

## Original Article

## Effect of early enteral nutrition on outcomes of trauma patients requiring intensive care

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## ABSTRACT

**Purpose:** To investigate the effect of early enteral nutrition on outcomes of trauma patients in the intensive care unit (ICU).

**Methods:** Clinical data of trauma patients in the ICU of Daping Hospital, China from January 2012 to December 2017 was retrospectively analyzed, including patient age, gender, injury mechanism, injury severity score (ISS), nutritional treatment, postoperative complications (wound infection, abdominal abscess, anastomotic rupture, pneumonia), mortality, and adverse events (nausea, vomiting, abdominal distention). Only adult trauma patients who developed bloodstream infection after surgery for damage control were included. Patients were divided into early enteral nutrition group (<48 h) and delayed enteral nutrition group (control group, >48 h). Data of all trauma patients were collected by the same investigator. Data were expressed as frequency (percentage), mean  $\pm$  standard deviation (normal distribution), or median (Q<sub>1</sub>, Q<sub>3</sub>) (non-normal distribution) and analyzed by Chi-square test, Student's *t*-test, or rank-sum test accordingly. Multiple logistic regression analysis was further adopted to investigate the significant variables with enteral nutrition.

**Results:** Altogether 876 patients were assessed and 110 were eligible for this study, including 93 males and 17 females, with the mean age of (50.0  $\pm$  15.4) years. Traffic accidents (46 cases, 41.8%) and fall from height (31 cases, 28.2%) were the dominant injury mechanism. There were 68 cases in the early enteral nutrition group and 42 cases in the control group. Comparison of general variables between early enteral nutrition group and control group revealed significant difference regarding surgeries of enterectomy (1.5% vs. 19.0%,  $p = 0.01$ ), ileum/transverse colon/sigmoid colostomy (4.4% vs. 16.3%,  $p = 0.01$ ) and operation time (h) (3.2 (1.9, 6.1) vs. 4.2 (1.8, 8.8),  $p = 0.02$ ). Other variables like ISS ( $p = 0.31$ ), acute physiology and chronic health evaluation  $\geq 20$  ( $p = 0.79$ ), etc. had no obvious difference. Chi-square test showed a much better result in early enteral nutrition group than in control group regarding mortality (0 vs. 11.9%,  $p = 0.03$ ), length of hospital stay (days) (76.8  $\pm$  41.4 vs. 81.4  $\pm$  44.7,  $p = 0.01$ ) and wound infection (10.3% vs. 26.2%,  $p = 0.03$ ). Logistic regression analysis showed that the incidence of wound infection was related to the duration required to achieve the enteral nutrition standard ( $OR = 1.095$ ,  $p = 0.002$ ). Seventy-six patients (69.1%) achieved the nutritional goal within a week and 105 patients (95.5%) in the end. Trauma patients unable to reach the enteral nutrition target within one week were often combined with abdominal infection, peritonitis, bowel resection, intestinal necrosis, intestinal fistula, or septic shock.

**Conclusion:** Early enteral nutrition for trauma patients in the ICU is correlated with less wound infection, lower mortality, and shorter hospital stay.

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Early enteral nutrition for trauma patients in the intensive care units (ICUs) is a great advance in clinic. Nutritional treatment is important for a comprehensive care of severe trauma

patients. The high nitrogen demand following severe trauma soon leads to malnutrition in those patients. However, nutritional treatment for such patients is very complicated because of tissue damage, hemorrhagic shock, planned multiple-staged surgeries, and anesthesia. A meta-analysis shows that trauma patients with early enteral nutrition present a shorter hospital stay and lower mortality, but with no significant difference in the

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incidence of pneumonia.<sup>1</sup> Ten years ago, three world-renowned researchers in early enteral nutrition figured out that early enteral nutrition reduces the length of hospital stay and mortality.<sup>2</sup>

However, in July 2019, Herbert et al.<sup>3</sup> proposed that early enteral nutrition produced no statistical difference in the mortality rate of patients. They reaffirm that the common causes of death after surgery were anastomotic fistula and septic shock. Then, in the era of damage control surgery for trauma patients,<sup>4</sup> the treatment strategy for severe trauma patients is quick damage control, resuscitation and definitive surgery. Trauma patients need to undergo repeated trauma stress response and resuscitation as well as two or more damage control operations. As we know, long duration and increased postoperative complications have obvious and lasting effects on the metabolism of severe trauma patients and can easily cause repeated acute intestinal injury, leading to long-time dependence on nutritional therapy.<sup>5</sup>

In this study, we collected clinical data of trauma patients in the ICU and retrospectively analyzed them to investigate the effect of early enteral nutrition on the outcome of such patients.

## Methods

This study has been approved by the ethics committee of our hospital, abiding by Helsinki Declaration II.

### Inclusion and exclusion

Adult trauma patients admitted to ICU of our hospital from January 2012 to December 2017 who developed bloodstream infection after surgery in the trauma center were retrospectively analyzed, regardless of their nutritional status. Trauma patients younger than 18 years old or those who required no critical care but ICU monitoring for insulin-dependent diabetes mellitus, renal or liver dysfunction, or inflammatory bowel diseases were excluded. Prophylactic antibiotics were used dependent on the surgery types.

### Grouping

Patients were divided into early and delayed enteral nutrition group according to the time they received the treatment of enteral nutrition, i.e.  $\leq 48$  h or  $>48$  h after surgery. The delayed enteral nutrition group was taken as the control group.

### Variables collected

Data of age, gender and injury mechanism, injury severe score (ISS), surgery parameters (total operation time, blood transfusion volume), acute physiology and chronic health evaluation II (APACHE II) score, enteral nutrition treatment, postoperative complications, length of hospital stay, mortality and adverse events were retrospectively collected and analyzed (Table 1). All case data were collected by the same investigator.

### Enteral nutrition treatment

Treatment of enteral nutrition was conducted according to the clinical guideline: if oral intake is not possible in critically ill patients, early enteral nutrition should be given within 48 h, rather than delayed enteral nutrition. To avoid overfeeding, early full feeding of enteral nutrition or parenteral nutrition cannot be given to critically ill patients. For such patients, the enteral nutrition treatment should be conducted gradually to reach the target amount within 3–7 days; if the patients have reached the full feeding target within 1 week, it is regarded as successful enteral nutrition. In this study, the full feeding amount was set as  $30\text{--}35 \text{ kcal} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$  ( $1 \text{ kcal}=4.186 \text{ kJ}$ ). For patients failed to reach the feeding target within 1 week, the severity of intestinal dysfunction was classified and corresponding intestinal rehabilitation measures were conducted to gradually recover the bowel function from zero load to full feeding. The duration patients needed to achieve the standard nutrition was classified as 7 groups: within 48 h, 1 week, 2 weeks, 3 weeks, 4 weeks, 7 weeks and failure to achieve the target.

**Table 1**

Clinical data of the 110 trauma patients who developed bloodstream infection after surgery in the ICU.

Variables	Total (n = 110)	Enteral nutrition after ICU admission		p value
		<48 h (n = 68)	>48 h (n = 42)	
Age (years)	50.1 ± 15.5	50.7 ± 16.7	49.0 ± 13.5	0.57
Gender (Male: Female)	93:17	57:11	36:6	0.95
APACHE II score $\geq 20$	56 (50.9)	31 (45.6)	25 (59.5)	0.79
ISS	22.3 ± 7.6	24.7 ± 9.9	25.1 ± 6.6	0.31
Injury mechanism				
Falling from height	31 (28.2)	23 (33.8)	8 (19)	0.66
Traffic accidents	46 (41.8)	32 (47.1)	14 (33.3)	0.16
Hitting by heavy objects	15 (13.6)	6 (8.8)	9 (8.2)	0.09
Falling injury	10 (9.1)	7 (10.2)	3 (7.1)	0.57
Crush injury	4 (3.6)	0 (0)	4 (9.5)	0.01
Twisting and squeezing injury	2 (1.8)	0 (0)	2 (4.8)	0.07
Others	2 (1.8)	0 (0)	2 (4.8)	0.07
Intra-abdominal hypertension	6 (5.5)	3 (4.4)	3 (7.1)	0.31
Enterectomy	9 (8.2)	1 (1.5)	8 (19)	0.01
Ileum/transverse colon/sigmoid colostomy	10	1/0/2	5/1/1	0.01
Blood transfusion volume (mL)	1800 (400, 4250)	1600 (400, 2800)	3100 (1000, 6145)	0.04
Total operation time (h)	3.2 (1.9, 6.4)	3.2 (1.9, 6.1)	4.2 (1.8, 8.8)	0.02
Time of CVC (d)	7.5 (3.0, 14.5)	6.5 (2.0, 11.0)	9.0 (5.0, 22.3)	0.20
Multiple drug resistance	33 (30.0)	24 (35.3)	9 (21.4)	0.34
Time of ventilator use (d)	13.0 (4.8, 21.0)	12.0 (6.0, 21.0)	13.5 (20, 20.3)	0.38
Days after surgery to start enteral nutrition	1 (1, 2.6)	1 (1, 1)	4 (2, 6)	0
Days required to achieve the enteral nutrition standard	3 (2, 9)	2 (1, 3)	9 (5, 18)	0

Data are expressed as mean ± standard deviation, median (Q<sub>1</sub>, Q<sub>3</sub>) or frequency (percent).

CVC: central venous catheterization; ICU: intensive care unit; APACHE II: acute physiology and chronic health evaluation II.

In early enteral nutrition group, the protein-containing enteral nutrition formula (Newy, Baple) was given within 48 h after admission to the ICU. The contraindications of enteral nutrition such as uncontrolled bleeding, shock, intestinal rupture, intestinal mechanical obstruction, and intestinal ischemic necrosis were precluded in advance. A nasogastric tube or nasointestinal tube was used for enteral nutrition according to the patient's condition. Enteral nutrition formula was continuously pumped at a constant speed by a nutrition pump. The initial feeding speed was 20 mL/h, and then adjusted according to the patient's tolerance (maximum: 100 mL/h). The energy for initial nutritional support was  $25\text{--}30 \text{ kcal} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$  (1 kcal = 4.186 kJ), and increased to  $30\text{--}35 \text{ kcal} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$  under stress and metabolic status. When the protein provided by enteral nutrition formula cannot meet the energy requirements, supplemental enteral protein or parenteral nutrition was provided.

In control group where enteral nutrition was started 48 h after surgery, the feeding was gradually increased to full amount ( $30\text{--}35 \text{ kcal} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$ ) within 3–7 d after admission to ICU. Others were the same as early enteral nutrition group.

For patients with enterectomy, treatment of enteral nutrition was carried out within 48 h after surgery if they present no severe shock, circulatory failure/severe hypoxemia or abdominal hypertension. Enteral nutrition was given in the same way, i.e. initial feeding speed of 20 mL/h and then adjusted according to the patient's tolerance, maximally 100 mL/h.

Clinical parameters like antibiotic use, gastrointestinal functions and infection-related blood parameters were closely monitored for a better nutrition treatment. Primary outcome parameter – length of hospital stay and mortality, and secondary parameters – post-operative complications (wound infection, intra-abdominal abscess, anastomotic rupture, pneumonia) and adverse events related to enteral nutrition (nausea, vomiting, abdominal distention, diarrhea, gastric retention, gastrointestinal bleeding, abdominal infection, and intestinal fistula) were observed. Moreover, the time to start nutritional feeding, time to reach the nutritional target, measures for intestinal rehabilitation to reach the state of autonomous enteral feeding, and reasons for inadequate enteral nutrition and corresponding management were recorded to promote the treatment.

### Statistical analysis

Statistical analysis was performed using SPSS 23.0 software. The measurement data of normal distribution were expressed as mean  $\pm$  standard deviation (SD). Student's *t*-test was used for comparisons between two groups. The measurement data of non-normal distribution were expressed as median ( $Q_1$ ,  $Q_3$ ) and processed using the rank-sum test. The counting data were expressed as cases (percentage) and analyzed using the Chi-square test. A *p* value less than 0.05 was considered significantly different. Multiple logistic regression analysis was used to further analyze the significant outcome results influenced by enteral nutrition.

## Results

### General and clinical variables

Altogether 110 patients met the inclusion and exclusion criteria from 876 trauma patients admitted to ICU during the study period, including 93 male and 17 female (Fig. 1).

High-energy injury was the most frequent injury mechanism, including fall from height in 31 patients (28.2%) and traffic accident injuries in 46 patients (41.8%). All patients received damage control surgery, planned surgery or definitive surgery. There were 68 cases (61.8%) in early enteral nutrition group with the mean age of

( $50.7 \pm 16.7$ ) years and 42 cases (38.2%) in delayed enteral nutrition group (control group), with the mean age of ( $49.0 \pm 13.5$ ) years. Days to start enteral nutrition treatment after surgery were median 1 for the former and 4 for the latter. To achieve the nutritional goal, the early group spent a median of 2 days and control group 9 days. Comparison of patient proportions in two groups regarding general data, ISS, APACHE II  $\geq 20$ , and injury mechanisms showed no significant differences (Table 1). But the operation time ( $p = 0.02$ ), blood transfusion volume ( $p = 0.04$ ), surgeries of enterectomy ( $p = 0.01$ ) and intestinal fistula ( $p = 0.01$ ) presented a significant difference.

### Time to reach the nutrition standard

In our study, 76 patients (69.1%) achieved the nutritional treatment standard within a week (45 patients in 48 h and 31 after then). With various intestinal rehabilitation measures, finally 105 (95.5%) patients with gastrointestinal impairment achieved autonomous intestinal feeding. The detailed distribution of time periods patients achieved the nutritional goal is shown in Fig. 2. Five patients (4.6%) failed to achieve the nutritional goal. Because of uncontrollable intestinal fistula, abdominal infection and shock until death. We found that trauma patients unable to reach the enteral nutrition target within one week were often combined with abdominal infection, peritonitis, bowel resection, intestinal necrosis, intestinal fistula, or septic shock.

### Postoperative complications

The outcome after early and late enteral nutrition treatment was compared and shown in Table 2. It is found that the rate of wound

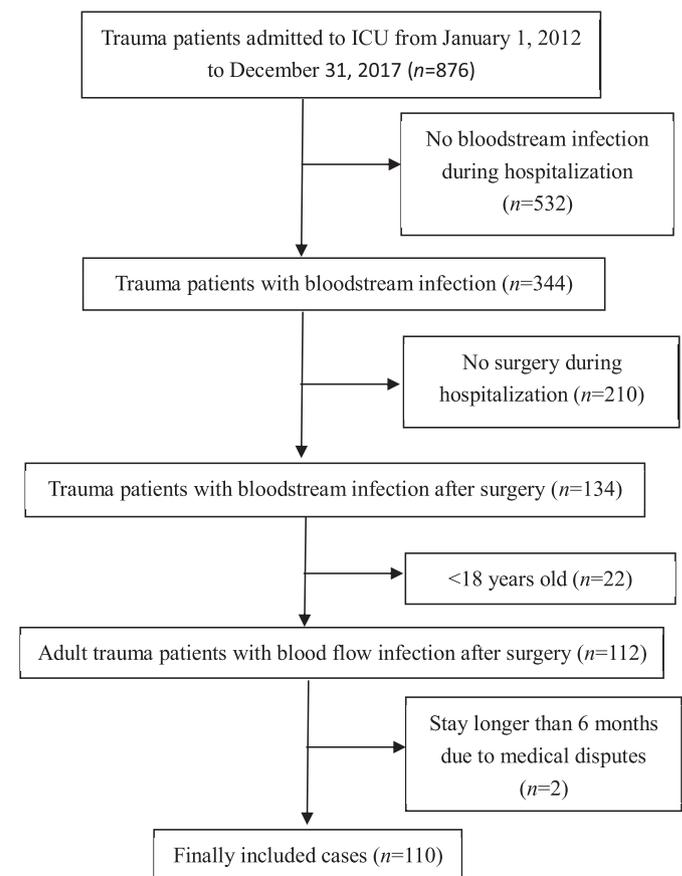


Fig. 1. Flow chart of adult trauma patient screening.

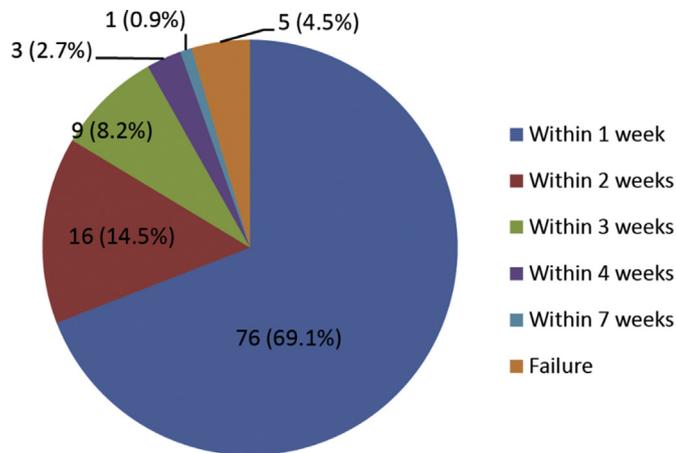


Fig. 2. Distribution of patients regarding nutritional goal achieve time.

infection (10.3% vs. 26.2%,  $p = 0.03$ ) and length of hospital stay (d) ( $76.84 \pm 41.4$  vs.  $81.4 \pm 44.7$ ,  $p = 0.01$ ) presented a much better result in the early enteral nutrition group than in control group. While other complications like anastomotic rupture ( $p = 0.20$ ), vomiting ( $p = 0.58$ ) and abdominal distention ( $p = 0.79$ ) showed no significant difference.

No death occurred in the early enteral nutrition group, but 5 patients died of intestinal fistula, uncontrolled abdominal infection, or septic shock in the control group, suggesting a significant difference ( $p = 0.01$ ).

Logistic regression analysis showed that the incidence of wound infection was related to the duration required to achieve the enteral nutrition standard ( $OR = 1.095$ ,  $p = 0.002$ ) (Table 3).

## Discussion

This retrospective study was to investigate the effect of early enteral nutrition on the outcomes of trauma patients in the ICU. The common causes of death in postoperative patients are reported to be anastomotic fistula and septic shock.<sup>3,6,7</sup> In critically ill trauma patients with hemorrhagic or septic shock, gastrointestinal

**Table 2**  
Outcome of 110 traumatic patients who developed bloodstream infection after surgery in the ICU.

Variables	Total (n = 110)	Enteral nutrition after ICU admission		p value
		<48 h (n = 68)	>48 h (n = 42)	
Wound infection	18 (16.4)	7 (10.3)	11 (26.2)	0.03
Anastomotic rupture	1 (0.9)	0	1 (2.4)	0.20
Vomiting	4 (3.6)	3 (4.4)	1 (2.4)	0.58
Abdominal distension	25 (22.7)	16 (23.5)	9 (21.4)	0.79
Diarrhage	3 (2.7)	1 (1.5)	2 (4.8)	0.31
Gastrointestinal hemorrhage	4 (3.6)	1 (1.5)	3 (7.1)	0.12
Urinary tract infection	14 (12.7)	9 (13.8)	5 (11.9)	0.84
Pulmonary infection	24 (21.8)	14 (20.6)	10 (23.8)	0.69
Hospital stay (d)	$55.6 \pm 35.4$	$76.8 \pm 41.4$	$81.4 \pm 44.7$	0.01
Postoperative death	5 (4.5)	0 (0)	5 (11.9)	0.01

ICU: intensive care unit.

**Table 3**  
Logistic regression analysis of significant outcomes influenced by enteral nutrition.

Variable	95% confidence interval	B	Exp (B)	p value
Days required to achieve the nutritional goal	1.033–1.161	0.091	1.095	0.002

function is impaired by a variety of factors, including immune, hemochemical, biological, and mechanical barrier disruption, and bacterial flora dislocation, causing multiple organ failure. Surgery-caused gastrointestinal injury associated with abdominal infection often resulted in intestinal paralysis and abdominal distention. Therefore, our study analyzed the effect of early enteral nutrition on outcomes of adult trauma patients with bloodstream infection in the ICU. Previous studies have revealed that early enteral nutrition reduces the mortality and hospital stay of trauma patients.<sup>2,3</sup> We found a significantly better result in early enteral nutrition group compared with control group, regarding wound infection, post-operative mortality, and length of hospital stay. This is consistent with the study of Doig et al.<sup>8</sup> A forward surgical team in Afghanistan also suggests that early enteral nutrition containing proteins is conducive to saving lives of trauma patients.<sup>9</sup>

In the management of enteral nutrition obstacles, the damage to gastrointestinal function after shock, septic shock, and exposure of the intestine to the air is mostly temporary and reversible. If the patient is at hemodynamic stability and there is no anatomical injury of the intestine, enteral nutrition should be performed as early as possible. According to the European Society for Clinical Nutrition and Metabolism guideline on clinical nutrition in ICU, if oral intake is not possible, early enteral nutrition (within 48 h) should be performed in critically ill patients, rather than delayed enteral nutrition.<sup>1</sup>

A prospective study of 100 patients with perforation of the digestive tract by Malhotra et al.<sup>10</sup> showed that early enteral nutrition can reduce the relative risk of wound infection, wound dehiscence, pneumonia, anastomotic fistula and septicemia. In our study 7 patients (10.3%) in early enteral nutrition group and 11 patients (26.2%) in control group developed wound infection ( $p = 0.03$ ). We speculated that early enteral nutrition containing proteins provides the substrate of nutrition metabolism, promotes wound healing and prevents infection, maintains intestinal function, reduces the displacement of intestinal flora, and reduces the risk of infection.

According to a meta-analysis of the prognosis comparison between early enteral nutrition and intravenous nutrition after gastrointestinal surgery, Weng et al.<sup>11</sup> pointed out that early enteral nutrition can reduce the incidence of incision dehiscence and infection, and definitely reduce the length of stay. This is consistent with our finding: the hospital stay (d) in early enteral nutrition group was  $76.8 \pm 41.4$ , compared to  $81.4 \pm 44.7$  in control group. Moreover, none of the patients in enteral nutrition group died but 5 in the control group. Both hospital stay ( $p = 0.01$ ) and postoperative mortality ( $p = 0.01$ ) revealed significant difference.

Regression analysis showed that the complications of post-operative wound infection were related to the days required to achieve the goal of enteral nutrition treatment ( $p = 0.002$ ). We believe that this is considerably due to the improved nutritional status, fast recovered intestinal function and better protection.

In 1983, Moore and Jones<sup>12</sup> reported that early nutritional support reduced the incidence of septicemia in severe injury patients. For trauma patients in the ICU, based on the digestive physiology of the gastrointestinal tract, the enteral nutrition tolerance at each stage should be considered to prevent complications, and the physicians should pay attention to graded nutrition and nursing and treatment for nutritional disorders.<sup>13</sup> No statistically significant differences in the incidence of clinically common complications such as abdominal distension, diarrhea, vomiting, gastrointestinal bleeding, urinary tract infections, and lung infections were found, suggesting that it is safe to develop early enteral nutrition actively. Standardized enteral nutrition programs and procedures can avoid adverse consequences. The timing, methods and approach of enteral nutrition depend on the

assessment results of trauma, gastrointestinal function, location of the fistula, and previous nutritional status. If the whole gastrointestinal tract is well preserved, enteral nutrition is the first choice. Only in patients whose nutritional needs cannot be met by enteral nutrition, parenteral nutrition should be applied. Nutritional treatment strategies include gastrointestinal stress management, bowel rehabilitation procedures, and a gradual transition from zero load to treatment standard.

In this study, among the 110 patients, 76 (69.1%) achieved the nutritional treatment standard within a week. After corresponding treatment, 105 patients (95.5%) achieved the nutritional goal in the end. Trauma patients unable to reach the enteral nutrition target within one week were often combined with abdominal infection, peritonitis, bowel resection, intestinal necrosis, intestinal fistula, or septic shock. Five patients died of intestinal fistula combined with septic shock. In those cases, abdominal infection was not successfully controlled. Most of fistulas are located in the small intestine and ileum, and intestinal fistula is accompanied by imbalance of water and electrolytes, malnutrition, sepsis, and hypermetabolism,<sup>14–16</sup> which emphasized the overall management of trauma patients.

Because this is a retrospective study, the quality of evidence is low, and more multiple centered studies are needed to explore implementation of intestinal rehabilitation and graded nutrition in traumatic patients. In this study, although the proportion of patients with APACHE score  $\geq 20$  revealed no significance between early nutrition group and control group, the operation time and blood transfusion volume showed a significant difference, which implied different severity between early and late enteral nutrition trauma patients. In addition, the control group had more patients with intestinal resection and intestinal fistula. The difference in injury severity may be one underlying factor for different mortality and length of hospital stay.

In conclusion, the treatment of trauma patients in the ICU is challenging because of multiple surgeries, abdominal infections and nutritional metabolic problems. Early enteral nutrition is associated with less wound infection, lower mortality, and shorter hospital stay for trauma patients requiring intensive care. Abdominal infection and intestinal fistula are commonly observed in trauma patients with delayed enteral nutrition in the ICU. It is helpful to monitor the nutritional progress of trauma patients, pay attention to the potential factors of substandard nutritional treatment and timely manage nutritional disorders in order to avoid the interaction between intestinal fistula caused by gastrointestinal tract injury and abdominal infection, even septic shock.

## Funding

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## Ethical Statement

This study has been approved by the ethics committee of our hospital, abiding by Helsinki Declaration II.

## Declaration of Competing Interest

The authors declared no competing interest.

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