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Original article

Enteral nutrition improves clinical outcome and reduces costs of acute mesenteric ischaemia after recanalisation in the intensive care unit

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SUMMARY

Background: Little data evaluate the enteral nutrition (EN) for patients with acute mesenteric ischaemia (AMI) in the intensive care unit (ICU). This study assessed the outcomes of EN for recanalised AMI patients in the ICU.
Methods: In this retrospective study, 183 AMI patients with mesenteric recanalisation admitted to two surgical ICUs were included. Patients were divided into EN (EN within first week, n = 95) and total parenteral nutrition (TPN) group (TPN in 1st week, n = 88). The etiology, outcomes and complications were compared. Nutritional, immunologic, inflammatory response and mesenteric reperfusion were evaluated. Subgroup analysis and cost-assessment were performed.
Results: No significant difference of demographics and illness severity at baseline were found. The rates of TPN for ≥6 months (7.4% vs. 18.2%, $P < 0.01$), infectious complications (7.4% vs. 20.5%, $P = 0.01$) and acute respiratory distress syndrome (4.2% vs. 13.6%, $P < 0.01$) were lower in EN group. For patients with mesenteric infarction (n = 101), EN was associated with earlier bowel continuity restoration ($P < 0.01$) and lower 30-day mortality (7.3% vs. 26.1%, $P = 0.01$). For patients without initial bowel resection (n = 82), length of ICU and hospital stay was significantly shortened in EN group. The 1-year survival was 88.4% in EN group and 78.4% in TPN group ($P = 0.031$). EN was cost-effective, with improved inflammatory response and elevated peak velocity of mesenteric flow.
Conclusions: For recanalised AMI patients, EN starting within the first week represents a favourable alternative to TPN. A multicentre randomised controlled trial with high level of evidence is warranted in the future.
Clinical relevancy statement: Acute mesenteric ischaemia (AMI) is a catastrophic abdominal vascular emergency in the surgical intensive care unit (ICU), and the mortality of AMI remains unchanged despite significant progress of endovascular techniques. A multidisciplinary and multimodal management approach of AMI in the ICU has been recently proposed to improve patient's survival and prevent the intestinal failure. Post-recanalisation nutrition therapy may significantly improve the overall survival of AMI patients is quite underemphasised in the ICU. Definitive data comparing EN with TPN for this patient population are very lacking. This study provides the clinical data to suggest that early EN starting after ICU admission represents a favourable alternative to TPN for recanalised AMI patients. The nutrition therapy protocol in the ICU for this special cohort needs to be updated with more high-level evidence in the future.

1. Introduction

Acute mesenteric ischaemia (AMI) is a catastrophic abdominal vascular emergency in the surgical intensive care unit (ICU) despite more than 50 years of advances in the treatment. AMI patients have a daunting mortality of 58% and high risk of extensive intestinal

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infarction, complicated by short bowel syndrome (SBS) and permanent intestinal failure requiring long-term total parenteral nutrition (TPN) [1]. Endovascular therapy has been the primary recanalisation modality of AMI and has shown favourable clinical outcomes [2,3]. However, the mortality associated with AMI remains unchanged despite significant increase in utilisation of endovascular techniques [4]. Considering AMI's complex pathophysiologic process, mesenteric recanalisation is only the first step of successful treatment. Emergent laparotomy remains imperative for patients with signs of transmural bowel infarction. In a study by Edwards et al., intestinal infarction was found in 81% of cases, and perioperative mortality was as high as 62% [5]. Without effective postoperative management, AMI can lead to lean body mass loss, visceral hypoperfusion, systemic immune compromise and even multiple-organ dysfunction syndrome (MODS).

A multidisciplinary and multimodal management approach of AMI has been proposed to improve overall patient survival and prevent intestinal failure in the ICU [6]. The goal-directed nutrition support to ensure appropriate energy and protein intake is associated with reduced morbidity and mortality in critical illness [7]. Early enteral nutrition (EN) delivered to appropriate patients can promote gut-mediated immunity, balance metabolic response, maintain microbial diversity and improve clinical outcome compared to TPN therapy [8]. Nevertheless, clinicians usually withhold early EN and prescribe TPN for recanalised AMI patients due to the risks of hemodynamic failure and exacerbation of bowel ischaemia. Recent data have shown that early EN can be achieved with careful monitoring and adequate delivery in patients after cardiac surgery even with hemodynamic instability [9]. In addition, enteral feeding has shown a protective effect for ischaemic injury of intestinal mucosa which is associated with reduced major complications and enhanced functional recovery in hypotensive patients [10].

At present, the post-recanalisation treatment that may greatly improve the survival of AMI patients is quite underemphasised in ICU. Definitive data comparing EN with TPN among this patient population are lacking. The aim of this study was to compare the clinical outcome, mesenteric reperfusion, nutritional, immunologic and inflammatory response of recanalised AMI patients receiving EN with those receiving TPN therapy in the ICU. A cost-analysis of two nutritional regimens was also carried out.

2. Patients and methods

2.1. Patients and study design

This was a retrospective study conducted in two separate surgical ICUs of a national intestinal failure unit. The unit was part of an integrated intestinal stroke centre where a stepwise management strategy of AMI was practiced [11]. The study protocol was approved by the Institutional Ethical Committee, and the written informed consent was obtained from all the patients. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patients with at least one of the four diagnostic procedures (computed tomography [CT] scan, digital subtraction angiography, gastrointestinal endoscopy or laparotomy) supporting the diagnosis of AMI from January 2007 to February 2014 were included. The exclusion criteria were: 1) age <18 years; 2) patients with secondary causes of mesenteric infarction (e.g., volvulus, adhesions, strangulated hernia); 4) irreversible acute hepatic or renal failure before ICU admission; 5) pregnancy or lactation; 6) absence of nutrition therapy in ICU or early transfer [within 7 days] to other hospitals; 7) incomplete medical records or follow-up data. All eligible patients were subsequently divided into the EN group (receiving EN within the first week of ICU admission) and TPN group (receiving TPN throughout the first week of ICU admission) (Fig. 1).

2.2. Mesenteric recanalisation strategy

Mesenteric recanalisation includes open and endovascular surgery in a hybrid operating room. Intraoperative thrombectomy or embolectomy is performed during emergent laparotomy for patient with peritonitis. For patients without peritonitis, endovascular therapy (aspiration embolectomy or thrombectomy, stenting and thrombolysis) are used. Antegrade aortomesenteric bypass is considered for only fast restoration of flow from proximal SMA thrombosis. Endovascular procedures for mesenteric vein thrombosis (MVT) include mechanical thrombectomy and thrombolysis via percutaneous transjugular intrahepatic portosystemic route, percutaneous transhepatic route or superior mesenteric artery (SMA) approach. Damage control surgery was applied for patients with bowel infarction. The viability-questionable segments are preserved and bowel resection is performed with staples instead of primary anastomosis, leaving the creation of anastomoses or stomas until the second-look laparotomy. For patients with high risk of intra-abdominal hypertension, the skin-only closure or temporary closure with an abdominal VAC® dressing (Kinetic Concepts, San Antonio, TX, USA) was used. After mesenteric recanalisation procedures, all patients were transferred into surgical ICU receiving aggressive fluid resuscitation, multiple-organ function support, and nutrition therapy.

2.3. Nutrition management protocol

Commercial EN products were administrated via a nasogastric tube, nasojejunal tube or jejunostomy feeding tube. Amino acid formula (Vivonex, Nestle, Minneapolis, MN, USA) or peptide-based formula (Peptisorb, Nutricia, China) was initially prescribed, followed by a transition towards whole protein formula (Nutrison Fiber, Nutricia, China). The calorie density was 1 kcal/mL with an osmolarity of 400 mOsm/L. The enteral formula was infused continuously by a peristaltic pump. The dosage and infusion speed of EN were gradually increased from 33.3% to 50.0% to the full strength over 5–7 days (adaptation phase) under close monitoring of 72 h. To avoid low-calorie intake and dehydration, supplemental parenteral nutrition (PN) was considered when EN is insufficient for more than 2 days during the adaptation phase [12]. The ideal body weight was calculated according to the Broca formula. For men, ideal body weight (kg) = [height (cm)−100]−([height (cm)−100] × 10%); for women, ideal body weight (kg) = [height (cm)−100] + ([height (cm)−100] × 15%). Full enteral feeding of 25 kcal/kg/d and 1.5 g of protein/kg/d was granted as a primary nutrition support goal. For obese patients with body mass index (BMI) > 30 kg/m^2, this was calculated as (25 kcal/kg of ideal body weight) + 30%. Then a full-strength maintenance dose was administered based on the results of indirect calorimetry per day.

Prescribed TPN (all-in-one TPN) was given to patients by an indwelling 2–3 lumen central venous catheter (Centra-Line™, Biometrix Medical, Gronsveld, The Netherlands). The basic regimen consisted of 1.25 g amino acids/kg/d, 3 g glucose/kg/d and 1 g fat/kg/d. Lipid was fish oil supplemented soybean oil (Omegaven 10%; Fresenius, Germany). Artificial nutrition, either TPN or EN, was continued until patients achieved an adequate oral food intake (800–1000 kcal/day).

Succus entericus reinfusion (SER) was performed for patients with double ostomy. The output from the proximal stoma was collected with a triple catheterisation cannula connected to

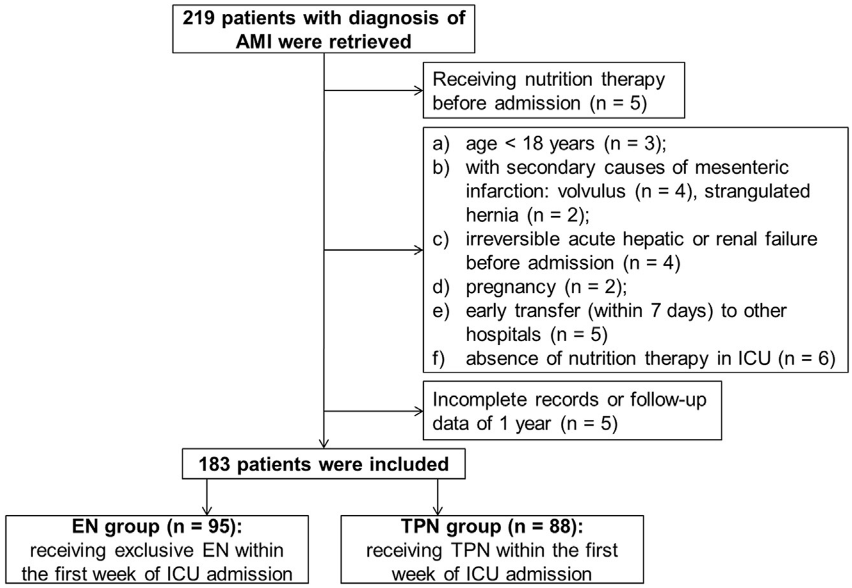

Fig. 1. Flow chart of the study design. ICU, intensive care unit; TPN, total parenteral nutrition; EN, enteral nutrition.

aspiration pumps of negative pressure. The freshly collected succus entericus was drained into a sterile catheter bag and reinfused into the distal stoma through a Foley catheter at a specific rate.

2.4. Data collection

The medical records of eligible patients were reviewed, and the following data were retrieved from an institutional medical database system: demographics, BMI, etiologic factors, types of AMI, CT mesenteric angiography, date of the emergent operation, initial recanalisation modality, length of remaining bowel after recanalisation and comorbidity. The small bowel lengths were measured using methods of radiology (barium follow through and/or CT enterography) and surgery for restoration of bowel continuity (measured along the antimesenteric border of unstretched bowel). The acute physiology and chronic health evaluation (APACHE) II score was calculated at ICU admission.

Laboratory tests, including nutritional parameters (e.g., albumin, prealbumin, transferrin), inflammatory and immunologic parameters (e.g., total lymphocytes, polymorphonuclear cells, C-reactive protein, L-lactate) were performed using Bayer ADVIA Centaur automated immunoassay system (Bayer, Leverkusen, Germany) on hospital admission (baseline), and then on post-recanalisation day (PRD)-1 and -7. Quantitative determination of human interleukin (IL)-6, intestinal fatty acid-binding protein (I-FABP) and tumour necrosis factor (TNF)-α were performed in microtitre plates using a commercially available enzyme-linked immunosorbent assay according to the procedures recommended by the manufacturer (Genzyme Diagnostics, Cambridge, UK). Lymphocyte subpopulations (CD4+/CD8+ ratio) were determined by flow cytometer (Becton Dickinson, San Jose, CA, USA). Fluorescent-activated cell-sorting analysis was carried out on a FACScalibur (Becton Dickinson) flow cytometer.

Doppler ultrasonography was performed to measure the peak velocity of SMA flow using a convex 5.0 MHz probe provided by a pulse-Doppler device operating at 2.5 MHz (SSD-5500SV, Aloka, Japan). The sampling volume cursor was placed at an angle of less than 60° to the longitudinal axis of the vessel. The spectrum of the Doppler signals or backscatter caused by blood cells was analysed while patients held their breath for about 4 s.

2.5. Clinical outcome measures

Clinical outcomes of interest included: 1) time from recanalisation to EN; 2) initial route of EN; 3) rate of bowel ischaemia recurrence, relaparotomy and repeat bowel resection; 4) time to restoration of bowel continuity; 5) length of ICU stay and hospitalisation; 6) APACHE II score on PRD-7; 7) incidence of SBS, MODS and long-term TPN (requirement of TPN for $\geq$6 months); 8) 30-day mortality and 1-year survival.

In this study, major complications were defined as events required further therapy, an unplanned increase in the level of care, prolonged hospitalisation (>48 h) or resulted in permanent adverse sequelae and death. All major complications during ICU stay were noted. Microbiological analysis and positive culture proved all infectious complications. Abdominal bloating, delayed gastric emptying (defined as gastric residual volume $\geq$ the cutoff value of 150 ml), abdominal cramps, severe diarrhoea, vomiting and displacement of jejunostomy or nasojejunal tubes were considered as indication of EN intolerance. Organ failure was defined according to the latest international recommendations on septic shock [13].

In addition, the subgroup analysis of AMI patients with mesenteric infarction requiring initial bowel resection or endovascular recanalisation without initial bowel resection was performed respectively.

2.6. Cost analysis

The cost analysis of nutrition therapy was performed according to the following variables: a) infusion set (e.g. tube, catheter, pump, line, dressing); b) nutrition formulas (e.g. all vitamins, electrolytes and trace elements); c) ICU care (e.g. general care, medical treatment, organ function support); d) tests for monitoring (e.g. laboratory, radiologic procedures, microbiology); e) sanitary personnel (e.g. physicians, nurses, technicians, pharmacists).

2.7. Statistical analysis

Continuous variables were defined as means ± standard deviation if they were normally distributed; otherwise, median values and interquartile ranges M (P25, P75) were represented.

Differences between the two groups were determined by t test for normally distributed continuous variables and the Mann–Whitney test for nonparametric data. Categorical data between the two groups were compared using the χ2 test or χ2 corrections for continuity. Continuous variables, including Lactate, I-FABP and peak velocity of SMA flow over time between the groups, were analysed using repeated measures analysis of variance followed by Bonferroni's *post hoc* testing. The survival rate within 1 year between the two groups was compared by Log-Rank test. The SPSS software (version 12.0; SPSS, Inc., Chicago, IL, USA) was used for statistical analysis. Statistical significance was accepted for a *P*-value ≤0.05.

3. Results

3.1. Demographics and etiology

A total of 183 patients (103 males and 80 females, age 47.0 ± 12.8 years) were included: 95 patients in EN group and 88 in TPN group (Fig. 1). The two groups were similar for baseline characteristics, comorbidity and surgical variables. The primary etiology included SMA embolism (27.9%), MVT (38.3%) and spontaneous isolated dissection of SMA (17.5%). Acute mesenteric infarction was found in 55.2% patients, and the rate of SBS was 6.0% during emergent laparotomy. Mesenteric recanalisation was performed by endovascular techniques in 63.4% patients and open surgery in 36.6% patients. The ostomy was carried out in 20.7% patients after initial bowel resection (Table 1).

3.2. Nutrition management

In EN group, the initial routes of EN include nasogastric tube (38.9%), nasojejunal tube (25.3%), and jejunostomy feeding tube (35.8%). Twenty-two (23.2%) patients received SER, and 9 (9.5%) out of 95 patients in EN group experienced enteral feeding intolerance. Supplemental PN was given in 23 patients (24.2%). Occlusion of the jejunostomy or nasojejunal tube was observed in 10 patients. All were recovered by flushing or insertion of a stylet. Delayed gastric emptying was reported in 5.3% of patients, and abdominal distension in 6.3% of the patients who were fed early EN. The symptoms related to EN were resolved by temporary discontinuation or reduction of infusion (Table 2). During the first week of admission, the mean energy intake per day was 1134 ± 412 kcal in EN group vs. 1271 ± 359 kcal in TPN group. Then delivered energy of both EN and TPN group was escalated to the similar level of energy target during the second week (Fig. 2). In EN group, the duration of nutrition support is 24.0 ± 9.0 days. The duration of nutrition support is 34.7 ± 25.7 days in TPN group.

3.3. Nutritional, inflammatory and immunologic response

No significant differences of the nutritional and immunologic variables were found between the groups. In both groups, serum levels of albumin, prealbumin and transferrin dropped significantly after mesenteric recanalisation procedures and remained stable until PRD-7 ($P < 0.01$). The immunologic response (i.e., total lymphocytes, CD4/CD8 ratio, polymorphonuclear cells) were depressed from PRD-1 to PRD-7 ($P < 0.01$). The inflammatory parameters (i.e.,

Table 1
Baseline characteristics of eligible patients on admission of ICU.

Variables	EN (n = 95)	TPN (n = 88)	*P* value
Age (y), mean ± SD	47.7 ± 12.7	46.2 ± 12.9	0.438
Male gender, n (%)	55 (57.9)	48 (54.5)	0.648
BMI, mean ± SD	21.2 ± 1.3	21.4 ± 1.3	0.295
AMI type, n (%)			
Embolism of SMA	27 (28.4)	24 (27.3)	0.863
Spontaneous isolated dissection of SMA	15 (15.8)	17 (19.3)	0.530
Thrombosis of SMA	14 (14.7)	13 (14.8)	0.995
Thrombosis of SMV	37 (38.9)	33 (37.5)	0.840
Nonocclusive mesenteric ischemia	2 (2.1)	1 (1.1)	1.000[a]
Acute mesenteric infarction, n (%)	55 (57.9)	46 (52.3)	0.445
SBS after initial surgery, n (%)	6 (6.3)	5 (5.7)	0.857
Recanalization modality, n (%)			
Endovascular recanalization	59 (63.2)	57 (64.8)	0.708
Thrombolysis	46 (48.4)	40 (45.5)	0.688
Thrombectomy/embolectomy	35 (36.8)	29 (33.0)	0.582
Stenting	18 (18.9)	20 (22.7)	0.529
Angioplasty	30 (31.6)	25 (28.4)	0.640
Open surgical recanalization	36 (36.8)	31 (35.2)	0.708
Open thrombectomy	30 (31.6)	26 (29.5)	0.766
Aortomesenteric artery bypass	6 (6.3)	5 (5.7)	0.857
Initial bowel resection, n (%)	55 (57.9)	46 (52.3)	0.445
Primary anastomosis	35 (36.8)	28 (31.8)	0.475
Ostomy	20 (21.1)	18 (20.5)	0.921
Open abdomen	9 (9.5)	8 (9.1)	0.929
Comorbidity, n (%)			
Diabetes mellitus	23 (26.1)	18 (20.5)	0.543
Hypertension	23 (24.2)	25 (28.4)	0.519
Liver disease	30 (31.6)	26 (29.5)	0.766
COPD	20 (21.1)	18 (20.5)	0.921
Cardiac disease	19 (20.0)	14 (15.9)	0.472
Malignancy	3 (3.2)	3 (3.4)	1.000[a]
CKD (Cr > 1.5 mg/dL)	2 (2.1)	1 (1.1)	1.000[a]
APACHE II score, M (P25, P75)	21 (18, 25)	22 (18.3, 24)	0.934

SD, standard deviation; EN, enteral nutrition; TPN, total parenteral nutrition; BMI, body mass index; AMI, acute mesenteric ischemia; SMA, superior mesenteric artery; SMV, superior mesenteric vein; SBS, short bowel syndrome; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney diseases; Cr, creatinine; APACHE, acute physiology and chronic health evaluation.
[a] χ2 correction for continuity were used.

Table 2
Outcome and complications of all patients.

Variables	EN (n = 95)	TPN (n = 88)	*P* value
Initial route of EN, n (%)			
NGT	37 (38.9)	–	–
NJT	24 (25.3)	–	–
JFT	34 (35.8)	–	–
Succus entericus reinfusion, n (%)	22 (23.2)	–	–
Re-laparotomy, n (%)	27 (28.4)	26 (29.5)	0.867
Bowel ischemia recurrence, n (%)	9 (9.5)	17 (19.3)	0.057
Bowel resection after initial surgery, n (%)	10 (10.5)	17 (19.3)	0.094
Length of ICU stay (d), M (P25, P75)	13 (10, 21)	18 (14.3, 21.5)	<0.001
Length of hospital stay (d), M (P25, P75)	20 (16, 29)	26 (23, 30.8)	<0.001
SBS, n (%)	9 (9.5)	14 (15.9)	0.189
MODS, n (%)	9 (9.5)	8 (9.1)	0.929
Long-term TPN (requirement of TPN for > 6 months), n (%)	7 (7.4)	16 (18.2)	0.027
30-day mortality, n (%)	7 (7.4)	14 (15.9)	0.070
Complications			
Enteral feeding intolerance, n (%)	9 (9.5)	8 (9.1)	0.929
Delayed gastric emptying	5 (5.3)	4 (4.6)	1.000
Severe diarrhea	3 (3.2)	4 (4.6)	0.918[a]
Abdominal distension	6 (6.3)	5 (5.7)	0.857
Vomiting	3 (3.2)	3 (3.4)	1.000[a]
Infectious complications, n (%)	7 (7.4)	18 (20.5)	0.010
Abdominal abscess	4 (4.2)	4 (4.6)	1.000[a]
Wound infection	4 (4.2)	3 (3.4)	1.000[a]
Pneumonia	3 (3.2)	9 (10.2)	0.054
Urinary tract infection	2 (2.1)	2 (2.3)	1.000[a]
Catheter-related infection	1 (1.1)	6 (6.8)	0.100[a]
Sepsis	3 (3.2)	8 (9.1)	0.092
Noninfectious complications, n (%)	18 (18.9)	17 (19.3)	0.949
ACS	5 (5.3)	5 (5.7)	1.000[a]
Anastomotic leak	6 (6.3)	5 (5.7)	0.857
Hemoperitoneum	7 (7.4)	5 (5.7)	0.645
GI bleeding	7 (7.4)	7 (8.0)	0.882
ARDS	4 (4.2)	12 (13.6)	0.024
Cardiac failure	1 (1.1)	1 (1.1)	1.000[a]
Liver dysfunction	1 (1.1)	6 (6.8)	0.100[a]

SD, standard deviation; EN, enteral nutrition; NGT, nasogastric tube; NJT, nasojejunal tube; JFT, jejunostomy feeding tube; ICU, intensive care unit; SBS, short bowel syndrome; MODS, multiple organ dysfunction syndrome; APACHE, acute physiology and chronic health evaluation; TPN, total parenteral nutrition; PRD, post-recanalization day; ACS, acute compartment syndrome; GI, gastrointestinal; ARDS, acute respiratory distress syndrome.
[a] $\chi 2$ correction for continuity were used.

C-reactive protein level, IL-6 and TNF-α, increased significantly in both groups on PRD-1 [$P < 0.01$]). Then on PRD-7, the levels of inflammatory response were lower in patients receiving EN than those receiving TPN (Table 3).

3.4. Mesenteric perfusion evaluation

As shown in Fig. 3, serum levels of lactate and I-FABP decreased gradually after mesenteric recanalisation in both groups. The lactate and I-FABP levels were lower in EN group on PRD-7 and PRD-5 ($P < 0.01$). The elevation of peak velocity of SMA flow on ultrasonography was greater in the EN group than in the TPN group from PRD-3 ($P < 0.01$).

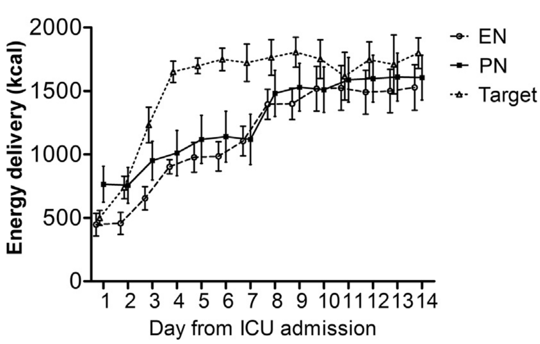

Fig. 2. Energy delivery and energy target in ICU. Energy was expressed as means ± standard deviation (kcal). ICU, intensive care unit; TPN, total parenteral nutrition; EN, enteral nutrition.

3.5. Clinical outcomes and complications

There is no significant difference of the rate of relaparotomy, bowel ischaemia recurrence and incidence of SBS and MODS between the two groups. The 30-day mortality (7.4% vs. 15.9%) is lower in the EN group than in the TPN group but with no statistical significance. However, the length of ICU stay and hospitalisation was significantly shorter in patients receiving early delivery of EN ($P < 0.01$). Fewer patients had long-term TPN (7.4% vs. 18.2%, $P < 0.01$) infectious complications (7.4% vs. 20.5%, $P = 0.01$) and acute respiratory distress syndrome (4.2% vs. 13.6%, $P < 0.01$) in the EN group (Table 2). During 1-year follow-up, the cumulative survival rate was better in the EN group (88.4% vs. 78.4%, $P = 0.031$) (Fig. 4).

The subgroup analysis showed that for patients with mesenteric infarction requiring initial bowel resection (n = 101), EN was associated with earlier bowel continuity restoration after ostomy ($P < 0.01$) and lower 30-day mortality ($P = 0.01$). For patients with endovascular recanalisation without initial bowel resection (n = 82), patients in the EN group had shorter ICU and hospital stay than those in the TPN group ($P < 0.01$) (Table 4).

By cost analysis, average cost per day in the TPN group was significantly higher than that of the EN group ($934.8 vs. $595.8,

Table 3
Nutritional, inflammatory, and immunologic response.

Variables	EN (n = 95)	TPN (n = 88)	*P* value
Nutritional response			
Albumin (g/L) (normal range 35–50), mean ± SD			
Baseline	36.0 ± 2.3	36.1 ± 2.2	0.673
PRD-1	30.3 ± 1.1[a]	30.2 ± 1.3[a]	0.604[b]
PRD-7	34.5 ± 2.2[a]	34.8 ± 2.0[a]	0.212
Prealbumin (g/L) (normal range 0.20–0.40), mean ± SD			
Baseline	0.25 ± 0.03	0.25 ± 0.03	0.269
PRD-1	0.16 ± 0.03[a]	0.16 ± 0.03[a]	0.222
PRD-7	0.18 ± 0.02[a]	0.17 ± 0.02[a]	0.379
Transferrin (g/L) (normal range 2.20–4.0), mean ± SD			
Baseline	2.60 ± 0.29	2.67 ± 0.35	0.147[b]
PRD-1	2.04 ± 0.27[a]	2.05 ± 0.28[a]	0.816
PRD-7	2.33 ± 0.22[a]	2.30 ± 0.21[a]	0.288
Immunologic response			
Total lymphocytes (cell/mm^3) (normal range 800–5000), mean ± SD			
Baseline	1693 ± 169	1560 ± 226	<0.001[b]
PRD-1	1339 ± 152[a]	1293 ± 116[a]	0.021[b]
PRD-7	1605 ± 162[a]	1400 ± 115[a]	<0.001[b]
CD4/CD8 ratio (normal value > 1), mean ± SD			
Baseline	1.85 ± 0.20	1.85 ± 0.21	0.980
PRD-1	1.53 ± 0.17[a]	1.52 ± 0.17[a]	0.952
PRD-7	1.70 ± 0.18[a]	1.71 ± 0.18[a]	0.555
PMN phagocytosis (%) (normal value > 40), mean ± SD			
Baseline	39.7 ± 1.7	40.0 ± 2.1	0.329[b]
PRD-1	31.1 ± 1.2[a]	31.0 ± 1.2[a]	0.649
PRD-7	35.3 ± 2.2[a]	35.4 ± 2.1[a]	0.682
Inflammatory response			
CRP (g/L) (normal value < 8), mean ± SD			
Baseline	92.4 ± 35.8	89.1 ± 36.1	0.533
PRD-1	145 ± 63.3[a]	141 ± 66.2[a]	0.614
PRD-7	39.3 ± 11.6[a]	83.9 ± 23.6	<0.001[b]
IL-6 (pg/mL) (normal range 56–150), mean ± SD			
Baseline	71.3 ± 12.4	69.4 ± 11.3	0.295
PRD-1	87.8 ± 18.6[a]	88.7 ± 18.1[a]	0.739
PRD-7	45.0 ± 9.2[a]	69.5 ± 6.1	<0.001
TNF-α (pg/mL) (normal range < 100), mean ± SD			
Baseline	148.2 ± 86.5	151 ± 94.8	0.832
PRD-1	187 ± 63.8[a]	198 ± 66.3[a]	0.237
PRD-7	89.6 ± 39.4[a]	116 ± 42.9[a]	<0.001

SD, standard deviation; PRD, post-recanalization day; CRP, C-reactive protein; IL-6, interleukin-6; TNF, tumor necrosis factor; PMN, polymorphonuclear cells.
[a] $P < 0.01$, compared with baseline.
[b] t′-tests were used because of heterogeneity of variance.

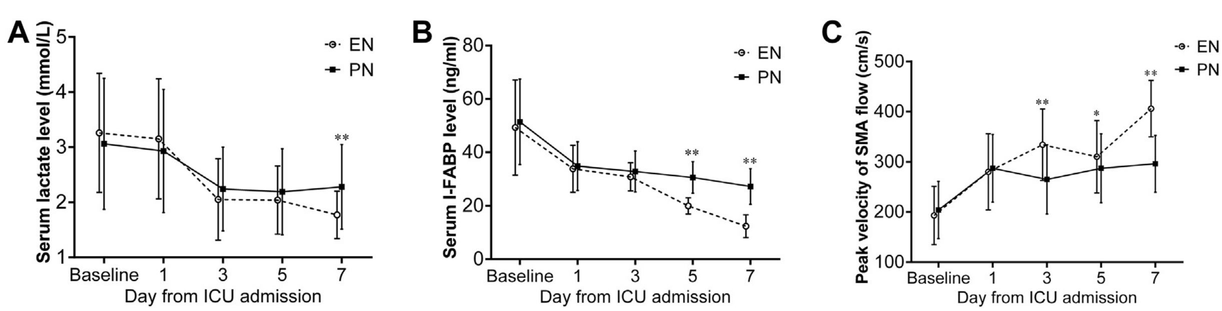

Fig. 3. Serum and hemodynamic parameters of mesenteric perfusion A, B. serum lactate and intestinal fatty acid-binding protein (I-FABP) levels of patients during the first week of ICU admission. C. variations of the peak velocity of SMA flow during the first week after mesenteric recanalisation. Values were expressed as mean ± standard deviation, **P* < 0.05, ***P* < 0.01 when compared among different groups. TPN, total parenteral nutrition; EN, enteral nutrition.

P < 0.01). Nutrition formulas (43.4% in TPN group vs. 6.8% in the EN group) and ICU care (27.2% in the TPN group vs. 37.0% in the EN group) represented most of the daily costs. The costs of the other variables were similar between the two groups (Fig. 5).

4. Discussion

In ICU, the incidence of AMI has risen recently because of increased elderly population and improved diagnostic techniques. AMI becomes a more common cause than expected of acute abdomen in the elderly, but only young patients had better treatment outcomes [14]. Acute mesenteric infarction is associated with a high early mortality, estimated at 28% during the first month [15]. Early recanalisation has been facilitated by modern endovascular technique, and the ‘second peak of mortality’ in the ICU becomes a great challenge to improve overall survival. Complications such as sepsis, electrolyte abnormalities, intestinal failure and malnutrition are the leading causes of high mortality for these patients in the ICU

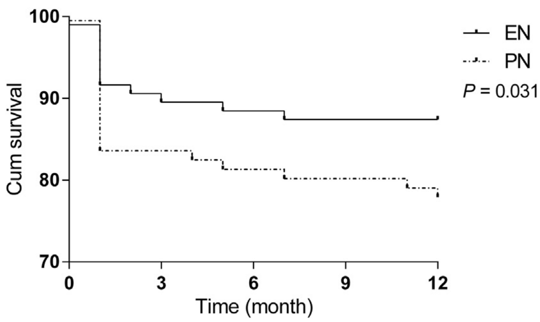

Fig. 4. Kaplan–Meier analysis of cumulative 1-year survival rate. Equality of survival distributions between the two groups were comparable by Log Rank test (P = 0.031). TPN, total parenteral nutrition; EN, enteral nutrition.

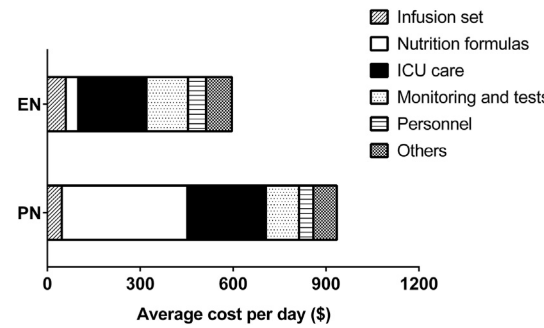

Fig. 5. Cost analysis of different nutritional regimens. TPN, total parenteral nutrition; EN, enteral nutrition.

[16]. TPN and bowel rest are often implemented to optimise the nutrition status. However, EN as opposed to TPN can reduce liver dysfunction, improve intestinal barrier function, avoid bacterial translocation and thus decrease infectious complications [17].

In a recent study of AMI patients in ICU, there were significantly more patients receiving EN in survivors than nonsurvivors [1]. For patients with cardiac surgery, EN increases the cardiac index and splanchnic blood flow [18]. In our study, early introduction of EN improves the mesenteric perfusion of recanalised AMI patients, indicated by augmented mesenteric blood flow and decreased serum levels of lactate and I-FABP. The metabolic response suggests that nutrients are well utilised. Although the mechanism is still unclear, these preliminary results suggest the mesenteric hemodynamic response to EN is adequate in AMI patients after recanalisation.

For AMI patients with suspected bowel infarction, immediate exploratory laparotomy is mandatory. Reestablishing bowel continuity should be considered in all patients with mesenteric infarction regardless of the length of residual small bowel to avoid TPN [19]. It is reported that early postoperative EN improves gut oxygenation and reduces overall costs [20]. Similarly, our study showed that EN resulted in early restoration of bowel continuity, and improved mesenteric perfusion. Enteral feeding is also more cost-effective than TPN. The significance of cost difference was essentially made by the nutritional formulas, as well as the complications related to an extended ICU stay.

The gut is considered as a motor of organ system dysfunction because impaired digestive and barrier function, altered intestinal morphology and architecture and reduced turnover of the epithelial layer are all associated with critical illness [21]. In this situation, bacterial overgrowth and massive translocation to remote organs may become significantly relevant when intestinal failure is coupled with mesenteric hypoperfusion. Thus, the nutrients in the gut lumen are essential stimulus for intestinal function maintenance [22]. Our data suggested that infectious complications and acute respiratory distress syndrome were reduced in recanalised AMI patients receiving EN, which might result from decreased microbial translocation from intestine. The serum tests showed nutritional and immunologic variables were decreased immediately after recanalisation, and this alteration persisted until PRD-7 regardless of the route of nutrient administration. However, the inflammatory response after recanalisation, which was a part of the ischaemia-reperfusion injury, was significantly improved in the EN group.

Based on the practice guidelines for nutrition therapy in the ICU, nutrition should be initiated as soon as possible, ideally within 24–48 h of admission, and early EN improves clinical outcomes and is considered the optimal route in patients with adequate

Table 4
Outcome in the subgroup of patients.

Groups	Variables	EN (n = 95)	TPN (n = 88)	*P* value
		n = 55	**n = 46**	
Mesenteric infarction requiring initial bowel resection (n = 101)	Re-laparotomy, n (%)	19 (34.5)	16 (34.8)	0.980
	Bowel resection after initial surgery, n (%)	8 (14.5)	9 (19.6)	0.502
	Bowel continuity restoration after ostomy (d), M (P25, P75)	15 (12, 23.8)	39 (29, 45.5)	<0.001
	Length of ICU stay (d), M (P25, P75)	20 (14, 26)	18.5 (15, 24.8)	0.687
	Length of hospital stay (d), M (P25, P75)	27 (22, 33)	25.5 (21.5, 31.8)	0.774
	SBS, n (%)	7 (12.7)	11 (23.9)	0.143
	MODS, n (%)	7 (12.7)	6 (13.0)	0.962
	30-day mortality, n (%)	4 (7.3)	12 (26.1)	0.010
	Infectious complications, n (%)	5 (9.1)	14 (30.4)	0.006
	Noninfectious complications, n (%)	10 (18.2)	9 (19.6)	0.859
		n = 40	**n = 42**	
Endovascular recanalization without initial bowel resection (n = 82)	Re-laparotomy, n (%)	8 (20.0)	10 (23.8)	0.677
	Bowel resection after initial surgery, n (%)	2 (5.0)	8 (19.0)	0.108[a]
	Length of ICU stay (d), M (P25, P75)	4 (2, 6)	24.5 (19.8, 31.5)	<0.001
	Length of hospital stay (d), M (P25, P75)	10 (7.3, 11)	17 (14, 19)	<0.001
	SBS, n (%)	2 (5.0)	3 (7.1)	1.000[a]
	MODS, n (%)	3 (7.5)	2 (4.8)	0.955[a]
	30-day mortality, n (%)	3 (7.5)	2 (4.8)	0.955[a]
	Infectious complications, n (%)	2 (5.0)	4 (9.5)	0.717[a]
	Noninfectious complications, n (%)	8 (20.0)	9 (21.4)	0.873

EN, enteral nutrition; TPN, total parenteral nutrition; ICU, intensive care unit; SBS, short bowel syndrome; MODS, multiple organ dysfunction syndrome.
[a] $\chi 2$ correction for continuity were used.

gastrointestinal function [23]. Although PN may result in negative outcomes, recent randomised controlled trials have shown that PN may not harm the critically ill [24]. On account of the conflicting results, the energy dose is suspected as an important factor. But current data are insufficient to draw conclusions regarding the optimal initial calorie and protein intake in critical illness [25]. For more effective delivery, supplemental PN is recently attempted. However, consensus regarding the early use of supplemental PN was not obtained from different trials [26–28]. Because the weak gastrointestinal function of AMI patients can limit the effective delivery of EN, initial moderate low calorie (33.3%–50% of the goal energy) with a high protein intake and low-dose supplemental PN was prescribed in our clinical practice. In addition, micronutrients were supplied to prevent refeeding syndrome. As current evidence does not support glutamine supplementation early in critical illness, we did not administer glutamine during the first week [29].

In our centre, ostomy was applied in a high percent of AMI patients during emergent laparotomy. Inadequate nutrition intake, increased nutrition requirements related to sepsis and catabolism and nutrient losses through the stoma output can lead to malnutrition [30]. However, the somatostatin that can decrease the stoma output is detrimental to AMI patients by reducing splanchnic blood flow and nutrient absorption. In this study, the SER was successfully used together with EN. SER provides essential enzymes and bile acids for optimal utilisation of EN and prevents excessive loss of fluid and electrolytes. This treatment can reduce the length of hospitalisation and improve the liver function as well as nutritional status with significant cost savings [31,32]. However, limited data about the optimal enteral formula for patients requiring SER is available due to lack of comparative studies. According to our experience, a peptide-based enteral formula (semi-elemental or elemental) is recommended. Further, chyme from the proximal stoma is filtered because chyme reinfusion is very demanding on the nursing staff and may cause hygiene and aesthetic issues.

In the present study, early EN was safe and well tolerated. The total length and function of residual bowel segments should be well assessed to ensure adequate absorption of nutrients and avoid ileus. The evaluation may be accomplished based on the characteristics of ostomy effluent, surgical findings, radiologic imaging and fistulogram. An unobstructed bowel in continuity and of sufficient length (at least 75 cm) for nutrient absorption should be demonstrated. It is noted that a lack of correlation between residual length of intestine and EN tolerance exists, and every patient needs to be managed individually.

This study has certain limitations. Its retrospective and non-randomised controlled design, possibilities exist of selection bias and inaccurate data collection. Because of the rareness of AMI, our sample size was not large enough to detect the benefits of early nutrition support in nutritional and immunologic response. Our institute is a national referral centre of intestinal failure, and most patients are transferred from other hospitals. Therefore, outcomes can be influenced by initial resuscitation needs, timing of surgery and variability of care before admission. Moreover, the consistency of energy intake between the two groups failed to be guaranteed. In addition, we did not consider strict glucose control during the management, and blood glucose levels can be elevated more frequently by PN than EN. Furthermore, consistent with the lack of evidence-based guidelines for these subjects, the detailed therapeutic strategies, such as the timing of nutrition initiation, route of nutrition delivery and nutrition ingredients were determined by the severity of critical illness, tolerance to EN, surgical intervention, nutrition status and surgeon's preference. All these may account for some differences between both groups. Finally, our data did not explore nutrition therapy's role in subgroup of malnourished AMI patients in the ICU.

In conclusion, this retrospective cohort study shows that EN is well tolerated in AMI patients with recanalisation within the first week of ICU admission and associated with better 1-year survival than TPN. Patients with intestinal infarction receiving enteral feeding had earlier bowel continuity restoration and increased 30-day survival than those receiving TPN. Patients without initial bowel resection had shorter length of ICU stay and hospitalisation with early delivery of EN than those with TPN. A large multicentre prospective randomised controlled trial with higher level of evidence for this issue is still warranted in the future.

Statement of authorship

SY and JG completed most of the scientific work. SY drafted the manuscript. SY, QN and JC collected all the clinic data. SY and XG completed the statistic work. GX and YZ helped to conceptualize and design the study. MY and LZ made the critical revision and final approval of the article.

Shuofei Yang and Jianming Guo contributed equally to the manuscript.

Meng Ye and Lan Zhang were both the corresponding authors.

Conflict of interest statement and funding sources

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