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Randomized Control Trials

Tolerability of proactive enteral nutrition post allogeneic haematopoietic progenitor cell transplant: A randomised comparison to standard care

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SUMMARY

Background & aims: Nutrition support is an important component of care to prevent malnutrition during allogeneic haematopoietic progenitor cell transplantation (HPCT) however there is no consensus on the optimal method of nutrition support. It is currently unclear whether enteral nutrition (EN) via nasogastric (NG) feeding is tolerated and improves clinical outcomes in comparison with parenteral nutrition (PN). This randomised study aimed to determine the tolerability and outcomes of proactive EN in comparison to PN (standard care).

Methods: Patients aged ≥18 years undergoing allogeneic transplantation with reduced intensity (fludarabine/melphalan) or myeloablative (cyclophosphamide/TBI) conditioning at a tertiary Australian hospital were eligible to participate. Patients were recruited pre-transplant and randomised to proactive enteral nutrition (EN) or standard care. The EN group underwent NG tube insertion the day after stem cell infusion with feeding commenced at 30 ml/h. Rate of feeding was increased to goal as oral intake declined. If patients were intolerant to NG feeding they were changed to PN if required. The standard care group commenced PN when oral intake was ≤60% of requirements for three days and was unlikely to improve for at least another week as per standard unit protocol. The primary endpoint was tolerance of EN.

Results: Forty-four patients, (median age [Q1–Q3]: 52 [38–59], 25 male, 19 female) were recruited and randomised to EN (n = 22) or standard care (n = 22). In the EN group eleven tolerated EN (55%), nine changed to PN and two withdrew from study. The median (Q1–Q3) duration of NG feeding was nine days (4–13) and this provided 86% of goal nutrition. In the standard care group 68% required PN, the median duration was nine days (0–17) and patients met 97% of goal nutrition. There were no statistically significant differences between groups for any clinical outcomes or grade 3–4 (CTCAE version 4) complications.

Conclusions: Half of patients receiving allogeneic transplantation tolerate EN when commenced early post-conditioning. As the use of proactive EN will reduce the use of PN (and associated costs and risks), it should be considered first line nutritional support.

Registration: This trial was registered with the Australian New Zealand Clinical Trials Registry (ANZCTR) trial number ACTRN12615000284561.

1. Introduction

The intensive conditioning during allogeneic haematopoietic progenitor cell transplantation (HPCT) frequently leads to significant gastrointestinal toxicity, elevated nutrition requirements and poor oral intake [1]. Malnutrition can develop quite rapidly unless

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timely nutrition support is initiated [2,3]. Weight loss and malnutrition post-transplant have been associated with poorer clinical outcomes including increased length of hospital stay [4], increased relapse risk [5] and reduced survival [5–7]. Therefore close monitoring of adequacy of oral intake is essential, with nutrition support initiated early to avoid or minimize further weight loss [1]. There is currently no consensus on whether enteral nutrition (EN) delivered via a nasogastric (NG) tube or parenteral nutrition (PN) is the optimal method of nutrition support during HPCT, leading to wide variation in practice [8]. Some non-randomised studies have indicated that EN compared to PN may improve patient outcomes [9–11]; however, there remains some uncertainty in practice about the tolerability of NG feeding in this patient group [12].

PN is easy to administer during HPCT as most patients have existing central venous access, and it offers the benefit of bypassing the inflamed gastrointestinal tract in those with mucositis [13]. There are, however, concerns regarding increased risk of hyperglycaemia, catheter related infections, suppression of appetite [14], delayed platelet engraftment [11,15,16] and potentially higher mortality [11]. EN has been associated with fewer central line complications, reduced need for antifungal therapy, lower duration of fever, lower rate of transfer to ICU [9], earlier neutrophil engraftment [11] reduced risk of graft versus host disease, and improved survival [11,17].

Concerns about the use of EN during HPCT include apprehension about possible gastrointestinal intolerance of the feed and NG tube, management of conditioning side effects such as vomiting and mucositis and tube occlusion and dislodgement [12,18]. The few studies that have examined NG tolerance during HPCT report varying results, potentially due to differences in timing of feeding commencement. Our group demonstrated that >1/3 of patients who required nutrition support had established severe mucositis or typhlitis at day seven after transplant; therefore NG feeding was either contraindicated or poorly tolerated [12]. Other groups have suggested that tolerance of NG feeding is improved if commenced prophylactically on day one after transplant [9,11].

The level of tolerance of proactive EN, whether it can meet nutritional requirements, optimal timing for initiation of nutrition support, and whether EN improves clinical outcomes over PN remains unknown and has not been explored in a randomised study. This study aimed to explore the feasibility, tolerance and clinical outcomes of proactive (early) EN in a prospective randomised comparison to standard care (PN) during allogeneic HPCT.

2. Materials and methods

2.1. Study protocol

This study was approved by the Royal Brisbane and Women's Hospital Human Research Ethics Committee and University of Queensland Human Research Ethics Board. The trial was registered with the Australian New Zealand Clinical Trials Registry (ANZCTR) trial number ACTRN12615000284561**.** Patients aged ≥18 years undergoing allogeneic HPCT with reduced intensity fludarabine and melphalan (FluMel) or standard myeloablative cyclophosphamide and total body irradiation (CyTBI) conditioning at a tertiary Australian Hospital who could give written informed consent were eligible to participate. Exclusion criteria included a non-myeloablative conditioning regimen, the presence of an anatomical deformity preventing EN or NG tube insertion or enrolment in a concurrent research study on the unit. All patients were seen by the unit Dietitian at least twice weekly from admission pre transplant through to hospital discharge after engraftment. All patients were provided with nutrition counselling and a high protein high energy diet with snacks and high protein supplement drinks. On admission, nutritional status was assessed using the Patient Generated Subjective Global Assessment (PG-SGA) [19] and nutritional requirements estimated as per clinical practice guidelines (125–145 kJ/kg/day and 1.2–1.5 g protein/kg/day; adjusted body weight used if BMI >25 kg/m^2) [20].

Informed consent was obtained from all patients prior to transplantation. Patients were randomised on enrolment to nutritional support by proactive EN or standard care (PN when nutrition support required) on a 1:1 basis. Randomisation was stratified according to type of conditioning (standard versus reduced intensity) and carried out by an independent member of the research team not involved in direct patient care. Blocked randomisation was completed using a computer generated list of random numbers generated prior to study commencement using the Research Randomiser website [21]. The allocation sequence was concealed from the researcher enrolling participants. After allocation there was no blinding of participants or researchers. Patients randomised to EN had a narrow gauge (8–10fr) NG tube inserted on day one after stem cell infusion (after platelet transfusion if platelet count $<30 \times 10^9$/L) and feeding commenced immediately at 30 ml/h with a polymeric non-fibre ready to hang formula (1.25 kcal/ml, 63 g protein/L), providing 720 ml per 24 h (3.7 MJ, 45 g protein). When oral intake fell below 60% requirements for three days NG feeding increased to 50 ml/h and when oral intake became minimal (<20% requirements) increased to the goal of 1 ml/kg/h (maximum 80 ml/h) providing 125–130 kJ/kg/day. Nasogastric feeding ran continuously via an enteral feeding pump. If patients receiving NG feeding could not tolerate the goal rate they continued the tolerated rate and commenced 'top-up' PN if less than 60% of requirements was being met via EN (oral plus nasogastric nutrition). If patients did not tolerate NG feeding (Table 1) it was discontinued and they were converted to PN if oral intake was below 60% of requirements and PN was anticipated to be required for at-least a week.

The standard care group commenced PN when required as per unit protocol; that is, when oral intake was ≤60% of requirements for three consecutive days and was unlikely to improve for at least another week. PN was administered through a central venous catheter using a central parenteral nutrition solution (4495 kJ, 57 g protein, 40 g lipid, 110 g glucose per litre) including intravenous vitamin and trace element supplementation administered separately. The rate of PN provided met the deficit between oral intake and goal nutritional requirements. If patients developed an acute kidney injury, current EN/PN was changed to a low electrolyte

Table 1
Reasons for cessation of nasogastric feeding.

Recurrent displacement of the nasogastric tube requiring reinsertion more than three times in 24 h, or reinsertion which is deemed unacceptable by the patient, or the presence of grade 3–4 mucositis at the time that the tube is displaced, or the development of a transplant-related complication which contraindicates reinsertion
Development of an ileus, bowel obstruction or other gastrointestinal complication which contraindicates enteral nutrition
Grade 3–4 diarrhoea or stool volume >1000 ml/day which is not attributable to infection, chemotherapy or medication effect
Suspected or proven graft versus host disease necessitating gut rest
Persistent gastrointestinal symptoms including nausea, vomiting, heartburn, nasopharyngeal pain/discomfort, or other symptoms which are attributable in the opinion of medical staff to enteral nutrition and which are not relieved by standard supportive care including parenteral antiemetics and analgesia
Withdrawal of patient consent for any reason

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solution. Throughout the study, patients were encouraged by the Dietitian and multidisciplinary team to continue oral intake if tolerated. Nasogastric feeding or PN was ceased when oral intake met ≥60% of nutritional requirements for at least one day post neutrophil engraftment.

2.2. Endpoints

The primary endpoint was tolerance in the EN group, defined as the percentage of patients randomised to EN who did not require change to PN or addition of 'top-up' PN. In this study EN included both nasogastric nutrition support plus oral intake. If a patient ceased NG feeding prior to meeting the criteria for feeding cessation post neutrophil engraftment but did not require commencement of PN they were still considered tolerant of EN. Secondary endpoints included the percentage of prescribed nutrition received in each group, oral intake and duration of requirement for nutrition support, incidence of biochemical derangements including elevation of liver enzymes, hyperglycaemia and hypertriglyceridemia, duration of neutropenia, (neutrophils $<0.5 \times 10^9$/L), length of hospital stay, grade 3–4 catheter related infection, platelet engraftment, day 100 rate of graft versus host disease (GVHD) and day 100 survival. Liver enzymes, blood glucose levels, neutrophil and platelet levels were tested daily and triglycerides tested weekly (all non fasting) as per routine clinical practice. If a patient was diagnosed with gastrointestinal GVHD, data collection on duration of requirement for nutrition support ceased on day of diagnosis. Clinical outcomes were assessed using Common Terminology Criteria for Adverse Events (CTCAE) version 4 criteria [22]. GVHD was assessed and graded as per the Seattle criteria [23].

Based on benchmarking with transplant units who primarily use EN for nutritional support and published non-randomised studies [9,11] we estimated that 70% of patients would tolerate EN as per study protocol. Statistically it was not possible to perform a sample size calculation therefore sample size was set pragmatically as the number that could be recruited at 12 months, estimated to be 40–50 patients per year. Due to competing research projects on the unit only 23 patients had been recruited at 12 months therefore recruitment was continued for another 14 months until the target was reached.

2.3. Statistics

Standard descriptive statistics were used to evaluate patient demographics and feeding outcomes including frequencies and percentages for categorical variables and mean and standard deviation or median and quartiles for continuous variables. Microsoft Excel 2016 and SPSS (IBM Corp. IBM SPSS Statistics for Windows, Version 23.0 and 25.0, Released 2015/2017. Armonk, NY: IBM Corp) was used for all analyses. To evaluate if there were any differences in baseline characteristics between groups categorical variables were assessed using Chi squared or Fishers exact test and continuous variables using the Independent samples T test or Mann Whitney U test where data was not normally distributed. Odds ratios with 95% confidence intervals were produced using binary logistic regression for binary outcomes and marginal means with 95% confidence intervals were produced using general linear models for continuous outcomes. Statistical significance was set at $p < 0.05$. Intention to treat analysis was completed.

3. Results

Forty-four patients, (median age [Q1–Q3]: 52 [38–59], 25 male, 19 female), were enrolled in the study between March 2015 and May 2017. Twenty-two patients were randomised to proactive NG feeding (EN group) and 22 to standard care. Two patients in the EN group withdrew from the study prior to transplant. Patient characteristics are detailed in Table 2. There were no statistically significant differences between groups.

Of the twenty patients allocated to EN, seventeen patients received the intervention with three patients not commencing feeding due to intolerance of NG tube placement. In the EN group eleven patients tolerated EN (55%) as per the primary endpoint definition and nine changed to PN (see Fig. 1). The reasons for changing to PN are detailed in Fig. 1. No patients remaining on NG feeding required top up PN as they tolerated an adequate rate of feeding. Table 3 outlines the nutrition and clinical outcomes of all patients in the study. Data on complication rates was available for all patients who received feeding; 15 patients who received PN in the standard care group and 19 patients in the EN group (one patient who failed NG insertion did not require PN). Duration of feeding was a median of 16 days for the EN group and nine in the standard care group due to proactive commencement of NG feeding on day one post transplant versus waiting until oral intake declined. The median percent of nutrition met via feeding was statistically significantly different between groups, 90% in the EN group and 97% in the PN group ($p = 0.001$) however this is not considered clinically significant. For clinical outcomes and complications there were no statistically significant differences between groups. Table 4 outlines the nutrition outcomes of all patients randomised to EN and Table 5 summarises the nutrition outcomes of the group that received nasogastric feeding. In a per protocol analysis for the patients who received PN (n = 15) it was

Table 2
Patient characteristics.

Patient characteristics	Enteral nutrition (n = 20)	Standard care (n = 22)
Age		
Median (Q1-Q3)	51 (39–60)	52 (34–60)
Sex		
Male	9 (45%)	14 (64%)
Female	11 (55%)	8 (36%)
Diagnosis		
AML	4 (20%)	10 (45%)
ALL	4 (20%)	3 (14%)
MDS	4 (20%)	5 (23%)
Other	8 (40%)	4 (18%)
Donor type		
Volunteer unrelated donor	12 (60%)	12 (55%)
Sibling	8 (40%)	10 (45%)
HLA matched		
Volunteer unrelated donor[a]	7 (35%)	6 (27%)
Conditioning		
CY-TBI	7 (35%)	8 (36%)
Fludarabine/melphalan	13 (65%)	14 (64%)
Weight (kg)		
Median (Q1–Q3)	70 (62–90)	73 (61–92)
BMI (kg/m^2)		
Median (Q1–Q3)	26 (21–28)	25 (22–28)
PG-SGA		
A well nourished	19 (95%)	21 (95%)
B moderately malnourished	1 (5%)	1 (5%)
C severely malnourished	0	0
Requirements/day		
kJ, mean (SD)	8565 (1517)	8800 (1634)
Protein grams, mean (SD)	82 (15)	84 (14)
Number of prior therapies		
0–2	13 (65%)	20 (91%)
2–4+	7 (35%)	2 (9%)

Abbreviations, AML: acute myeloid leukemia, ALL: acute lymphoblastic leukemia, MDS: myelodysplastic syndrome, HLA: human leukocyte antigen, BMI: body mass index, PG-SGA: patient generated subjective global assessment, kJ: kilojoules.
[a] HLA 8/8 match, all mismatched donors 7/8 matched.

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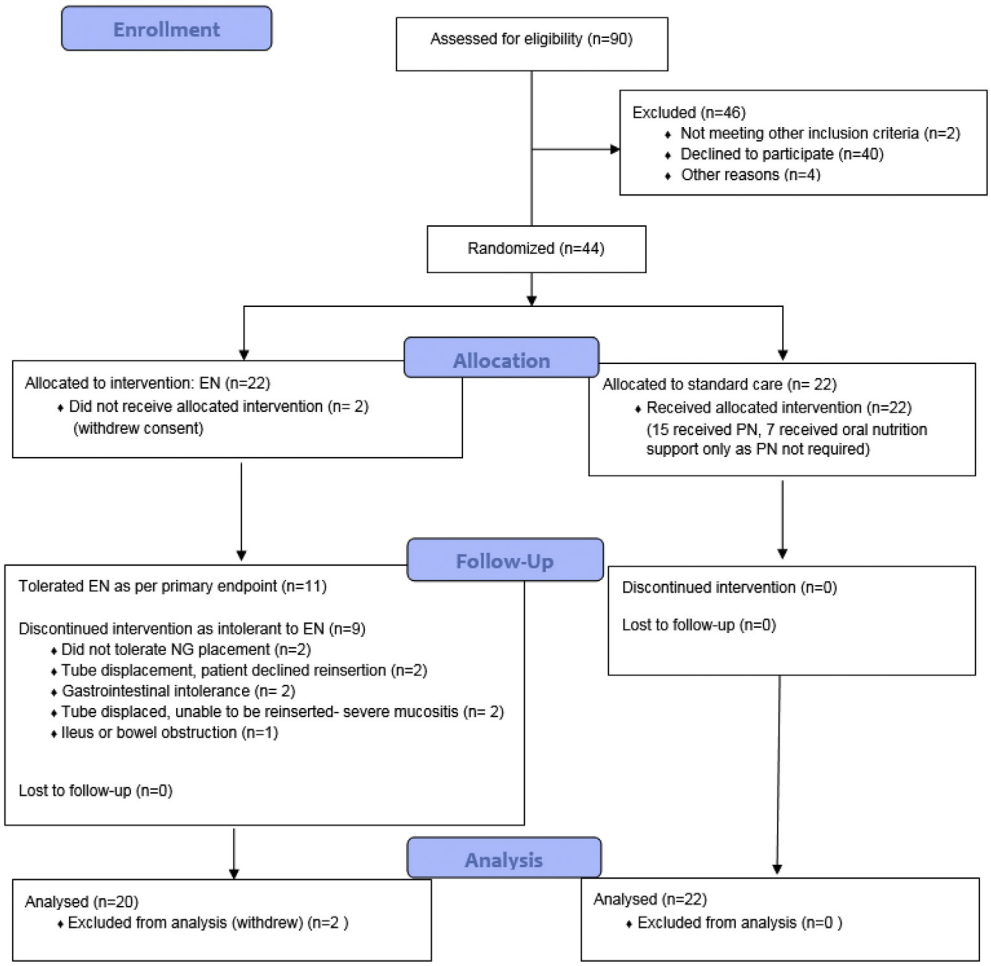

Fig. 1. CONSORT flow diagram of patient recruitment and randomization.

commenced a median of five days [5–8] post-transplant with a median duration of 12 days [9–21].

Twenty-nine percent of patients receiving CyTBI conditioning had grade 1–2 mucositis and 71% had grade 3–4 mucositis. In the FluMel group 58% of patients had grade 1–2 mucositis and 33% had grade 3–4. Despite more severe mucositis in the CyTBI group the median duration of NG feeding was 8 days [5–12] and the median amount of goal feeding received was 73% (57–92). In comparison, the FluMel group had a median 9 days NG feeding [2–12] meeting 80% (68–91) of goal feeding. When examining the effect of type of conditioning on tolerance 43% of patients receiving CyTBI myeloablative conditioning tolerated EN versus 62% of those receiving FluMel (reduced intensity). Overall 67% of patients with grade 1–2 mucositis tolerated EN and 33% of patients with grade 3–4.

4. Discussion

A recent systematic review on nutrition support during allogeneic transplant highlighted the limited available evidence to guide decisions in this area, with only three observational studies published since 2009 [24]. Despite the limited evidence, the authors concluded that 'considering the important side effects of PN, current evidence points to a beneficial role of EN as a first choice' [24]. A large observational study published since this review found a reduced risk of GVHD and improved survival with EN compared to PN [17]. The recently updated ESPEN guidelines also recommend EN unless in the presence of severe mucositis, intractable vomiting, ileus, severe malabsorption, protracted diarrhea or gastrointestinal GVHD, in which case PN is preferred [1]. Prior work from our group demonstrated that commencing NG feeding at the time patients fail to meet nutritional requirements was not tolerated due to the high incidence of mucositis and/or enterocolitis [12]. Results of two observational studies commencing EN proactively prior to mucositis development have suggested greater tolerance of EN, with only 32–42% of patients requiring a change to and/or supplementary PN [9,11]. On this background our current study randomised patients to receive standard care (PN when required) or proactive EN commencing on day one after transplantation. In comparison to our previous findings this studies results demonstrate improved NG feeding tolerance when started proactively, with half of patients undergoing reduced intensity or standard myeloablative allogeneic HPCT tolerating EN.

There is minimal literature on how to define NG feeding tolerance during HPCT with studies often reporting the number changing to PN without defining the reasons for this or a measure for NG feeding success. Although frequency of gastrointestinal symptoms or gastric aspirate volume are common measures of tolerance in other patient groups, these are not suitable for use during HPCT. In this study clear definitions of EN intolerance and reasons for NG feeding cessation were used. Almost 90% of patients ceased NG feeding before meeting the feeding cessation criteria described in the protocol. Due to this some patients required commencement of PN however for others the nutritional impact was minimal with NG feeding ceasing only a day or two prior to resuming adequate oral intake. The most

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Table 3
Nutrition and clinical outcomes.

	Enteral nutrition group (n = 20)	Standard care group (n = 22)
Nutrition Outcomes		
PN received		
Yes	9 (45%)	15 (68%)
No	11 (55%)	7 (32%)
Duration of feeding[a] (days)median (Q1–Q3)	16 (12–21)	9 (0–17)
% of goal nutrition met via feeding[b] (n_{EN} = 19, n_{SC} = 15) median (Q1–Q3)	90 (80–93)	97 (96–98)
Clinical Outcomes		
Mucositis (n_{EN} = 19, n_{SC} = 15)		
None	1 (5%)	1 (7%)
Grade 1–2	9 (47.5%)	5 (33%)
Grade 3–4	9 (47.5%)	9 (60%)
Hyperglycaemia (n_{EN} = 19, n_{SC} = 15)	7 (37%)	5 (33%)
Elevated triglycerides (n_{EN} = 17, n_{SC} = 13)[c]	8 (47%)	9 (69%)
Elevated LFTs (n_{EN} = 19, n_{SC} = 15)	9 (47%)	7 (47%)
Grade 3–4 catheter related infection (n_{EN} = 19, n_{SC} = 15)	2 (11%)	1 (7%)
Days neutropenic post HPCT (n_{EN} = 19, n_{SC} = 15) median (Q1–Q3)	13 (11–16)	12 (11–16)
Length of hospital stay from day 0 median (Q1–Q3)	28 (21–33)	20 (19–28)
Platelet engraftment by day 100	17 (85%)	18 (82%)
GVHD by day 100	10 (50%)	13 (59%)
Gastrointestinal GVHD by day 100	4 (20%)	5 (23%)
Survival at day 100	18 (90%)	19 (86%)

PN: parenteral nutrition, EN: enteral nutrition, LFTs: liver function tests, GVHD: graft versus host disease.
n_{EN}: patients randomised to enteral nutrition who received either enteral nutrition, parenteral nutrition or both.
n_{SC}: patients randomised to standard care who received parenteral nutrition.
[a] For the enteral nutrition group this includes days of nasogastric feeding plus days of parenteral nutrition if this was also required.
[b] for the enteral nutrition group this includes nutrition met via nasogastric feeding plus parenteral nutrition if this was also required.
[c] Triglyceride testing not completed for 2 patients in each group.

common reasons for early feeding cessation were tube displacement, tube blocking or gastrointestinal intolerance. In this study 8–10fr NG tubes were used, however it was observed that 8fr tubes appeared to block more frequently than 10fr. If tubes were unable to be unblocked and required removal they could often not be replaced due to the presence of grade 3–4 mucositis. Gastrointestinal side effects from conditioning are common during HPCT and 20% of patients ceased feeding due to vomiting, pain or bloating. Interestingly no patients ceased EN due to diarrhoea or required 'top–up' PN due to tolerating only a low rate of EN. Other studies report similar reasons for EN cessation including repeated vomiting [9,11,25] nausea, diarrhoea [25] psychological intolerance, tube displacement or blocking [9].

Prior to this study, EN was used infrequently on the HPCT unit therefore a limitation of this study is that some staff were unfamiliar with this mode of feeding despite ward education sessions on EN management. One study reporting a high rate of EN tolerance was conducted in a transplant unit where EN is part of standard supportive care. The authors noted that 'tolerance to NGT improved over the course of the study because of better acceptance by the nursing team after initial reluctance owing to the reputation of harshness of nasogastric feeding' [11]. Other authors agree that multidisciplinary counselling to educate patients and encourage EN is required for enteral feeding success [26,27]. It is noteworthy that 44% of potentially eligible patients screened for our study declined to participate. Patient and staff attitudes and perceptions to EN were not explored in this study but are likely to effect successful use of EN and should be explored in future research to assist in optimising EN tolerance.

Table 4
Outcomes of the patients randomised to enteral nutrition.

Enteral Nutrition Outcome	Randomised to enteral nutrition (n = 20)
NG feeding received	
Yes	17 (85%)
No, failed NG placement	3 (15%)
Primary Endpoint: tolerance of enteral nutrition	
Yes tolerated EN, no change to PN or top-up PN required	11 (55%)
Not tolerated as PN commenced	9 (45%)
Change to parenteral nutrition	
Yes change to PN required	9 (45%)
No PN required as tolerated NG feeding	9 (45%)
No PN required as maintained oral intake post cessation of NG feeding	2 (10%)

NG: nasogastric, EN: enteral nutrition, PN: parenteral nutrition.

In this study the EN group met an average of 90% of goal nutrition with the PN group meeting 97%. This difference although statistically significant is unlikely to be clinically meaningful in practice. Unlike observational studies investigating EN during adult HPCT [9,11,17] or paediatric HPCT [28] no statistically significant differences were found between groups for clinical outcomes or rate of complications. Possible explanations for this include the small study size or the randomised study design which avoids the limitations and biases associated with observational designs. Interestingly, a trend towards longer length of stay was noted in the EN group (28 days EN vs 20 days PN), however it did not reach statistical significance. Whilst reasons for this trend are unknown, this is a clinically significant result and should be examined in future trials with a larger sample size. This finding highlights the need for ongoing randomised comparisons to understand the true impact of different nutrition support pathways on clinical outcomes.

Patients receiving non myeloablative conditioning were excluded from this study therefore due to conditioning intensity and side effects patients eligible for this study rarely meet nutrition requirements at day one after transplantation. Due to this the risk

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Table 5
Outcomes of the patients who received nasogastric feeding.

Enteral Nutrition Outcome	Received nasogastric feeding (n = 17)
NG tube failure	
Yes blocked	3 (18%)
Yes dislodged	7 (41%)
No	7 (41%)
NG feeding ceased early	
Yes	15 (88%)
No	2 (12%)
Reason for early NG feeding cessation (n = 15)	
Tube displacement: patient declined reinsertion	7 (47%)
NG dislodged/blocked, grade 3–4 mucositis prevented reinsertion	3 (20%)
Contraindication to EN - ileus	1 (6.5%)
Gastrointestinal intolerance eg: vomiting, pain, bloating, nausea	3 (20%)
Withdrawal of patient consent for feeding (disliked elevated positioning)	1 (6.5%)
Top up parenteral nutrition required	
Yes	0
No	17 (100%)
Tolerated goal rate of NG feeding	
Yes	10 (59%)
No	4 (23%)
Goal rate not trialled	3 (18%)
Number of NG tube placements	
1	15 (88%)
2–4	2 (12%)
Amount of goal NG feeding received (%)	
Median (Q1–Q3)	86 (71–93)
Duration of NG feeding (days)	
Median (Q1–Q3)	9 (4–13)

NG: nasogastric, EN: enteral nutrition, PN: parenteral nutrition.

of overfeeding with EN was low. Due to incorporating oral and nasogastric nutrition in the primary endpoint definition of EN tolerance, two patients who either failed NG placement or ceased NG feeding in the first two days and did not require PN were still considered tolerant of EN. If these patients are excluded from the analysis the rate of NG feeding tolerance was 45% (n = 9). The advantage of this approach is that it is representative of clinical practice where some patients may still tolerate oral intake, making these results more transferable to practice. While most patients undergoing myeloablative HPCT require intensive nutritional support, the criteria used to instigate it vary and in this study we could not identify pre HPCT factors predictive of requiring nutrition support. While future large studies may provide clarity on this, at present commencement of early EN can only be recommended based on the likely toxicity of the conditioning regimen. The higher cost of PN in comparison to EN has been reported in the literature [10,25] and confirmed in this study with the cost of PN per patient $1350 higher than the cost of EN for the median duration of nutrition support.

This is the first randomised study to investigate the tolerance and clinical outcomes of proactive EN during allogeneic HPCT. The results of this study indicate that half of all patients receiving reduced intensity or myeloablative allogeneic transplantation can tolerate EN when commenced proactively on day one post transplant, prior to mucositis development. This has the potential to significantly reduce the use of PN and its associated complications and cost, and therefore, we recommend proactive EN be considered as first line nutritional support for this patient cohort.

Statement of authorship

S Andersen carried out the literature review, study design, data collection, data analysis, interpretation and manuscript drafting.

N Weber assisted with study design, data collection, analysis, interpretation and manuscript drafting.

T Brown, G Kennedy, M Banks and J Bauer assisted with study design, data analysis, interpretation and manuscript drafting.

All authors assisted in manuscript revision and have read and approved the final manuscript.

Conflict of interest

None to declare.

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