

Supplemental Material Table of Contents

Supplemental Table 1. Prior studies of Acute Kidney Injury in Allogeneic

Hematopoietic Stem Cell Transplantation

Supplemental Table 2. Timing of Max AKI, AKI, stratified by Max AKI Stage

Supplemental Table 3. NRM cumulative rate (95%CI) at 6 months and 1 year by AKI stage in d100 landmark cohort (n= 536).

Supplemental Table 4. Transplant type and GVHD prophylaxis regimen stratified by max AKI Stage

Supplemental Table 5. AKI subgroup analyses

Supplemental Table 5a. Medication exposures in AKI subgroup

Supplemental Table 5b. Comparison of Vancomycin and tacrolimus use in patients with AKI, based on severity.

Supplemental Table 1. Prior studies of Acute Kidney Injury in Allogeneic Hematopoietic Cell Transplantation

Publication	Author/Center	Trial Design	Years of Enrollment	AKI Outcomes	Risk Factors	AKI Criteria
BMT 2003 ¹³	Hahn/ Roswell Park Center Institute, Buffalo, NY	Retro-spective, n = 97	1996-1999	Grade 1: 100%; Grade 2: 60%; Grade 3*: 19% (*100% mortality by day 132)	Severe VOD, severe acute GVHD, age, unrelated donor	Bearman criteria: ⁵⁰ Grade 1: increase in baseline serum creatinine, Grade 2: Cr \geq 2x baseline, Grade 3: Requiring Dialysis
Kidney International, 2005 ⁵	Hingorani/ Fred Hutchinson Cancer Research Center, USA	Pro-spective case control, n=147	1997-2000	36%	SOS, Amphotericin. No association with GVHD, TBI, CsA levels.	Doubling of baseline SCr during first 100 days
BMT 2007 ⁵¹	Kersting et al/ University Medical Centre, Utrecht, Netherlands	Retro-spective, n=363	1993-2004	49.6% (severe)	Hypertension	Grades 0-4; Grade 0 <25% of eGFR decline, Grade 1 2x rise in creatinine, Grade 2, >2x rise, Grade 3 requiring dialysis
BMT , 2009 ¹⁶	Pinana/ Autonomous University of Barcelona, Spain	Retrospective, n=188, reduced intensity conditioning	1999-2006	52% (1 year)	CsA, MTX, >3 lines of chemotherapy, GVHD III-IV	>25% eGFR decline by MDRD
BMT , 2009 ¹⁴	Liu/ Zhongda Hospital, Huaian Hospital, Zhenjiang First People's Hospital	Retrospective, n=62, Non-myeloablative	2002-2007	29%	VOD, acute GVHD, sepsis, incomplete HLA-match	AKIN

IJKD, 2010 ⁶	Saddadi/ Shariati Hospital, Tehran, Iran	Prospective, n=292	2000-2002	42.1% of allografts (vs 22.1% of auto-logous)	Age, CsA, high CsA levels (>209 ug/L), GVHD	Doubling of SCr during first 180 days post-transplant
Chinese Journal of Cancer, 2010 ¹⁵	Yu/ Zhongda Hospital Southeast University, China	Retrospective, n=96	2003-2009	29.2%	Myeloablative conditioning, acute GVHD, sepsis, VOD	Grade 0-3, based on severity of eGFR decline
NDT Supplement, 2016 (Abstract) ⁵²	Esposito/ Policlinico San Matteo, Pavia Italy	Retrospective, n=57	Not reported	31.6%	Hypertension, GVHD	Grades 1-4; Grade 1: >2x increase in Cr, Grade3: >4x increase in Cr
Indian Journal of Nephrology, 2017 ⁴	Sehgal/ Christian Medical College, Ludhiana	Retrospective, n=65	2008-2014	85.2% in allogenic HCT; AKI in first 2 weeks was risk for mortality, p =0.016	Inotrope use, nephrotoxic drugs, SOS, fungal infection. GVHD showed no statistical significance	RIFLE
PeerJ, 2019 ³	Mima/ Kindai University Nara Hospital	Retrospective, n=108	2006-2016	15.7%	ABO-incompatible, GVHD incidence	AKD defined as AKI or subacute decline in GFR <60ml/min, >35% decline in GFR, or >50% increase in creatinine for less than 3 months
International Journal of Stem Cells, 2019 ⁵³	Khalil / University of Jordan Hospital	Retrospective, n=70 (61% allogeneic)	2002-2016	31.6% by 90 days	Allogeneic, Male donor, high-dose melphalan	RIFLE

BMT, 2020 ⁵⁴	Gutiérrez-García / Hospital Clinic of Barcelona, Spain	Retrospective, n=422	2001-2012	46% at 30 days, 58% at 100 days, and 63% at 1 year; AKI Stage 3 was 15%	Age >55 years, TBI, CMV reactivation, methotrexate for GVHD prophylaxis; Acute GVHD associated with higher risk for CKD	KDIGO
Acta Haematologica, 2020 ⁵⁵	Sakaguchi / Nippon Medical School Hospital, Japan	Retrospective, n = 114	2001-2015	64.9% AKI ; 21.9% CKD	Age ≥46, use of ≥3 nephrotoxic drugs; acute GVHD was not significant	KDIGO
BBMT, 2020 ¹⁷	Gutgarts/ Memorial Sloan Kettering Cancer Center, USA	Retrospective, n=153, cord blood transplants	2006-2017	83% (54% with Grade 2-3 AKI)	Baseline albumin, ICU admission, African ancestry, Nephrotoxic meds	KDIGO

Summary of the largest analyses of Acute Kidney Injury in Allogeneic HCT. Abbrev: IJKD, Iranian Journal of Kidney Diseases; BMT, Bone Marrow Transplantation; PeerJ, Journal of Life and Environmental Sciences; NDT, Nephrology Dialysis Transplantation; BBMT, Biology of Blood and Marrow Transplantation ; SOS, Sinusoidal Obstructive Syndrome; VOD, Veno-occlusive Disease; HD, Hemodialysis; HCT, hematopoietic stem cell transplantation; GVHD, Graft vs Host Disease; AKI, Acute Kidney Injury; AKD, Acute Kidney Disease

Supplemental Table 2. Timing of Max AKI, stratified by Max AKI Stage

Max AKI Stage	N	Days Onset
1	220	32 (16,58)
2	117	31 (12,49)
3	60	16 (9,49)

Median onset of Max AKI, stratified by Max AKI stage; data represented is median (IQR)

Supplemental Table 3. NRM cumulative rate (95%CI) at 6 months and 1 year by AKI stage in d100 landmark cohort (n= 536).

AKI Stage	n	NRM at 6 months; rate (95% CI)	NRM at 1 year; rate (95% CI)
0	194	0.016 (0, 0.033)	0.089 (0.048, 0.129)
1	206	0.034 (0.009, 0.059)	0.117 (0.073, 0.161)
2	100	0.04 (0.001, 0.079)	0.08 (0.027, 0.133)
3	36	0.139 (0.024, 0.254)	0.194 (0.063, 0.326)

Non-relapse mortality (NRM) at 6 months and 12 months, stratified by max AKI stage. Statistics presented: rate (95% CI); 80 patients omitted due to competing events

Supplemental Table 4. Transplant type and GVHD prophylaxis regimen stratified by max AKI Stage

Treatment	N	AKI Stage 1	Stage 2	Stage 3
Chemo	462	0.379 (0.335, 0.423)	0.201 (0.165, 0.238)	0.095 (0.068, 0.122)
Total Body Irradiation	154	0.292 (0.22, 0.364)	0.156 (0.098, 0.213)	0.104 (0.056, 0.152)
Myeloablative	367	0.316 (0.268, 0.364)	0.131 (0.096, 0.165)	0.076 (0.049, 0.103)
Nonablative	50	0.46 (0.32, 0.6)	0.2 (0.087, 0.313)	0.06 (0, 0.127)
Reduced Intensity Conditioning	199	0.407 (0.339, 0.475)	0.296 (0.233, 0.36)	0.146 (0.097, 0.195)
T-Cell Depleted	242	0.244 (0.19, 0.298)	0.124 (0.082, 0.166)	0.244 (0.19, 0.298)
Tacrolimus-based	263	0.452 (0.392, 0.513)	0.232 (0.181, 0.283)	0.452 (0.392, 0.513)
Tacrolimus/Siroli mus-based	37	0.432 (0.269, 0.596)	0.243 (0.101, 0.385)	0.432 (0.269, 0.596)
Cyclophosphami de-based	71	0.366 (0.253, 0.48)	0.225 (0.127, 0.324)	0.366 (0.253, 0.48)

Transplant type and GVHD prophylaxis regimen stratified by max AKI Stage. Data represented by: rate (95% CI).

Supplemental Table 5. AKI subgroup analyses

Supplemental Table 5a. Medication exposures in AKI subgroup

Characteristic	N = 403
Number of Nephrotoxic medications	
0	357 (89%)
1	40 (9.9%)
2	6 (1.5%)
Amphotericin	18 (4.5%)
Cidofovir	5 (1.2%)
Foscarnet	27 (6.7%)
Gentamicin	2 (0.5%)

Subgroup analysis of medication exposures prior to development of any AKI. Nephrotoxic medication as defined by Amphotericin, Cidofovir, Foscarnet, and Gentamicin. Statistics presented: n (%)

Supplemental Table 5b. Comparison of Vancomycin and tacrolimus use in patients with AKI, based on severity.

Characteristic	AKI Max Stage			
	1, N = 220	2, N = 119	3, N = 64	p-value
Vancomycin use prior to AKI	50 (23%) ^a	68 (57%)	45 (70%)	<0.001
Vancomycin level pre-AKI onset, mcg/mL	14(3, 27)	13(4, 41)	18(3, 52)	0.080
Tacrolimus use prior to AKI	145 (66%)	55 (46%)	28 (44%)	<0.001
Average levels of tacrolimus 7 days pre-AKI onset	10.08(6.15, 16.32) ^b	10.40(3.00, 16.00)	10.34(5.80, 18.72)	0.3

Subgroup analysis of vancomycin use and levels, and tacrolimus use and levels, stratified by the max stage AKI. Statistics presented: ^an (%); ^b median (minimum, maximum); Statistical tests performed: chi-square test of independence; Kruskal-Wallis test.