Graft Failure after Matched Sibling Donor Transplant for Severe Aplastic Anemia

Ahmed Kotb, Muhned Alhumaid, Ali M. Assiri, Mona Hassanein, Imad Ghabashi, Ahmed Alshomer, Ahmed Balbaid, Husam Alsadi, Anas Alhakim, Mohammed Assiri, Tusneem Elhassan, Syed Osman Ahmed, Marwan Shaheen, Walid Rasheed, Fahd Almohareb, Naeem Chaudhri, Fahad Al-sharif, Hazzaa Alzharani, Amr Hanbali, Feras Alfraihi, Saud Alhayli, Shahrukh K. Hashmi, Wedian Rawas, Mahmoud Aljurf, Riad El fakih.

Adult Hematology/BMT, King Faisal Specialist Hospital and Research Center, Riyadh, KSA.

Context

Aplastic anemia is a bone marrow failure disorder that results from immune-mediated destruction of stem cells. The first line treatment for patients younger than 40 years is MSD transplant if a MSD is available. The goal of transplant is to restore hematopoiesis without GVHD. Graft failure and GVHD are the major causes of transplant failure in this population.

Objectives

To calculate the frequency of graft failure after MSD transplant for SAA in a homogenously treated cohort of patients (MSD, bone marrow graft, same conditioning), and to study the risk factors that correlate with graft failure.

Patients and methods

Retrospective study for SAA patients who underwent MSD between January 2003 and January 2017. Logistic regression was used to test the association between graft failure and proposed risk factors. 95 patients were included after excluding myelodysplasia, congenital BMF, conditioning other than fludarabine and cyclophosphamide and peripheral blood graft (Table 1)

Table 1

Diagnosis	
SAA	95
Sex	
Male	53
Female	42
Median Recipient age at HCT	18.5
Median TNC-dose (×108/kg)	3
Median CD34 cell dose (×106/kg)	3
Donor Sex	
Male	62
Female	33
Median donor age	20.5
Donor/recipient sex	
FF	20
MF	21
FM	13
MM	41
Donor recipient ABO match	
Major	16
Minor	19
Bidirectional	3
No mismatch	57
Conditioning	
Flu/Cy	95
Graft Source	
BM	95
GVHD prophylaxis	
CsA+MTX	95
Donor-recipient CMV status	
Donor +/-recipient +	95
Graft Failure	
Primary	0
Secondary	10
No	85

Table 2

Outcome	Graft Failure	P-value	Mixed Chimerism	P-value	Volume of PRBC transfusion	P-value	Length of PRBC transfusion	P-value
Risk Factor								
ABO match								
Major and bidirectional	1		1	0.04	3800(2295,6020)	0.003	12(5,52.5)	0.01
Minor	0.2(0.02,2)		0.28(0.07,1.1)		1520(1080,2280)		3(2,10.8)	
Mismatch	0.36(0.08,1.5)		0.26(0.08,0.87)		1520(990,3405)		3.6(2.3,13.1)	
CD34 10 ⁶								
<=2	1		1		1520(1479,3841)		5.1(2.9,42.6)	
>2	0.85(1.6,4.4)	0.8	0.5(0.2,2.7)	0.8	1625(1102.5,4147.7)	0.9	3.8(2.1,14.1)	0.5
TNC 10 ⁸								
<=2	1		1		2280(1509,5895)		5.1(3,22.3)	
>2	0.18(0.04,0.7)	0.02	0.7(0.3,1.8)	0.5	1537(1000,3869.5)	0.6	3.4(2.1,14.1)	0.05
Donor age								
< =20 Y	1		1		1557(1137,4619)		4.2(2.5,14.8)	
> 20 Y	1.2 (0.3,1.6)	0.7	0.58(0.2,1.4)	0.2	1690(1095,3968)	0.9	3.7(2.2,16.2)	0.6
Recipient age								
14-20 Y	1		1		1520(1110,4078)		4(2.7,13.2)	
> 20 Y	8.7(1.06,72)	0.04	1.14(0.4,2.7)	0.7	1625(1234,4581)	0.9	4(2.1,20.7)	0.6
CMV Reactivation								
No	1		1		1557(1018.7,4317.5)		3.1(1.8,11.6)	
Yes	0.7(0.18,2.7)	0.6	.6(0.2,1.5)	0.2	1810(1145, 3573.5)	0.9	5.1(3.1,16.2)	0.09
Time from Diagnosis to Transplant								
<= 2 months	1		1		1870(1142,4137)	0.2	4(2.5,14.8)	0.9
>2 months	2.1(05,8.4)	0.2	0.8(0.3,2.3)	0.7	1520(1016,4799.5)		4.3(1.9,16.4)	

Results

The rate of secondary graft failure was 10.5%. TNC < 2×10⁸ and recipient age >20 were significantly associated with graft failure (p=0.02, 0.04 respectively). Donor age, CD34, time from diagnosis to transplant and ABO incompatibility did not significantly affect failure rate. Major ABO mismatch was statistically significantly associated with higher risk of mixed chimerism, larger volume and longer period of PRBC transfusion post-transplant (p=0.03, p=0.003 and 0.01 respectively). TNC dose ≤2×10⁸ /kg was statistically significantly associated only with longer period of PRBC transfusion post-transplant (p=0.05) (Table 2).

Discussion & Conclusion

Known risk factors for GF include HLA mismatch, alternate donor, T-cell depleted graft, reduced intensity conditioning, low graft cell dose, prior transfusions, and progressive mixed chimerism. Studies focusing on GF in SAA patients suffer from heterogeneity in regards of stem cell source, donor types, GVHD prophylaxis and conditioning regimens. To minimize these confounders, we focused our review on a homogenous population of patients suffering from SAA who received an unmanipulated BM graft from a matched sibling, conditioned with Flu/Cy and received same GVHD prophylaxis with MTX/CsA. We concluded that graft failure after MSD transplant for SAA at our institution matched published results. Lower TNC and higher recipient-age were significantly associated with graft failure.