

First of all, we would like to thank the three reviewers for their review of this paper and their comments and valuable suggestions. Here are the answers to each of the reviewer' questions:

Reviewer #1:

Q1:Please mention how sample size was determined?

A: Before the start of study, the sample size of this study was initially formulated as 10 cases in each group and a total of 30 cases according to the sample size of the study on intestinal flora in patients with sepsis published in 2021^[1] (10 cases in each group). After the initial completion of patient sample collection and clinical nutrition index examination, the calculation and verification of the minimum sample size were carried out: Due to this study is a study related to nutritional support, the change of prealbumin can represent the effect of nutritional support. Based on the mean and standard deviation of prealbumin in three groups of patients, the sample size of multi-group parallel control design was calculated (the calculation formula is as follows). SAS calculated λ (when $\alpha = 0.05$, Power = 0.8, K = 3), $\lambda = 9.64$. The means of prealbumin in the three groups were 0.15,0.13,0.11, and the standard deviation was 0.03. According to the formula, the final sample size of each group was $n \approx 10$.

$$\begin{cases} n = \lambda / \Delta \\ \Delta = \frac{1}{\sigma^2} \sum_{i=1}^k (\mu_i - \mu_0)^2 \end{cases}$$

Note: n: sample size; σ : standard deviation; k: number of groups; μ_i : the mean of each group; μ_0 : The average of the means of each group.

Q2: please provide some detail on how initial 30 patients were enrolled (sampling method), how they were randomized.

A: This study was grouped according to random number table and random number remainder methods:

Firstly, 30 patients were expected to be enrolled in the group and numbered 1-30 in order; starting from the selection of any row and column in the random number table, the random numbers starting from row 2 and column 5 to the right and to the right are grouped by the remainder of the random number divided by 3 in this study, the remainder is 1 that is divided into the first group, the remainder is 2 that is divided into the second group, and the remainder is 0 that is divided into the third group (group: 1 = TEN; 2 = TPN; 3 = SPN). After the first grouping, group 1: 9 cases; group 2: 11 cases; group 3: 10 cases. (Details in the following table)

Secondly, the next random number 98 divided by the remainder of 3 is 2, adjusting the patient number 2 from group 2 to group 1. There were 10 patients in each group.

numeration	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
Remainder	2	1	0	0	2	1	2	1	1	1	2	2	0	0	0	0	2	2	2	1	0	2	2	0	0	0	1	2	1	1
Group	2	1	3	3	2	1	2	1	1	1	2	2	3	3	3	3	2	2	2	1	3	2	2	3	3	3	1	2	1	1
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Q3:looks like patients were enrolled at various time, so please provide more detail on how exactly the patient were selected for various mode of nutrition.

A: As the answer of Q2 above, the patients were randomly grouped after numbering, and it would give patients different nutritional support according to different groups. During the period of nutritional support, due to the change of the patient 's condition (improved discharge/deterioration of the condition cannot continue to give nutritional support), the patients with less than 5 days of nutritional support were regarded as invalid observation cases and excluded, and the next enrolled patient was given nutritional

support according to the same nutritional support route of invalid cases.

Q4: Please mention if other patient factors were considered besides randomization, for selection of mode of nutrition.

A: In order to avoid the patient's own factors that cannot lead to nutritional support, the inclusion criteria^④ pointed out: with nutritional support pointer (hemodynamic stability (no/small dose of vasoactive drugs to maintain vital signs and lactic acid levels ≤ 2 mmol/L), and NUTRIC score (nutritional risk scoring tool for critically ill patients) ≥ 6 points). In order to exclude the contraindications of intravenous or enteral nutrition support and achieve a relatively uniform state of the basic state of the enrolled patients, the exclusion criteria ②、③ pointed out that the following patients need to be excluded: gastrointestinal tract, abdominal open injury; there are serious acid-base balance and electrolyte metabolism disorders.

[1] Yang XJ, Liu D, Ren HY, Zhang XY, Zhang J, Yang XJ. Effects of sepsis and its treatment measures on intestinal flora structure in critical care patients. *World J Gastroenterol.* 2021;27(19):2376-2393. doi:10.3748/wjg.v27.i19.2376.

Reviewer #2:

Q1: Please provide the information about the missing data, if it occurred in this study, and how to deal with it.

A: There was no missing data in this study. All data included flora and short-chain fatty acids, if not detected, the content was 0.

Q2: In the discussion, please correct the word “improveme” in the phrase “early TEN supports can improveme gut microbiota.” - In the legend of Figure 1, please correct the word “bacteial”.

A: Thanks for reading carefully and finding the errors, which have been corrected.

Q3: In Figure 3, please reconsider changing the color code between the group as the author mentioned in the legend of Figure 3. Red as before nutrition support and blue as after nutrition support are used in Figure 1, Appendix Figure 1, and Appendix Figure 2. However, blue as before and red as after nutrition support are alternately used in Figure 3, which might confuse the reader. Also, please reconsider changing the color code: red as before nutrition support and blue as after nutrition support in Figure 4.

A: Thanks for your valuable comments, and I have modified the corresponding diagram as recommended.

Q4: In the result, the authors reported, "Comparison of genus and OTU level in gut microbiota composition using Mann-Whitney U-test showed that some gut bacteria changed significantly in the three groups after 5 days ..." However, Mann-Whitney U-test is a statistical analysis to compare two groups in general rather than among three groups, as the authors mentioned. Please reconsider

using the appropriate statistics.

A: This partial statistics is indeed finished with the Mann-Whitney U-test, but not for comparison between the three groups, but for comparison between the each group of three groups of patients before and after nutrition. The statement may make the reader ambiguous and has been modified.

Q5: As the author mentioned, "... this study is limited with the small sample size ..." Please provide the study size estimation in the method section.

A: Before the start of study, the sample size of this study was initially formulated as 10 cases in each group and a total of 30 cases according to the sample size of the study on intestinal flora in patients with sepsis published in 2021^[1] (10 cases in each group). After the initial completion of patient sample collection and clinical nutrition index examination, the calculation and verification of the minimum sample size were carried out: Due to this study is a study related to nutritional support, the change of prealbumin can represent the effect of nutritional support. Based on the mean and standard deviation of prealbumin in three groups of patients, the sample size of multi-group parallel control design was calculated (the calculation formula is as follows). SAS calculated λ (when $\alpha = 0.05$, Power = 0.8, K = 3), $\lambda = 9.64$. The means of prealbumin in the three groups were 0.15, 0.13, 0.11, and the standard deviation was 0.03. According to the formula, the final sample size of each group was $n \approx 10$.

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