in 3 (6.8%), and a myelodysplastic syndrome in 2 (4.5%) patients, respectively. Eighteen children (40.9%) received HSCT due to nonmalignant disorders: 14 had a primary immunodeficiency (PID, 31.8%), 3 a bone marrow failure syndrome (6.8%), and 1 a sickle cell disease (SCD, 2.2%). The majority of children (65%) received a myeloablative conditioning regimen including TBI or busulfan. Acute GvHD was reported in 48.5% of patients who received allogeneic HSCT; it was grade III-IV in 59% of these. Acute GvHD was the most frequent indication for SOT in LuTx recipients followed by recipients of LTx and KTx (35% and 33%, respectively). Chronic-GvHD was responsible for SOT in 37% of patients; the highest incidence (83%) was observed in patients who subsequently received a LuTx.

TABLE 2 Characteristics of 44 patients who underwent SOT following HSCT

	Liver transplant N = 20 (45%)	Lung transplant N = 12 (27%)	Heart transplant N = 6 (14%)	Kidney transplant N = 6 (14%)	Total transplant N = 44
Age (y) at HSCT, median (range)	4.7 (0.6-15.9)	7.8 (0.9-17.2)	7.4. (1.6-13.3)	8.2 (4.1-17.1)	7.2 (1.8-15.9)
Age (y) at SOT, median (range)	6.5 (1.0-16.3)	13.7 (4.2-20.4)	19.8 (13.1-31.3)	9.0 (5.2-22.7)	12.1 (5.9-22.7)
Underlying disease					
Malignant	12 (60%)	7 (58.3%)	6 (100%)	4 (66.7%)	29 (66%)
Nonmalignant	8 (40%)	5 (41.7%)	0	2 (33.3%)	15 (34%)
Type of HSCT					
Allogeneic	16 (80%)	12 (100%)	2 (33.3%)	5 (83.3%)	35 (78%)
Autologous	4 (20%)		4 (66.7%)	1 (16.7%)	9 (22%)
Type of donor					
Related donor	7 (35%)	7 (58.3%)	2 (33.4%)	4 (66.6%)	20 (45%)
Unrelated donor	9 (45%)	5 (41.7%)	0	1 (16.7%)	15 (43%)
Unknown	4 (20%)		4 (66.6%)	1 (16.7%)	9 (12%)
TBI					
Yes	4 (20%)	3 (25%)	5 (83.3%)	3 (60%)	15 (35%)
No	16 (80%)	9 (75%)	1 (16.7%)	2 (40%)	28 (64%)
Bus					
Yes	5 (25%)	7 (58.3)	1 (16.6%)	1 (16.6%)	14 (32%)
No	15 (75%)	5 (41.7%)	5 (83.4%)	5 (83.4%)	30 (68%)
a-GVHD					
Absent	8 (50%)	4 (33.3%)	2 (100%)	3 (60%)	17 (48.5%)
Grade I-II	1 (6.3%)	5 (41.7%)		1 (20%)	7 (20%)
Grade III-IV	7 (43.7%)	2 (16.6%)		1 (20%)	10 (28.5%)
Unknown	0	1 (8.3%)			1 (3%)
c-GVHD					
Yes	3 (18.7%)	10 (83.3%)			13 (37%)
No	13 (81.3%	2 (16.7%)	2 (100%)	5 (100%)	22 (63%)

a-GvHD, acute Graft vs Host disease; Bus, busulfan; c-GvHD, chronic-Graft vs Host disease; HSCT, hematopoietic stem cell transplantation; SOT, solid organ transplantation; TBI, total body irradiation.

TABLE 3 Indications for SOT

Indication of SOT	12 LuTx, n (%)	6 KTx, n (%)	6 HTx, n (%)	20 LTx, n (%)	44 Overall, n (%)
Acute or chronic GvHD	10 (83)	0	0	6 (30)	16 (36.3)
Acute or chronic toxicity	2 (16.6)	3 (50)	6 (100)	7 (35)	18 (40.9)
Organ dysfunction	0	3 (50)	0	7 (35)	10 (22.8)

GvHD, Graft vs Host disease; HTx, heart transplantation; KTx, kidney transplantation; LTx, liver transplantation; LuTx, lung transplantation; SOT, solid organ transplantation.

3.2 | Indications for SOT

Severe a-GvHD (10%) and c-GvHD (90%) were the primary indications to perform LuTx in 10 out of 12 patients (83.3%) and in 6 out of 20 patients who received LTx (30% a-GvHD and 50% c-GvHD). No patients received HTx or KTx due to GvHD. Acute and long-term HSCT therapy-related toxicity was responsible for HTx in all of the 6 patients reported (100%), 3/6 KTx (50%), 7/20 LTx (35%), and 2/12 LuTx (16.6%). Organ dysfunction related to the underlying disease was the indication for SOT in 7 patients who received LTx (35%) (3 hepatoblastoma, 1 lymphoma, 1 bone marrow failure syndrome, and 2 primary immunodeficiency) and in 3 who received KTx (50%, 1 Fanconi anemia, 1 Wiskott-Aldrich syndrome, and 1 SCD). Overall, the indications for SOT are summarized in Table 3.

TABLE 4 SOT characteristics

	Liver	Lung	Heart	Kidney	Total
	n = 20 (45%)	n = 12 (27%)	n = 6 (14%)	n = 6 (14%)	n = 44
Donor of HSCT = Donor of SOT	1	1	0	2	4
SOT source: from deceased donor	12 (60%)	1 (8%)	4 (60%)	3 (50%)	30 (68%)
From living donor	6 (30%)	11 (92%)	0	3 (50%)	10 (23%)
Unknown	2 (10%)	0	2 (40%)	0	4 (19%)
Major complications after SOT					
No complications	9 (45%)	3 (25%)	3 (50.0%)	4 (66.6%)	18 (41%)
Infections	0	5 (42%)	0	1 (16.6%)	6 (15%)
Graft rejection	3 (15%)	2 (16.6%)	1 (16.6%)	1 (16.6%)	7 (16%)
Organ failure	4 (20%)	1 (8.3%)	2 (33.3%)	0	7 (16%)
Other (surgical complications)	4 (20%)	1 (8.3%)	0	0	5 (12%)
IS in connection to SOT?					
No	0	1	0	1	2
Yes	18	11	5	5	39
Unknown	2	0	1	0	3
IS still ongoing at last follow-up					
No	0	1	0	3	4
Yes	18	11	5	3	37
Unknown	2	0	1	0	3
Survival at last follow-up					
Alive	13 (65%)	10 (83%)	4 (66.6%)	6 (100%)	33 (75%)
Dead	7 (35%)	2 (17%)	2 (33.4%)	0	11 (25%)
Age (y) at last follow-up, median (range)	14.6 (4.0-24.7)	17.2 (11.4-31.3)	30.0 (21.3-37.0)	25.1 (6.5-44.1)	
Age (y) at time of death, median (range)	7.3 (1.1-16.1)	21.5 (21.4-1.7)	23.0 (13.1-32.8)	–	

HSCT, hematopoietic stem cell transplantation; IS, immunosuppression; SOT, solid organ transplantation.

3.3 | Characteristics of SOTs

The characteristics of SOTs are illustrated in Table 4. The median follow-up of the 44 patients who received SOT was 10.9 years (1.7-29.5 years; 95% CI: 1.7-29.5). The median age at last follow-up was 14.65 years (range 4.09-24.77 years) for LTx, 17.27 years (range 11.46-31.36 years) for LuTx, 30.6 years (range 21.39-37.07 years) for HTx, and 25.17 years (range 6.58-44.16 years) for KTx.

The majority of patients (90%) received SOT from a donor different from the HSCT donor, except in 4 cases (1 LTx, 1 LuTx, and 2 KTx). Major complications following SOT were reported in 56.8% of patients and included organ failure in 7 (16%), infections in 6 (15%), graft failure in 7 (15.9%; in 3 associated with infections), and other complications including surgical complications in 5 patients (11%). Rejection occurred after LTx in 3 children (15%), after LuTx in 2 (16.6%), after HTx in 1 (16.6%), and after KTx in another 1 (16.6). Post HSCT, pharmacological IS was administered at the time of SOT in 39 patients (88.6%), while 2 patients (LuTx and KTx) did not receive any IS at the time of SOT (1 of them received SOT from the same HSCT donor). In 3 cases, this information was not available.

3.4 | Survival after SOT

At the last follow-up, patients who received KTx were all alive (100%), while patients who received LuTx, HTx, and LTx were alive in 83%, 66.7%, and 65% of cases, respectively.

The OS for all patients at 1 and 5 years after SOT was 85.7% (95% CI, 75.8%-97%) and 80.4% (95% CI, 69%-93.6%), respectively. The OS at 1 and 5 years after KTx and LuTx was 100% (95% CI, 100%-100); it was 74.7% after HTx (95% CI; 57.7%-96.6%), and 63.2% after LTx (95% CI, 44.7%-89.3%). Two patients died 5.36 years and 10.08 years after LuTx due infection and underlying disease (PID).

The causes of death were original disease related (n = 7), hemorrhages (n = 1), infection (n = 1), GvHD (n = 1), and other transplant-related cause (n = 1). In univariate analysis, different indications for SOT, such as a-GvHD and c-GvHD, toxicity, organ failure, organ dysfunction related to underlying disease, and type of SOT donor (living or deceased donor) did not impact on OS at 1 and 5 years (Table 5). Moreover, the univariate Cox analysis of factors related to HSCT such as the stem cells source, the type of the donor (autologous or allogeneic), the conditioning regimen, and age at HSCT did not have an impact on OS after SOT (Table 6).

TABLE 5 Risk factors impacting on OS at 1 and 5 years in patients who underwent SOT

Risk factors		OS at 1 y, % (95% CI)	OS at 5 y, % (95% CI)	*P* value
Reason for SOT	GvHD	92.3 (78.9-100)	84.6 (67.1-100)	.46
	Underlying disease	87.5 (67.3-100)	75 (50.3-100)	
	Organ failure pre-HSCT	68.6 (44.5-100)	68.6 (44.5-100)	
Source of SOT	From deceased donor	96.6 (90.1-100)	92.7 (83.4-100)	.070
	From living	78.8 (56.4-100)	67.5 (43-100)	

CI, confidence interval; GvHD, graft vs host disease; OS, overall survival; y, years; SOT, solid organ transplantation.

TABLE 6 Univariate analysis with Cox analysis of survival of patients who underwent SOT

Variables	HR	95% CI for HR	*P*
Diagnosis: nonmalignant vs malignant	0.17	(0.02, 1.34)	.09
Age of patients at HSCT (y)	0.99	(0.88, 1.11)	.85
Age of patients at HSCT			
<4 y (ref)	—	—	—
<4-11 y	1.11	(0.28, 4.38)	.88
>2 y	0.47	(0.05, 4.50)	.51
Age of patient at SOT	0.97	(0.89, 1.06)	.55
Age of patient at SOT			
<4 y (ref)	—	—	—
<4-11 y	0.93	(0.18, 4.79)	.93
<12-17 y	0.81	(0.13, 4.92)	.82
>18 y	0.33	(0.03, 3.66)	.37
Sex: female vs male	1.39	(0.37, 5.27)	.63
Type of HSCT: auto-HSCT vs allo-HSCT	2.07	(0.60, 7.20)	.25
Interval between HSCT and SOT (y)	0.94	(0.80, 1.11)	.49
Conditioning regimen			
TBI based (ref)	—	—	—
Bu based	0.64	(0.11, 3.60)	.61
Nonmyeloablative regimen	1.56	(0.37, 6.61)	.54
Stem cell sources: PBSC vs BM	2.78	(0.49, 15.66)	.25
Donor: AD vs RD	1.77	(0.39, 7.95)	.46

AD, alternative donor; Bu, busulfan; BM, bone marrow; CI, confidence interval; HR, hazard ratio; HSCT, hematopoietic stem cell transplantation; PBSC, peripheral blood stem cells; RD, related donor; SOT, solid organ transplantation; TBI, total body irradiation; y, years.

4 | DISCUSSION

The purpose of this study was to retrospectively collect data on the outcome of pediatric patients receiving SOT after a previous either auto- or allo-HSCT. After reviewing data obtained through a questionnaire-based survey, we were able to analyze data coming from 20 pediatric EBMT Centers, for a total of 44 SOTs performed after HSCT. As expected by the limit of a survey, the number of children who received SOT could have been underestimated, and also some specific information regarding complications that occurred after SOT can be missed, since only the HSCT center was contacted for this survey. Furthermore, SOTs performed in children in adult centers might have been missed. Notwithstanding these possible biases, the incidence of SOT (0.062%) in this pediatric survey is similar to the incidence of SOT (0.067%) reported in the recent EBMT published survey combining adult and pediatric data.[10]

In our cohort, the most frequent indications for SOT were acute or chronic HSCT-related toxicity (40.9%), followed by a-GvHD and c-GvHD (36.3%), and organ dysfunction related to the underlying disease (22.8%).

The indications for SOT collected in this survey were similar to those reported in the previous EBMT survey.[10] In particular, GvHD and acute and chronic toxicity represented the most frequent indications for SOT as shown by the current study.[10] Lungs and liver represent the organs more frequently transplanted in the presence of intractable acute or chronic GvHD (83.3% and 30%, respectively), and the majority of patients were already under IS therapies at time of SOT. While the indication for LuTx was represented by BO/c-GvHD (83.3%), an isolated and very often IS-resistant complication that leads to irreversible respiratory failure, acute or chronic GvHD represented more rare indications for LTx (30% and 50%, respectively). Of interest, the frequency of complications after LTx was lower than that reported after LuTx (55% vs 75%); by contrast, LTx recipients appear to be at increased risk of severe and irreversible complications, with a mortality rate more than double when compared to LuTx recipients (35% vs 17%). Moreover, the median interval between HSCT and LTx was shorter than the time between HSCT and LuTx (1.8 vs 12.9 years), suggesting that LTx was performed in more immunocompromised recipients and thus at increased risk of complications. The main difference between our survey and the one already published is represented by the more frequent use of SOT due to organ dysfunction related to underlying disease in the pediatric cohort (22.8 vs 4.4%). This result could be explained

by the highest number of patients transplanted for nonmalignant diseases in the pediatric group in comparison to the adult one. Our study shows that OS of all children at 5 years was 80.4% (95% CI, 69%-93.6%), similar to the OS of 78% (95% CI, 64%-92%) reported in the recent EBMT survey, which included both children and adults.[10] A review of the literature on pediatric patients who received SOT without a previous HSCT showed that OS at 5 years is 97% for KTx,[4] 80% for HTx[5] and LTx,[3] and from 49% [18] to 61%[19] for LuTx. In the present study, in comparison with published data, the 5-year OS is higher in the group of children who underwent LuTx (100% vs 49% or 61%), and lower in the group that received LTx (63.2% vs 80%), while it was similar for HTx- and KTx-recipients. The surprisingly favorable outcome of the relatively small number of patients who underwent LuTx might be explained by the strict selection of candidates in our series as compared to those included in the large cohort study reported by the Society for Heart and Lung Transplantation (n = 2171 since 1988).[20] Moreover, it has been reported[2] that the OS of patients who received LuTx for any cause decreased over time from 54.8% at 5 years to 44% at 10 years, whereas in our population, OS after LuTx started to decrease after 10 years, suggesting a potential role of HSCT as a tool of immune tolerance for SOT.[21]

The complications that occurred after SOT included failure of the transplanted organ (16%), graft rejection (16%), infections (15%), and surgical complications (12%). While graft rejection, organ failure, and surgical complications occurred more frequently after LTx, infections were more frequent after LuTx and they were mostly responsive to therapies.

In this study, none of the evaluated variables (stem cells source, type of the donor, conditioning regimen, age at HSCT) related to HSCT had statistically significant impact on the patients' outcome. The dismal outcome observed in patients who received peripheral blood stem cells as stem cell source (hazard ratio = 2.78) as well as from an alternative donor (hazard ratio = 1.77) could be related to the higher risk of developing c-GvHD, which is typical of these kinds of HSCT. In addition, the SOT rejection incidence in our cohort was similar (15.9%) to that reported in the EBMT survey (13.3%)[10] and similar to the incidence of rejection reported after SOT performed for other causes.

Our data confirm that SOT is a valuable and potentially life-saving treatment for patients who develop otherwise intractable end-stage organ failure after HSCT. When compared to children undergoing SOT for other indications, the OS of SOT recipients after HSCT performed in pediatric-age patients appears to be similar. For this reason, the decision to perform SOT after HSCT should involve patients, family, and the entire multidisciplinary team. The option of SOT should be limited to selected cases in which the failure of a single organ resistant to other treatment (as in the case of GvHD) or a consequence of a severe organ toxicity or pre-existing before the HSCT has been demonstrated. Social and psychological aspects should also deserve a specific evaluation.[2] Nevertheless, the success of this approach lay only in the presence of strict cooperation between the SOT and HSCT teams, to determine the eligibility for a post-HSCT SOT and for establishing an appropriate follow-up.

In conclusion, our study shows that SOT after either auto- or allo-HSCT is a feasible therapeutic option in pediatric patients. A close collaboration with the SOT team will improve the definition of the eligibility criteria and the appropriate timing for SOT in pediatric HSCT recipients.

DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

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