Original Article

Early jejunal feeding by bedside placement of a nasointestinal tube significantly improves nutritional status and reduces complications in critically ill patients versus enteral nutrition by a nasogastric tube

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Background and Objective: Unguided nasojejunal feeding tube insertion success rates are low. Controversy persists about how to safely and efficiently perform enteral nutrition (EN) in critically ill patients. This study explores an innovative blind nasointestinal tube (NIT) insertion method and compares nasogastric and nasointestinal feeding. **Methods:** Seventy critically ill patients admitted to the intensive care unit (ICU) were divided randomly into a nasogastric tube group (NGT; n=35) and an NIT group (NIT; n=35). After bedside NGT and blind-type NIT insertion, tube position was assessed and EN was started on day 1. Patients' nutritional status parameters, mechanical ventilation duration, average ICU stay, nutritional support costs, and feeding complications were compared. **Results:** Pre-albumin and transferrin levels on days 7 and 14 were significantly higher in the NIT group than in the NGT group (*p*<0.01, *p*<0.05). Bloating, diarrhea, upper gastrointestinal bleeding, and liver damage did not differ significantly between groups (*p*>0.05). Interleukin-6 and tumor necrosis factor-α levels and APACHE II score were significantly lower in the NIT group than in the NGT group (*p*<0.01, *p*<0.05). Reflux and pneumonia incidences, mechanical ventilation duration, average ICU stay length, and nutritional support costs were significantly lower in the NIT group than in the NGT group (*p*<0.01). **Conclusion:** Blind bedside NIT insertion is convenient and its use can effectively improve nutritional status, reduce feeding complications, and decrease nutritional support costs of critically ill patients.

Key Words: jejunal feeding, pre-albumin, aspiration pneumonia, interleukin-6

INTRODUCTION

Critically ill patients in intensive care units (ICU) are usually in a high metabolic state with an increased demand for energy and protein due to stress, trauma, infection, and other reasons.[1] At the same time, however, the presence of eating disorders and gastric motility disorders effectively impedes efficient nutrient uptake; therefore, these patients experience different degrees of malnutrition. Most of these patients cannot self-feed due to upper gastrointestinal (GI) dysmotility, an entity commonly found in the ICU setting that can lead to insufficient nutrient intake while increasing the risks of infection and mortality. Further, overcoming altered motility with early enteral feeding is associated with a reduced incidence of infectious complications in ICU patients.[2] Enteral nutrition (EN), compared with parenteral nutrition (PN), is associated with better blood glucose control, a lower incidence of septic complications, reduced need for surgical procedures, shorter hospital stay, and a significant reduction in patient mortality rates, possibly due to trophic action on the intestinal wall and prevention or reduction of bacterial translocation.[3-5]

Early EN can directly provide energy to intestinal epithelial cells, reverse intestinal mucosal injury, effectively improve intestinal mucosal barrier structure and function, stimulate the immune system, and prevent bacterial translocation.[6] More importantly, it reduces the incidence of infection and multiple organ dysfunction.[3,7] When energy is lacking, the incidence of diseases such as acute respiratory distress syndrome, sepsis, and renal failure are higher than that with a normal energy supply. When EN supplies mimic the target range, clinical outcomes are improved.[8]

EN in critically ill patients often needs to be carried out through a nasogastric tube (NGT) or nasointestinal tube (NIT). The NGT has been widely used for its qualities of being non-invasive, economical, easy to use, and high catheterization success rate. However, the disadvantage of feeding via an NGT is aspiration, especially in the pres-

ence of upper GI dysmotility.[2] EN delivered to the duodenum or jejunum is associated with a reduced risk of regurgitation and aspiration.[9]

Early EN in critically ill patients depends on the feeding tube, especially nasojejunal tubes (NJT). There are several current methods of NJT insertion. Endoscopic or x-ray interventional placement of an NJ tube is a possible alternative, but its complexity and potential risks to patients, especially the need to move the patient, inconsistent success rates, and high cost, have been reported.[10,11] The use of a new electromagnetically guided NIT system was recently proposed to improve tube positioning beyond the ligament of Treitz;[12,13] however, the results, although appealing, showed that it is very expensive in daily clinical practice, especially in small hospitals. Another spiral NIT is a passive wait-type tube that requires normal stomach motility. The overall success rate of blind spiral intubation tube was 57%-78%.[14]

Based on all the above-mentioned disadvantages of the NIT insertion process, this study consisted of practical research on unguided bedside NIT insertion that is easy to perform, features a high success rate, and may be suitable for use in clinical practice. Another purpose of this study was to determine whether early jejunal feeding by bedside placement of a NIT significantly improves nutritional status and reduces complications in critically ill patients versus EN by NGT.

Patient selection

This prospective study was performed in the ICU of the affiliated Hospital of Jiangsu University in China. Data were collected from February 2012 to April 2014. After the trial was approved by the institutional ethics committee and patient consent was obtained (ChiCTR-TRC-13003762), consecutive patients were recruited after admission to the ICU. The causes for their ICU admission included: traumatic brain injury and cerebral infarction; multiple injuries such as multiple rib fractures, hemothorax with pneumothorax, pulmonary contusion, ruptured spleen, and intestinal rupture; orthopedic hip replacement, pelvic fractures, and femoral shaft fractures; cancer such as lung, esophageal, stomach, colon, and pancreatic cancer as well as post-operative treatment after the removal of other tumors; severe acute pancreatitis, cirrhosis decompensation, severe pneumonia, and acute respiratory distress syndrome; shock, multiple organ dysfunction syndrome, and cardiopulmonary arrest resuscitation.

Seventy patients were randomized into blocks of four after stratification using random number tables and then divided into the NGT group or the NIT group.

EN tube material and directions for insertion of the new type NIT Corpak®10-10-10 Corflo® NIT series (USA) for EN

Directions for insertion

1. Explain procedure to patient (if applicable).
2. Administer an intravenous injection of metoclopramide 10 mg; insert the NIT 10 min later.
3. Position the patient in a sitting or Fowler's position as tolerated.
4. Measure the length of the tube to be inserted to ensure that tip/bolus enters the gastric region. Place the exit port of the tube at the tip of the patient's nose. Extend the tube to the patient's earlobe and then to the xiphoid process. Use the printed centimeter marks on the tubes to aid with intubation and confirm the tube migration.
5. Use 200 mL of saline to soak the catheter and inject 20 mL of saline from the connector end to activate the water activity lubricant of the lumen.
6. Direct the tube posteriorly, aiming the tip parallel to the nasal septum and along the surface of the hard palate. Advance the tube to the nasopharynx and allow the tip to seek its own passage. As the patient swallows sips of water, gently advance the tube through the esophagus into the stomach.
7. Confirm tube position per institutional protocol (eg, X-ary, PH measurement).

    When the NIT was inserted into the gastric cavity with 65-cm graduation, the sound of air over the water could be heard and the pH of the gastric juice was <6;[15] with 75-cm graduation, most of the catheter tips were moved through the pylorus; with 95-105-cm graduation, the catheter tip was inserted into the duodenum and jejunum, and the pH of secretions was >7. A plain abdominal radiograph was performed to further verify NIT position (Figure 1).
8. Activate the internal lubricant and remove the stylet.
9. Attach the feeding kit. Once NIT position is confirmed, begin feeding.

EN

Patients could be fed immediately after NIT position is confirmed by a plain abdominal radiograph. EN suspensions were used at full strength and a rate of 30 mL/h increasing to 100 mL/h over 24-72 h. At ICU admission (day 1), the caloric target was set for all admitted patients at 25 kcal/kg of ideal bodyweight/day for women and 30 kcal/kg of ideal bodyweight/day for men.[16]

The diets of the two groups were identical in caloric, lipid (35%), and protein (20%) contents. All patients received adjuvant peripheral PN consisting of a standard solution (Fat Emulsion, Amino Acids (17) and Glucose (11) Injection, Kabiven PI) as a supplement to reach the caloric target.
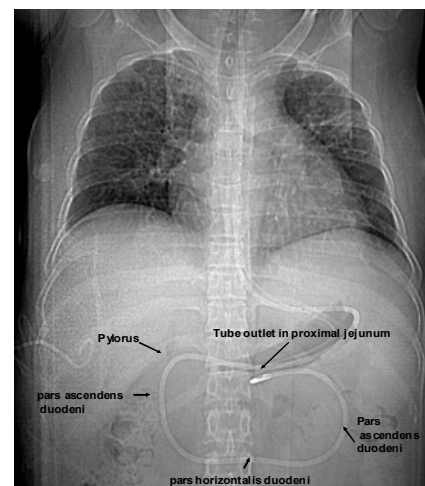

Figure 1. Abdominal radiograph showing appropriate feeding tube placement

Table 1. Comparison of basic characteristics between the two patient groups

Group	Patients (n)	Gender		Age, years
		Male	Female	Mean±SE
NGT	35	25	10	52.0±3.7
NIT	35	23	12	52.7±3.6

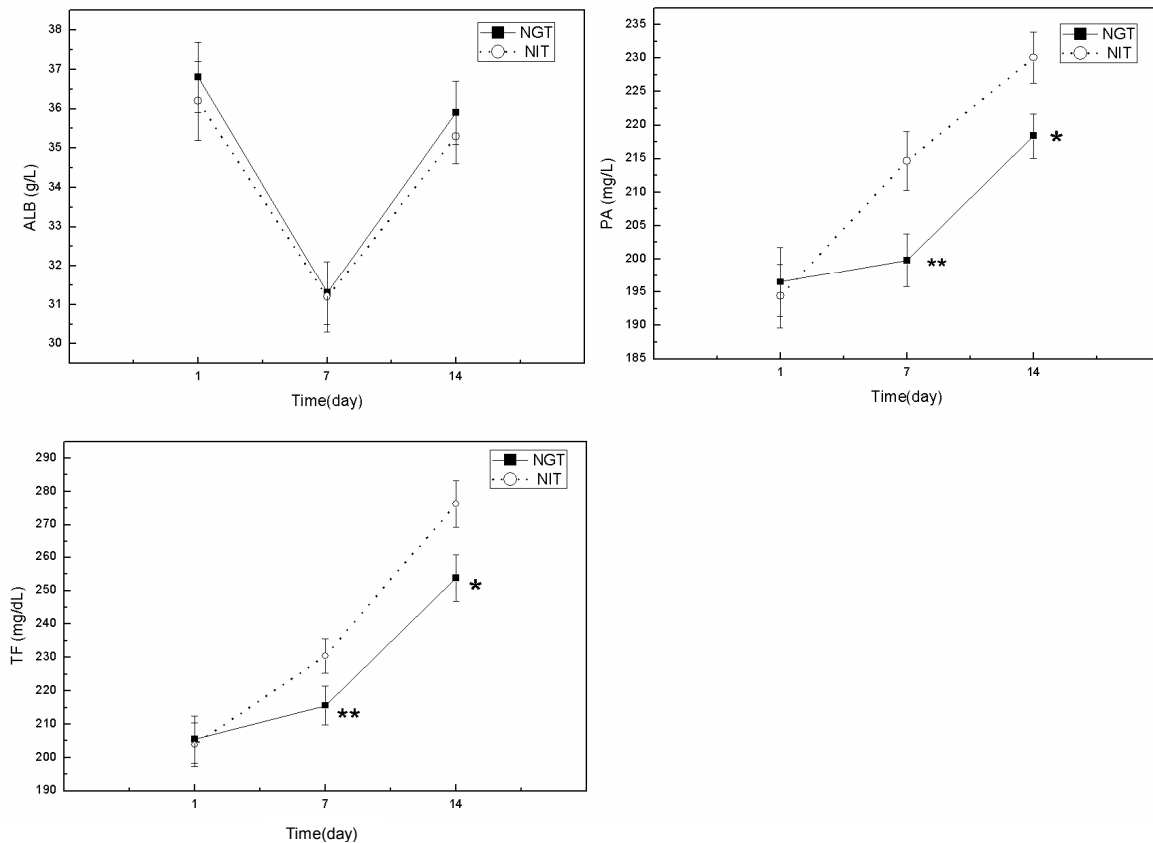NGT: nasogastric tube; NIT: nasointestinal tube.

Figure 2. Nutritional parameters at different times in the two groups. ALB: albumin; PA: pre-albumin; TF: transferrin. *$p<0.05$, **$p<0.01$ vs. the NGT group.

The patients in the NGT group who did not tolerate an EN product were defined as a single aspirated gastric residual volume>150 mL or two aspirated gastric residual volumes>120 mL during a 12-h period.[17] Patients received 10 mg of metoclopramide and continued to receive EN. The EN was discontinued if the residual gastric volume exceeded 250 mL or the patient vomited.[18]

Assessment
Venous fasting blood samples were obtained on days 1, 7, and 14 after feeding tube insertion. Three types of measurements were performed. First, a nutrition-associated assessment was carried out that included serum albumin, pre-albumin (PA), serum albumin (ALB), and transferrin (TF). Serum ALB, PA, and TF were determined by an automatic biochemistry analyzer (HITACHI 7600; Hitachi Co., Tokyo, Japan). Second, inflammatory cytokines including interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) were assessed using enzyme-linked immunosorbent assay. APACHE II score and average ICU stay were also recorded. Finally, clinical outcome was assessed based on EN complications including bloating, diarrhea, reflux, upper GI bleeding, liver damage, and

pneumonia.

Statistical analysis
Data were expressed as mean±SE or N and percentage. Continuous variables were compared using analysis of variance and the paired t-test, while categorical variables were compared using the chi-square test. Values of $p<0.05$ were considered statistically significant.

RESULTS
A total of 70 patients with different diseases requiring ICU admission were enrolled in the study: 35 patients (25 men, ten women; ages 23-91 years) were assigned to the NGT group and 35 patients (23 men, twelve women; ages 19-88 years) were assigned to the NIT group. There was no significance in age or gender between the two groups ($p>0.05$; Table 1).

In this study, the initial success rate of blind bedside NIT insertion was 94.3% (33/35). If the position of the catheter tip was above the pylorus confirmed by plain abdominal radiography, the operation failed. The procedure was repeated successfully.
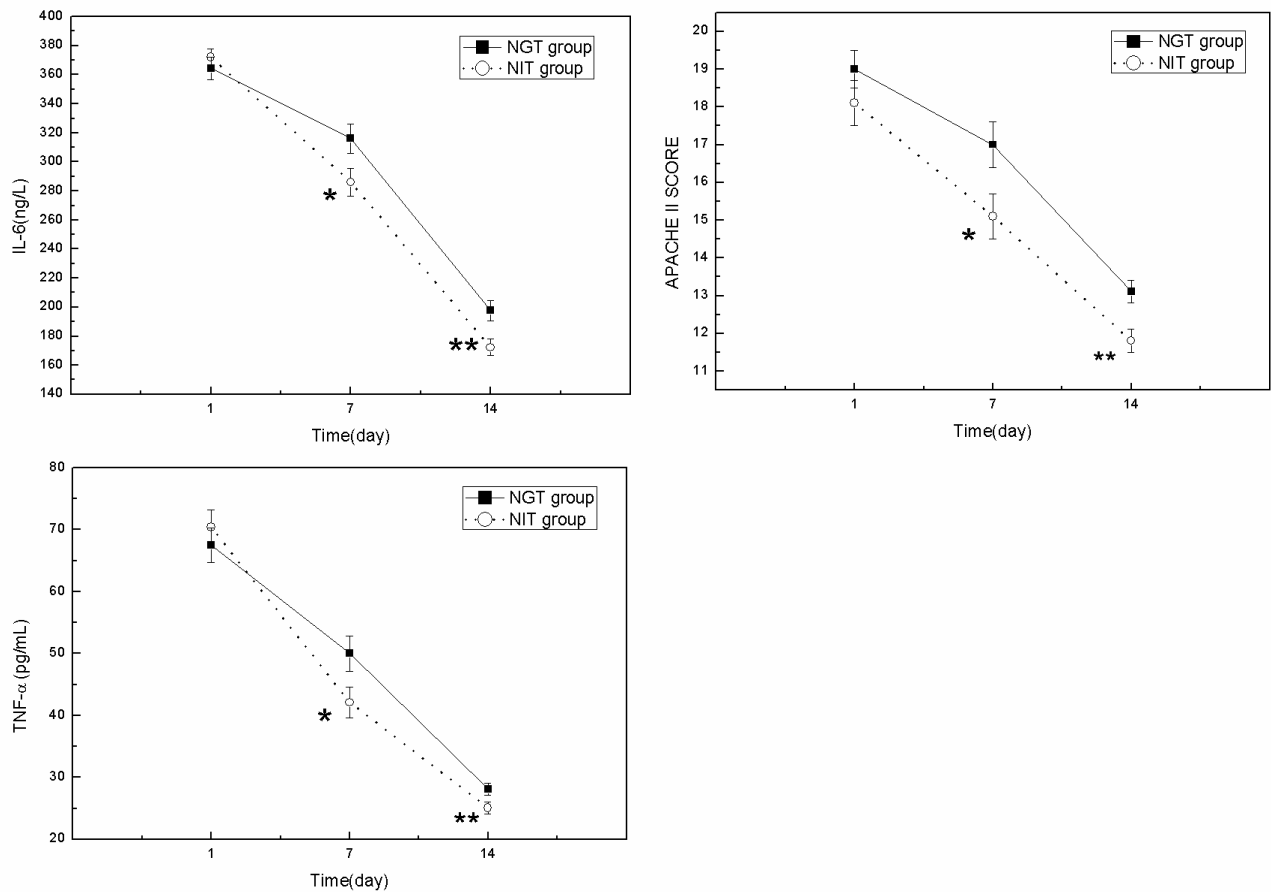
Figure 3. Levels of inflammatory factors at different time in the two groups. IL: interleukin; TNF: tumor necrosis factor. $^*p<0.05$, $^{**}p<0.01$ vs. the NGT group.

Table 2. The incidence (%) of enteric nutrition complications

Complication	Cases of complication NGT (n)	Cases of complication NIT (n)
Bloating, diarrhea	10	9
Liver damage	5	3
Hyperglycemia	9	7
Stress ulcer	2	1
Reflux	14	1[*]
Aspiration pneumonitis	10	0[*]

$^*p<0.01$ vs. the NGT

Nutrition-associated assessment

During the 14 days after admission, the ALB value was not significantly different between the two groups ($p>0.05$), whereas the serum PA and TF levels in the NIT group on days 7 and 14 were significantly higher than those in the NGT group ($p<0.01$, $p<0.05$; Figure 2).

Inflammatory-associated assessment

No significant difference in inflammatory markers was seen between the two groups on day 1 ($p>0.05$). Compared with the data of the NGT group, a significant decrease in APACHE II score and IL-6 and TNF-α levels was observed in the NIT group on day 7 ($p<0.01$) and day 14 ($p<0.05$; Figure 3).

Clinical outcome

The incidences of bloating, diarrhea, stress ulcers, and liver damage had not significantly different between groups ($p>0.05$; Table 2). The incidences of reflux and reflux-induced aspiration pneumonia in the NIT group were significant lower than those in the NGT group ($p<0.01$; Table 2). Mechanical ventilation times, ICU lengths of stay, and nutritional support costs in the NIT group were significantly reduced compared with those in the NGT group ($p<0.01$; Table 3).

DISCUSSION

In this research, bedside insertion method convenience and accuracy were studied and the differences in EN by feeding tube type were compared between NIT and NGT groups. The main conclusions were as follows. First, in most cases, bedside insertion of NIT (Corpak®10-10-10 tubes) could replace other NIT methods. Second, compared with the NGT group, EN by NIT could significantly decrease inflammation factors. Third, EN by NIT could reduce the complications of EN and provide cost savings. These results suggest that the timely use of NIT in critically ill patients for EN has significant clinical value.

Table 3. Mechanical ventilation duration, ICU stay length, and nutritional support costs in the two groups

Group	NGT	NIT
Duration of MV	8.5±0.5	5.2±0.3[*]
Length of ICU	17.1±1.0	12.2±0.7[*]
Nutritional support cost	7786±555	5203±247[*]

*$p<0.01$ vs. the NGT

Blind bedside insertion of the NIT in this study placed it directly into the duodenum and jejunum by an improved method, including the use of a drug to promote GI motility and anesthetics of lidocaine and mixture injection of gas and liquid. The initial insertion success rate of the new NIT was 94.3% in this study. The insertion success rate of straight NIT was 0%-14%, while that of the spiral was 57%-78% within 24 h.[14] The success rate of this new method was higher than that with air injection (90%) and was similar to that with an electromagnetically guided device (95%).[19] Failed NIT insertion was followed by reinsertion with 10 mL 2% Lidocaine injected into the gastric lumen through the NIT. Pyloric spasm might be a factor in such patients, and the use of Lidocaine causes pyloric relaxation.

EN by NGT was advocated for simplicity; however, many critically ill patients with gastroparesis in whom gastric tubes experienced multiple complications, some that worsened their conditions. The catheter insertion method in this study could be implemented at the bedside, which reduced the risk of insertion-related complications in the intervention and endoscopy room. Additionally, after NIT catheterization, this study compared the effect of EN delivered in two ways, and the results suggested that EN delivered by an NIT could significantly improve the nutritional status of critically ill patients. In addition, TF and PA values in the NIT group were significantly higher than those in the NGT group. PA and TF are the hepatic synthesis of negative acute phase protein. The half-life of PA is only 2 days, while that of TF is 8 days; neither is affected by the exogenous infusion of ALB, so they can be used to assess a patient's recent nutritional status.[20,21] In another study, TF and PA levels improved at the end of the period of early enteral feeding, and survivors had higher PA levels than non-survivors.[22]

Critically ill patients have varying degrees of consciousness disturbances, swallowing dysfunction, delayed gastric emptying, gastroparesis, and other complications.[23] The presence of malabsorption, reflux, and difficulty reaching target feeding amounts existed when early EN was performed through an NGT. Swallowing dysfunction in critically ill patients increases ventilation time and hospitalization days.[24] Our study showed that EN delivered through an NIT could compensate for this gastric dysfunction effect, reduce the incidence of complications such as aspiration, and decrease the duration of mechanical ventilation and ICU stay length. In this study, levels of the inflammatory cytokines TNF-α and IL-6 were significantly lower in the NIT group than those in the NGT group. The main reason for this might be the earlier EN delivered by NIT.

The use of early EN could reduce the risk of postoperative sepsis and postoperative mortality rates in patients with sepsis.[25,26] EN performed through an NIT ahead of time within 24 h after admission can effectively reduce reflux caused by gastric dysfunction. Furthermore, continuous EN leads to reduced PN input and prevents bacterial translocation, thereby reducing the systematic inflammatory response syndrome response and resulting in significantly decreased inflammatory marker levels.[27,28]. Additionally, EN by NIT could reduce the use of PN, an important reason to reduce IL-6 and other inflammatory cytokines.[29]

In this study, bedside insertion could achieve a higher success rate only when Corpak® 10-10-10 tubes were used and lidocaine was used when second insertions were required. This procedure must be performed by experienced physicians only. If the digestive tract of patients demonstrated variability, the success rate would be affected.

This study has several limitations. First, the use of lidocaine to increase the insertion success rate has not been reported elsewhere. As such, perhaps our observation was a coincidence, so this finding needs to be confirmed in future studies. Second, it included a small sample with only a few diseases. Third, all data were collected from a single center.

The correlation between the amount of gastric retention and aspiration is also worth exploring. In clinical practice, patients with GI disorders could regain a certain degree of GI function after treatment. Whether patients need EN by NIT or EN performed sequentially with NIT-NGT-oral insertion, as well as how to make patients more comfortable, requires further examination.

In conclusion, this study investigated the feasibility of bedside insertion in critically ill patients and achieved a satisfactory success rate. Further clinical studies are required. In critically ill patients, early EN by NIT has considerable practical value, features cost savings, could significantly decrease plasma inflammatory markers, improve patient nutritional status, and reduce complication rates. How to optimize NIT insertion and deliver EN is worthy of further exploration with a large sample.

AUTHOR DISCLOSURES
All authors have no conflict of interest of this paper.

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Original Article

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早期盲法置入鼻肠管行肠内营养与鼻胃管相比可以显著改善危重患者的营养及炎症状态

本研究探讨改良的盲插型鼻肠管的置入方法，并比较鼻肠管及鼻胃管进行肠内营养后患者的营养状态、炎症指标及肠内营养的费用及并发症发生率。入住ICU的危重症患者70例随机分为鼻胃管组（NGT；n=35）和经鼻腔置入鼻肠管组（NIT；n=35）。比较了患者的营养相关指标、机械通气及ICU住院日、记录肠内营养并发症发生率及肠内营养费用等。第7、14天，NIT组的PA及TF水平明显高于NGT组（$p<0.01$，$p<0.05$）。两组间腹胀、腹泻、上消化道出血及肝功能损害无统计学差异，但反流及吸入性肺炎发生率、机械通气时间、ICU平均住院日和肠内营养支持费用，NIT组均明显低于NGT组（$p<0.01$）。IL-6和TNF-α水平及 APACHE II评分，NIT组显著低于NGT组（Day 7，$p<0.01$；Day 14，$p<0.05$）。使用新型鼻肠管并改良盲插方式，可以提高盲插成功率。更重要的是，及时使用鼻肠管肠内营养，可以显著改善重症患者的营养状况、炎症反应及肠内营养的支持费用和相关并发症。

关键词：空肠置入、前白蛋白、吸入性肺炎、白细胞介素-6