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Beckerson, J

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Impact of Nutrition on Non-relapse Mortality and Acute Graft Versus Host Disease During Allogeneic Hematopoietic Cell Transplantation for Hematologic Malignancies

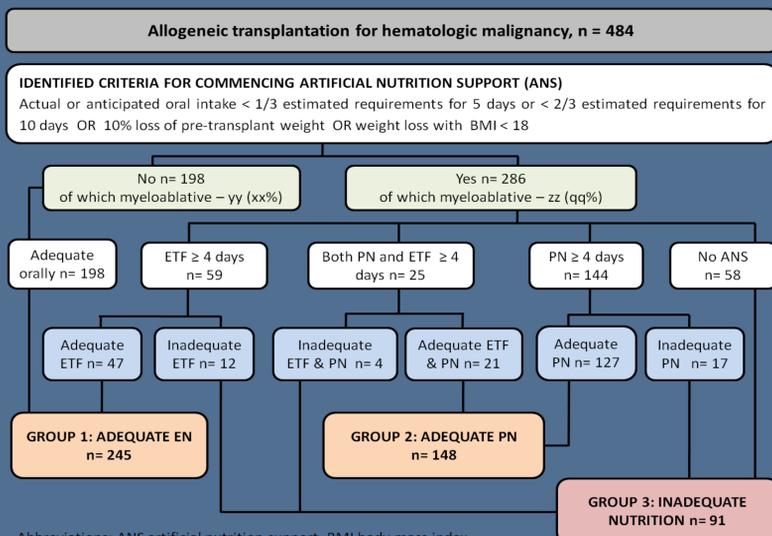


Julie Beckerson, Richard M. Szydlo, Mary Hickson, Catriona Mactier, Andrew Innes, Ian Gabriel, Renuka Palanicawandar, Edward J Kanfer, Donald MacDonald, Dragana Milojkovic, Amin Rahemtulla, Aris Chaidos, Anastasios Karadimitris, Eduardo Olavarria, Jane F. Apperley and Jiri Pavlu. Imperial College, Hammersmith Hospital, London, UK

Introduction Allogeneic hematopoietic cell transplantation (HCT) is often associated with poor oral intake and as a result, nutritional status declines. Although it might seem obvious that optimal nutrition is likely to improve outcomes of transplantation, there are no clinical data that directly support this assumption. It is also unclear whether artificial nutrition support (ANS) should be provided as enteral tube feeding (ETF) or parenteral nutrition (PN).

Methods A retrospective analysis of 100 day non-relapse mortality (NRM) and incidence of acute GvHD according to route and adequacy of nutrition, together with other known prognostic factors, after allogeneic HCT in a single centre between 2000 and 2014. Nutritional intake was reviewed from admission to engraftment and deemed inadequate where an unmet need for ANS was documented. Exclusion criteria were age < 16 years, non-hematological malignancy, cord blood or haplo transplant. Myeloablative conditioning was used in 285 (59%) patients, 272 of whom received a TBI based regimen. Reduced intensity conditioning was given to 199 (41%) patients. For the 236 (49%) unrelated donor cell recipients *in vivo* T-cell depletion with alemtuzumab was used.

Figure 1: Flow chart for nutritional intake group



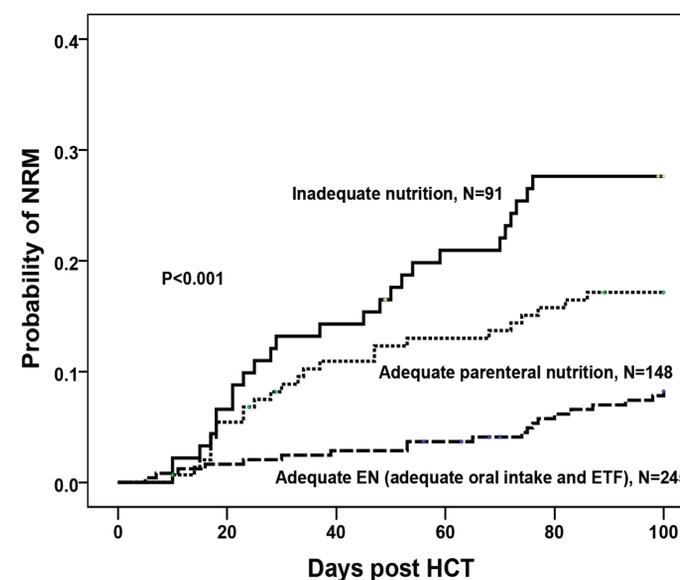
Abbreviations: ANS artificial nutrition support, BMI body mass index, ETF enteral tube feed, EN enteral nutrition, PN, parenteral nutrition

Results ANS was initiated in 228 (47%) of patients who met predefined criteria shown in figure 1. Myeloablative HCT recipients were advised to have an enteral feeding tube inserted prophylactically at day 1 post HCT. If ETF could not be established then PN was given. 198 (41%) of subjects never met the criteria for artificial nutrition and maintained an adequate oral intake. A further 47 (10%) of subjects required ETF for a median of 12 days to achieve adequate enteral nutrition. There were 148 subjects that required 4 or more days of PN to achieve adequate nutrition. 127 subjects required PN for a median of 17 days and 21 required a median of 16 days PN plus 8 days ETF. Episodes of ANS shorter than 4 days were excluded as likely inappropriate or ineffective.

Table 1: Univariate analyses of nutritional intake group on NRM and acute GvHD

	N	NRM at 100d % (95%CI)	p-value	AGVHD grade N (%)	p-value	Gut AGVHD N (%)	p-value	
				0-1	2-4	No	Yes	
Overall	484	14.6 (12-18)	-	260 (59)	179 (41)	285 (65)	153 (35)	-
Nutritional Intake Group								
Adequate EN	245	8.2 (5-12)	<0.001	157 (68)	75 (32)	169 (73)	63 (27)	<0.001
Adequate PN	148	17.1 (12-24)		59 (45)	73 (55)	68 (52)	63 (48)	
Inadequate	91	27.6 (20-38)		44 (59)	31 (41)	48 (64)	27 (36)	

Figure 2: Cumulative incidence for NRM at day 100



The effects of all known patient, disease and transplant factors were studied in univariate analyses on NRM and acute GvHD, following which multivariate analyses were performed. Univariate effects of nutritional intake group on NRM and acute GvHD are shown in Table 1 and Figure 2. (Univariate analyses of other factors not shown).

Factors significantly associated in multivariate analyses with NRM, acute GvHD grade 2 or above or gut acute GvHD of any grade are shown in Tables 2 and 3.

Table 2: Multivariate analyses of NRM

NRM at 100d			
	N	RR (95% CI)	p-value
Nutritional Group			
Adequate EN	242	1.0	
Adequate PN	148	2.9 (1.6 - 5.4)	<0.001
Inadequate	89	4.1 (2.2 - 7.2)	<0.001
Recipient age (yrs)			
< 40	212	1.0	
40-60	229	1.9 (1.1 - 3.1)	0.026
≥ 60	38	3.1 (1.5 - 6.8)	0.004
Previous autograft			
< 1	434	1.0	
> 0	45	2.4 (1.3 - 4.5)	0.007
Recipient CMV			
Negative	202	1.0	
Positive	277	1.8 (1.1 - 3.1)	0.027

Table 3: Multivariate analyses of acute GvHD

	Acute GVHD grade 2-4			Gut AGVHD any grade		
	N	OR (95% CI)	p-value	N	OR (95% CI)	p-value
Nutritional Group						
Adequate EN	231	1.0		231	1.0	
Adequate PN	132	2.0 (1.2 - 3.3)	0.006	131	1.8 (1.1 - 3.0)	0.018
Inadequate (all routes)	75	1.3 (0.7 - 2.2)	0.38	75	1.3 (0.7 - 2.3)	0.39
Recipient / Donor Sex						
Other combination	353	1.0		352	1.0	
Male / Female	85	1.7 (1.0 - 2.7)	0.047	85	1.8 (1.1 - 3.0)	0.025
Conditioning regimen						
Myeloablative	262	1.0	0.001	262	1.0	<0.001
Reduced intensity	176	0.5 (0.3 - 0.7)		175	0.4 (0.3 - 0.7)	

Conclusion Adequate nutrition during allogeneic HCT is associated with improved 100 day NRM. Adequate EN is associated with significantly better results for this outcome than adequate PN. Furthermore adequate EN, predominantly via oral intake may be associated with lower incidence of acute GvHD when compared to PN, perhaps because of its ability to maintain gut mucosal integrity and the gastrointestinal tract environment, including microflora. The significant associations reported here warrant further research into optimizing enteral nutrition in recipients of HCT.