Reviewer
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Effect of Early vs Late Supplemental Parenteral Nutrition in Patients Undergoing Abdominal Surgery: A Randomized Clinical Trial
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Context
This article investigates the effect and optimal timing of initiating supplemental parenteral nutrition (SPN) in patients after major abdominal surgery. The estimated prevalence of malnutrition in patients after major abdominal surgery ranges from 20-70% and is associated with increased morbidity and mortality. Infectious risk related to SPN has been a concern when compared to enteral nutrition (EN); however, this concern has been challenged by several observational studies suggesting the opposite finding. The objective was to examine the effect of early SPN (E-SPN) (Day 3 after surgery) vs late SPN (L-SPN) (Day 8 after surgery) on the incidence of nosocomial infections in patients who are at high nutritional risk and have poor tolerance of EN. This study adds to previous literature as it is the first multicenter, randomized clinical trial to evaluate the effect of the timing for initiating SPN on infections [1].

Methods
- Multicenter, open-label randomized clinical trial conducted from April 1, 2017 to December 31, 2018 involving 11 General Surgery departments in China
- Primary outcome: incidence of nosocomial infections between post-operative day 3 and hospital discharge
- Inclusion criteria: adult patients who underwent elective gastric, colorectal, hepatic, and pancreatic resections (benign and malignant). Risk of malnutrition was defined as a Nutrition Risk Screening 2002 score of 3 or higher. Patients were expected to have a post-operative LOS > 7 days and have received 30% or less of the energy target by enteral nutrition on Day 2 after surgery
- Exclusion criteria: psychiatric disorders, pregnancy or breast feeding, malnutrition (>10-15% weight loss in 6 months, BMI <18.5, Subjective Global Assessment (SGA) of Malnutrition Score Stage C, albumin <30g/L), hemodynamically unstable or refractory shock, mortality rates > 50% in 6 months with malignancy or irreversible disease, hepatic/renal insufficiency, metabolic disease, burn > 20% BSA, immunosuppression, INR >3 or Plt <30,000, intracranial hemorrhage 1month before enrollment, and/or nutritional support prior to surgery
- Investigators and participants were not masked to the treatment assignment, but follow-up was performed by blinded physicians and nurses
- Energy targets were calculated as 30 kcal/kg of ideal body weight for men and 25 kcal/kg of ideal body weight for women while protein requirements were 1.2 g/kg of ideal body weight
- Both groups received nutritional support for a minimum of 5 days, until 80% of the energy target was reached with EN, or until hospital discharge. The mean hospital LOS was 16.6

days (SD 8.8) in the E-SPN group and 17.6 days (SD 8.4) in the L-SPN group, 95% CI 1.0 (-1.1 to 3.1), p=0.39.
- Daily nutritional information was recorded for a maximum of 12 days or until a normal diet was resumed or the patient was discharged
- Power: sample size of 110 patients in each group

Findings
- 1560 patients were screened and ultimately a total of 230 patients were randomized – 115 E-SPN group, 115 in the L-SPN group (1 patient withdrew before intervention)
- Demographics included mean age 60.1 years; 140 men (61.1%); and all patients were of Han race and Asian ethnicity
- E-SPN group received more mean energy delivery between Days 3 and 7, 26.5 vs 15.1 kcal/kg daily, p<0.001. The mean protein intake was 1.02 (0.28)g/kg per day in the E-SPN group and 0.48 (0.17)g/kg per day in the L-SPN group, p<0.001. There was no statistical difference in the mean energy and mean protein intake between the two groups during the 8 to 12 days after surgery.
- E-SPN had fewer nosocomial infections 10/115 (8.7%) vs 21/114 (18.4%), risk difference 9.7%, 95% CI 0.9-18.5%, p=0.04, and there was no difference found in mean number of noninfectious complications, total adverse events, and rates of other secondary outcomes
- Mean serum albumin, 3.55 vs 3.37 g/dL, mean difference 0.19 g/dL, 95% CI 0.030.35 g/dL, p=0.02, and prealbumin, 15.84 vs 13.0 mg/dL, mean difference 2.85 mg/dL, 95% CI 1.88-3.82 mg/dL, p<0.001, levels at discharge were significantly higher in the E-SPN group than the L-SPN group
- 7 (6.1%) patients in the E-SPN group and 9 (7.9%) patients in the L-SPN group required ICU admission, 95% CI 1.8 (-4.8 to 8.4), p=0.62

Commentary
Various nutritional and advanced recovery societies recommend EN initiating as soon as possible after surgery; however, energy delivery in post-surgical patients using EN alone is less than estimated [1]. European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines recommend initiating SPN if energy requirements have not been met by EN for more than 7 days [2] and American Society of Parenteral and Enteral Nutrition (ASPEN) guidelines recommend SPN withing 3-5 days for patients who are at nutritional risk [3]. This study found a significant improvement in nutritional status in the E-SPN group with SPN started by Day 3 after surgery. This finding may be due to E-SPN combined with EN substantially improving energy delivery after surgery and preventing energy deficits during the initial postoperative days. Interestingly, there were fewer gastrointestinal dysfunctions were found in the E-SPN group than the L-SPN group.

This study primarily evaluated the incidence of nosocomial infections. They found the E-SPN group had significantly fewer nosocomial infections. Logically, total energy and protein intakes were significantly higher during the intervention periods after surgery in the E-SPN group leading to improved nutritional parameters. This study adds considerably to the literatures as it provides prospective data demonstrating E-SPN as a favorable strategy to reduce nosocomial infections among patients with high nutritional risk and poor tolerance to EN after major elective abdominal surgery. The limitations include the lack indirect calorimetry as it is the recommended method to measure resting energy expenditure in surgical patients; the study's inclusion of a select cohort of patients who had high nutritional risk and poor tolerance of EN; and the unblinded nature of the participants and investigators.

Implications for practice

This study performed nutritional screening using the Nutrition Risk Screening 2002 that asks 4 questions regarding BMI <20.5 kg/m2, weight loss within 3 months, reduced dietary intake in the last week, and if the patient is in the ICU. If the answer is "yes" to any, a Final Screening is performed which evaluates nutritional impairment, severity of disease on a scale from 0-3 points, and age < or > 70 yrs [2]. This screening does appear to take into account if the patient is in the ICU, but it is unclear if the additional metabolic demand of a critically ill state is accounted for. This does pose a question for the optimal timing to initiate SPN for nutritionally at risk patients undergoing emergent procedures or those in extremis. It appears earlier is better; however, this study was performed in the elective population. The EPaNIC trial compared the clinical prognosis of critical ill patients who receive SPN initiated 8 days after entering the ICU with the patients who had started SPN within 2 days and they found E-SPN associated with increased infectious complications [4]. It is unclear if the higher dose of glucose or some degree of overfeeding while under severe metabolic stress played a factor. This study starts SPN at the earliest post-operative Day 3 when the stress and inflammatory response to surgery has already decreased and there is improved metabolic tolerance. This could factor into the screening of critically ill patients and the initiation of nutrition when their clinical inflammatory response has resolved or is at least improved. Ultimately, there may be a benefit, such as reduced nosocomial infections, to screening elective surgery patients for malnutrition and initiating early supplemental nutrition.

References

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