

Associations between trajectories of dietary fiber supplement and the incidence of acute gastrointestinal injury and mortality in critically ill patients : a prospective observational study

Ting Liu, Bin Liu, Yi-qing Jiang, Omorogieva Ojo, Xiao-song Jiang, Yu-yu Wang, Can Wang, Xiao-hua Wang (2024) Effects of different dietary fiber supplement strategies on incidence of acute gastrointestinal injury in ICU patients: A prospective observational study. *Intensive and Critical Care Nursing*, Available at; <https://doi.org/10.1016/j.iccn.2024.103673>

Abstract

Background: Insufficient dietary fiber (DF) supplement is closely associated with adverse clinical outcomes in critically ill patients which has not been paid enough attention in China. The amount of DF supplement in critical settings is low and inconsistent. This study aimed to explore the associations between trajectories of DF supplement and the incidence of acute gastrointestinal injury (AGI) and other clinical outcomes.

Methods: This was a prospective observational study conducted from April 2021 to March 2023. Using a five-day dietary log counted the amount of DF supplement. The best fitting trajectories of DF supplement were determined based on the latent class trajectory modelling (LCTM). The data of AGI grade were evaluated on the day 5 (D5) and day 7 (D7) after ICU admission. The mortality of ICU and one-month were collected.

Results: A total of 179 patients were included in the study. The LCTM yielded a four-trajectories of models, named; sustained low (SL), slowly rising (SR), early supplement and slowly rising (ESR) and rapidly rising (RR) groups, respectively. The incidence of AGI on D5, D7 and one-month mortality were 51.39%, 40.0% and 15.1%, respectively. Taking the RR group as reference, the SL group had significantly higher risk in the incidence of AGI on D5 (*OR*, 3.30; 95% *CI*, 1.15 - 9.50; *P* = 0.017) and D7 (*OR*, 16.79; 95% *CI*, 3.96 - 71.14; *P* < 0.001); the SR group had a significant association with one-month mortality (*OR*, 9.62; 95% *CI*, 1.04 - 88.73; *P* = 0.046).

Conclusion: Early, consistent and sufficient dose of DF supplementation significantly

reduce the risk of the incidence of AGI and one-month mortality in critically ill patients.

Implications for clinical practice: In order to improve clinical outcomes, critically ill patients could be provided an early, consistent and sufficient dietary information on DF supplement.

Key words: dietary fiber; acute gastrointestinal injury; mortality; critically ill patients

1. Introduction

The maintenance of proper barrier function is one of the important functions of gastrointestinal (GI) tract^[1]. In critically ill patients, the GI is a vulnerable organ and its dysfunction has been considered as an important clinical concern^[2]. Hence, monitoring the status of GI is vital for patients in intensive care unit (ICU). In 2012, the Working Group on Abdominal Problems of the European Society of Intensive Care Medicine (ESICM) defined acute gastrointestinal injury (AGI) as the malfunctioning of the GI tract in ICU patients and recommended a four-grade classification for AGI severity^[3]. It was reported that the overall incidence of AGI in critically ill patients was 82.81% and the incidence of grade I-IV were 35.94%, 37.50%, 20.63% and 9.06%, respectively^[4].

AGI is closely related to adverse outcomes such as prolonged hospital stay^[5] and increasing ICU mortality^[1]. Besides, the severity or grade of AGI is correlated with mortality^[6]. A meta-analysis indicated that the patients with AGI had a higher risk of mortality [risk ratio (*RR*) = 2.01; 95% confidence interval (*CI*), 1.20 – 3.37; *P* = 0.008] and that patients with more severe AGI (grade III and IV vs grade II) had a higher risk of mortality (*RR* = 1.86; 95% *CI*, 1.48 – 2.34; *P* < 0.0001)^[1].

Dietary fiber (DF) is a class of dietary polysaccharides that are neither digested nor absorbed in the human small intestine^[7] and it could depolymerize and ferment into host-absorbable short-chain fatty acids (SCFAs) in the colon^[8]. It does not only promote the growth of probiotics, improve fecal microbial diversity, reduce the levels of enterococci and multi-drug resistant bacteria, stabilize intestinal flora, but also stimulates the production of intestinal mucins in the intestine to repair intestinal epithelial tight junctions and improve the intestinal mucosal barrier^[9-11]. Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) suggested that ICU patients that are hemodynamically stable could routinely be supplemented with 10 – 20 g/d of soluble DF to maintain the stability of the intestinal mucosal barrier and intestinal flora^[12]. Some clinical trials have examined the effect of DF supplement on the improvement of GI symptoms^[11, 13, 14] in ICU patients. Liu et al. ^[15] indicated that the DF group had a significantly decreased risk of vomiting, regurgitation, diarrhea, constipation, even mortality, compared with

the DF free group. Cara et al.^[14] also pointed that enteral nutrition formulations containing DF showed a lower risk of GI complications compared with non-fiber groups (*RR*: 0.61; 95% *CI*, 0.47-0.79). In addition, Liu PX et al.^[16] reported the ‘death group’ had significantly lower dose of DF supplement in the first 14 days of ICU than that of the ‘survival group’ [total intake: 26.45 (0.00 - 108.87) g VS 52.56 (0.00 - 126.30) g, *P* < 0.01]. Cox proportional hazard regression analysis showed that low DF intake was a risk factor for death in ICU patients.

However, at present, the use of DF supplementation has been inconsistent and not optimistic in clinical settings. While some patients may have continuous low-dose supplements, other patients may be quickly supplemented relatively sufficient amounts. The trajectory of DF supplementation is not consistent. Besides, the relationship of different trajectories about DF supplement with different incidences of AGI and other clinical outcomes is still unclear. Therefore, this study aims to explore the status of the trajectories of DF supplement and the associations between the trajectories of DF supplement and the incidence of AGI and other clinical outcomes.

2. Materials and methods

2.1 Study design

This was a prospective observational study conducted from April 2021 to March 2023. By convenience sampling of participants who met the inclusion criteria, we recruited the patients with critical illness in the intensive care unit (ICU) of the First Affiliated Hospital of Soochow University. The study protocol was approved by the ethics committee of The First Affiliated Hospital of Soochow University (No. 2021428) and implemented in accordance with the Declaration of Helsinki.

2.2 Study population

Inclusion criteria: (1) duration of ICU study >72 h; (2) age >18 years; (3) receiving nutrition support (orally or through enteral tube feeding) during the first five days of admission; (4) signing informed consent by patients themselves or members of their main family and voluntary participation. Exclusion criteria : (1) with GI diseases; (2) discharged or died within 72h of admission; (3) AGI could not be evaluated for any reason.

2.3 Five-day dietary log for counting the amount of Dietary fiber supplement

Two well-trained researchers recorded the five-day dietary log. It included (1) the names and the amount of all foods consumed for patients with an oral nutrition support and / or (2) the names and the amount of all nutrition solutions which contained dietary fiber for patients with an enteral (tube) nutrition support within the first 5 days of admission. Before collecting dietary data, the educational manual was developed. It contained (1) concept and types of dietary fiber and common foods rich in dietary fiber; (2) food standard portions developed by Chinese Dietary Guidelines (2016 Edition) and the methods of evaluating food portions; (3) the types and nutrient composition of common enteral nutrition solutions; (4) the dietary log which was used to record the portions and amount of consumed foods and supplemented enteral nutrition solutions was kept for the first five days of admission. Based on the educational manual, two researchers were trained for about one hour. During the process of research, the researchers accurately noted the types, portions and amounts of all consumed foods, snack and enteral nutrition solutions. The amount of DF supplement was calculated according to dietary logs using Feihua Nutrition Software (V2.7.6.10, Beijing, China).

2.4 AGI diagnosis

The AGI grades were defined following the 2012 ESICM recommendations as follows^[3]: AGI I grade: the function of the GI tract was partially impaired, expressed as GI symptoms related to a known cause, and perceived as transient. Clinically, it was common in nausea, vomiting, loss of bowel sounds, and diminished bowel motility in the early stages of shock; AGI II grade: the GI tract was not able to perform digestion and absorption adequately to satisfy the nutrient and fluid requirements of the body, for examples: gastroparesis with high gastric residuals or reflux, paralysis of the lower GI tract, diarrhea, intra-abdominal hypertension (IAH) grade I (intra-abdominal pressure 12-15 mmHg), visible blood in gastric content or stool. Feeding intolerance was present if at least 20 kcal/ kg / day via enteral route could not be reached within 72 h of feeding attempt; AGI III grade: loss of GI function, and restoration of GI function was not achieved despite interventions, and the general condition was not improving, for examples; despite treatment, there was feeding intolerance with persisting-high gastric residuals, persisting GI paralysis, occurrence or worsening of bowel dilatation, progression of IAH to grade II (intra-abdominal pressure 15–20 mmHg), low

abdominal perfusion pressure (below 60 mmHg); Feeding intolerance was present and possibly associated with persistence or worsening of multiple organ dysfunction syndrome (MODS); AGI IV grade: AGI had progressed to become directly and immediately life-threatening, with worsening of MODS, such as intestinal ischemic necrosis, GI bleeding leading to hemorrhagic shock, Ogilvie's syndrome, abdominal compartment syndrome requiring decompression. Based on these, AGI was divided three groups: grade 0 (without AGI), grades I/II (acute GI dysfunction), and grade III/IV (acute GI failure).

To accurately collect the data of AGI diagnosis, the training manual which was associated with AGI diagnosis and the estimation methods of AGI were formulated and two researchers were trained for about 1 hour. The AGI assessment was conducted at 9 am in the first, fifth and seventh days of admission.

2.5 Data collection

General information questionnaire was used to collect demographic and clinical data. The demographic data included age, sex, marital status, body mass index (BMI). The clinical data included disease condition which was represented by Acute Physiology and Chronic Health Evaluation II (APACHE II) score (within the first 24 h after ICU admission), the usage of mechanical ventilation (MV), vasopressor, continuous renal replacement therapy (CRRT) and sedative drugs. ICU mortality and one-month mortality were also collected. ICU mortality was defined as the death during the admission in ICU. One-month mortality was defined as the death within 30 days of ICU admission. If the patients transferred to another department, the data of one-month mortality was collected by medical record system. If the patient was discharged, it was followed by telephone.

2.6 Endpoints

The endpoints included (1) Incidence of AGI on days 5 and 7 of ICU admission and (2) ICU mortality and one-month mortality.

2.7 Statistical analyses

To determine the best fitting trajectories of DF supplement for first five days of admission, we used latent class trajectory modelling (LCTM) which allowed identifying unobserved groups of individuals following similar trajectories over age or

time of a single outcome or behavior^[17]. Models were assessed with statistical criteria using log-likelihood, Akaike information criterion (AIC), Bayesian information criterion (BIC) and relative entropy values. The smallest BIC was considered the most appropriate model^[18]. The posterior probabilities for each individual being a member of the trajectories were calculated in the final model. Statistical analysis was performed using R programming language (version 4.0.2; R Foundation for Statistical Computing, Vienna, Austria).

The baseline characteristics of the participants were summarized as counts and percentage for categorical data. Continuous data were reported as means \pm standard if normally distributed; otherwise, they were shown as median and interquartile range (IQR). Chi-squared test was used to compare the differences of the grades of AGI on the fifth and seventh days, ICU mortality and one-month mortality in the different trajectory groups. To further analyze the associations between the DF supplement and the grades of AGI on the fifth and seventh days, one-month mortality in different trajectory groups, we used univariate analysis and ordered or binary logistic regression. In ordered or binary logistic regression, the covariates which were P -values < 0.05 in the univariate analysis were included. Statistical analysis was performed using SPSS 25.0 software (SPSS, Chicago, IL, USA). A two-tailed value of P -values < 0.05 was taken to indicate statistically significant.

2.8 Sample size calculation

The sample size estimation was based on the incidence of AGI. According to previous study, the incidence of AGI in ICU was 40.0%^[1]. The sample size estimation was carried out using Power Analysis and Sample Size (PASS) software, version 15.0 (New Canaan, CT, USA), considering alpha = 0.05, power = 90% and applying a two-tail-test. The accepted sample size was at least 120, in consideration of 20% dropout rate.

3 Results

3.1 Baseline characteristics

The sampling flowchart is shown in Figure 1. A total of 201 participants were screened for inclusion, of which 17 were voluntarily discharged and 5 were transferred during the first four to five days after admission. Among the included 179 patients, 44

patients did not assess the grade of AGI on the seventh day because of discharging or transferring or refusing assessment on that day. A total of 179 participants with an average of 62.46 (standard deviation 19.01 years) were recruited for the study. Among them, 67.60% were men and the average BMI was 23.0 ± 3.5 (kg/m²).

3.2 DF supplement trajectories

Based on the DF supplement in the first five days after admission, the LCTM yielded four-trajectories of model as the best fit to the data which had lower BIC and highest entropy, named sustained low (SL) group, slowly rising (SR) group, early supplement and slowly rising (ESR) group and rapidly rising (RR) group (Figure 2). The fit statistics of trajectory model are reported in Table 1. The baseline characteristics of participants in four trajectory groups are demonstrated in Table 2.

3.3 Status of daily DF supplement in the groups with different trajectories

The average supplement of DF in ICU patients from D1 to D5 of admission were (7.50 ± 1.54) g/d, (15.00 ± 3.82) g/d, (18.25 ± 5.81) g/d, (23.50 ± 7.56) g/d and (23.60 ± 8.51) g/d. The SL group sustained a low DF supplement during the first five days after admission, with an average DF supplement of (0.67 ± 1.03) g/d. That of the SR group was characterized by a gradual increase in DF supplement during the first four days (average amount: 2.76 ± 2.36 g/d). The supplemented DF in the ESR group began on the first day (average amount: 4.14 ± 3.41 g/d), then slowly increased in the following days. The DF supplement of the RR group significantly increased from the second day to the maximum (15 g/d) on the fifth day after admission. The detailed DF supplement is showed in Table 3.

3.4 Incidences of AGI on the fifth and seventh days after admission

As outlined in the methodology, we categorized the enrolled patients into three groups: AGI grade 0, AGI grades I/II (acute GI dysfunction), and AGI grade III/IV (acute GI failure). The overall incidence of AGI on the fifth and seventh days after admission were 51.39% and 40.0%, respectively; of which about 46.37% and 31.86% had the grades I/II and 5.02% and 8.14% suffered the grade III/IV, respectively. As shown in Table 4, no patients with acute GI failure were found in the RR group, while there were 6 (9.38%) and 6 (15.00%) patients in the SL group on the fifth and seventh day, respectively. On the seventh day of admission, there was a significant difference

in the incidence of AGI among the groups of different DF supplement trajectories ($\chi^2 = 18.173$, $P < 0.001$). In addition, although there was no statistical significance in terms of AGI on the fifth day of admission, there was a rising trend in the SL, SR, and ESR groups, compared with that of the RR group ($\chi^2 = 9.644$, $P = 0.140$) (Table 4).

3.5 Associations between DF supplement trajectories and AGI on the fifth and seventh days after admission

Table 5 summarized the demographic and clinical characteristics of the patients with different AGI grades on the seventh day of admission. The variables with $P < 0.05$ were adjusted in subsequent Multiple Logistic Regression analysis. As shown in Table 5, statistically significant differences ($P < 0.05$) were found in the variables including mechanical ventilation time (MVT), acute physiology, and chronic health evaluation-II (APACHE-II score), use of Vasopressor and Sedative drugs.

An ordered logistic regression analysis was performed to determine the associations between DF supplement trajectory and incidence of AGI on the fifth and seventh day after admission (Table 6). Taking the RR group as a reference and adjusting for covariates including APACHE-II score, MVT, vasoactive drug and sedatives, the SL group demonstrated significantly higher risk in the incidence of AGI on both day 5 [odd ratio (*OR*), 3.30; 95% *CI*, 1.15-9.50; $P=0.017$] and day 7 (*OR*, 16.79; 95% *CI*, 3.96-71.14; $P < 0.001$). In addition, the vasoactive drug was found to increase significantly the odds of the incidence of AGI on day 7 (*OR*, 3.82; 95% *CI*, 1.06-13.77; $P=0.041$).

3.6 Incidence of ICU and one-month mortality

The ICU and one-month mortality rates were 10.1% and 15.1%, respectively. The lowest rates (3.7%) for both ICU and one-month mortality were in the RR group, while the highest proportions of ICU (18.8%) and one-month mortality (25.0%) were in the SR group. But no statistical differences ($P>0.05$) were found among the groups in the two observing points (Table 7).

3.7 Association between DF supplement trajectories and one-month mortality

There were statistically significant differences in the variables ($P < 0.05$) including age and APACHE-II. Thus, both of them were taken as the covariates in the analysis of association between DF supplement trajectories and one-month mortality (Table 8). A

Binary logistic regression analysis was performed to investigate the association between the DF supplement trajectories and the one-month mortality (Table 9). Taking the RR group as a reference and adjusting for the age and APACHE-II, the SR group demonstrated an association with one-month mortality (*OR*, 9.62; 95% *CI*, 1.04 - 88.73; *P* = 0.046).

4 Discussion

This study indicated that ICU patients had an insufficient and inconsistent DF supplement. In relation to the supplement of DF in the first five days, there were four trajectory groups named; the sustained low (SL), slowly rising (SR), early supplement and slowly rising (ESR) and rapidly rising (RR) groups, respectively. The results showed that SL group had the highest incidence of acute GI failure, while there was no patient with acute GI failure in the RR group. Besides, the lowest mortality was in the RR group. Compared with the RR group, after adjusting for covariates, the SL group had higher risks for AGI incidence on D5 and on D7. Furthermore, SR group had a higher risk for one-month mortality.

Population characteristics

Among 179 ICU patients, the average age was 62.5±19.0 years, and most patients were male (67.6%) which is similar to previous study^[19]. A BMI of 23.0±3.5 (kg/m²) indicates that most patients had a BMI within the normal range. The APECH-II was 12.68±7.53, indicating a mild case, which is similar to and an earlier study [14.0 (12.0-17.0)]^[20]. MVT was 5.82±10.63 day, which is comparable to previous study (7.5±7.0 day)^[21]. An observational study^[22] reported that 30.55% of the ICU patients used vasoactive drug, which is less than the findings of our study (44.1%). In our research, 53.1% (95/179) used sedative, and most of them maintained anesthesia in patients with tracheal intubation, which is similar to Hyun's research^[23].

Status of DF supplement

The results showed that the supplementation of DF in critically ill patients were insufficient, with a median DF intake of 5.0 g/d by D3 of admission. Freedberg et al.^[24] demonstrated that ICU patients received a median DF intake of 10.7 g/d by D3 of admission. Fu YC et al.^[11] pointed the median DF intake of ICU patients were only 13.4g during the 72 hours after ICU admission. In this study, the results of DF

supplement in different trajectory groups indicated that the SL group maintained very low doses during first five days of admission to ICU (D1, 0.37 ± 0.90 g/d to D5, 3.40 ± 3.75 g/d), the SR group had very low doses during first three days of admission to ICU (D1, 0.39 ± 1.57 g/d to D3, 3.18 ± 4.07 g/d), while the RR group had a significant increase from 0.24 ± 0.99 g/d on D1 (0.24 ± 0.99 g/d) to nearly 8 g/d on D2, 15.00 g/d on D5.

Incidence of AGI

In this study, 94.4% of the patients suffered from AGI, including 7.3% with acute GI failure. The overall incidence of AGI on the fifth and seventh day after admission were 51.39% and 40.0%, respectively. Sun JK et al.^[20] found there was 86.7% of patients with AGI, and 8.4% with acute GI failure during ICU hospital stay, which is consistent with the results reached in our study.

Further analysis found that SL group had the highest incidence of acute GI failure, with 12.2% and 15.0% on D5 and D7, respectively; while RR group did not have any incidence of acute GI failure. Taking the RR group as a reference and adjusting for covariates, the SL group demonstrated significantly higher incidence of AGI on both day 5 (*OR*, 3.30; *P*=0.017) and day 7 (*OR*, 16.79; *P* < 0.001).

In critically ill patients, the release of inflammatory mediators following trauma, surgery and infection causes intestinal flora translocation and injury to the intestinal mucus membrane, resulting in loss of barrier function, impaired immune protective system, and secretion dysfunction^[1]. AGI may manifest as delayed gastric emptying, changes in intestinal motility patterns, and impaired integrity of the intestinal barrier^[3]. Butyrate, one of SCFAs produced by DF, is well documented to be effective in maintaining intestinal epithelial integrity by providing energy to intestinal epithelial cells and inducing colonic mucin expression^[25,26]. Animal study has shown that acetate promoted intestinal barrier integrity^[27]. In addition, a recent animal study using fiber-deprived or high fiber diet to explore the effect of DF on intestinal permeability, the result indicated that the mice in fiber-deprived group manifested severe colitis and increased intestinal permeability^[28]. Hence, DF may be an important factor for maintaining the intestinal barrier and reducing the incidence of AGI. This study confirmed that the patients with sustained DF supplementation had a significant higher

incidence of AGI.

ICU mortality and one-month mortality

The results showed that the total ICU and one-month mortality rates were 10.1% and 15.1%, respectively. The SR group had the highest incidence, while the RR group had the lowest incidence of ICU and one-month mortality. The multiple logistic regression analysis showed that the one-month mortality in the SR group was 9.62 times that in the RR group. Hu et al.^[22] surveyed ICU patients and found there were as high as 29.3% of one-month mortality. The reason may be that the population in Hu's study had higher APACHE II scores (19.47 ± 7.12) and proportion of acute GI failure (26.17%). Many studies have indicated that APACHE-II score was an independent risk factor for mortality of ICU patients^[29, 30]. In addition, ICU patients with GI failure had higher mortality^[1].

5. Limitations

There are some limitations to the study. Firstly, this study was conducted in a single medical center. Secondly, some patients dropped off or refused to provide AGI information on D7 after admission, which may result in some bias. Furthermore, due to the high cost of relative biomarker about the assessment of AGI and limited support fund, the study was not involved in biomarker about accessing AGI. In future, some high quality RCTs are needed to determine the effect of different trajectories of DF supplement and the incidence of AGI and mortality in critically ill patients.

6. Clinical recommendations

Considering the current findings, medical staff should pay attention to the supplementation of not only the three macronutrients, but also dietary fiber in critically ill patients. In the clinic, nurses can educate family members of patients, give advice to doctors, or assist with feeding to ensure that critical care patients receive DF supplementation.

7. Conclusion

Early, consistent and sufficient dose of DF supplementation significantly reduced the risk of the incidence of AGI and one-month mortality in critically illn patients. In order to improve their clinical outcomes, professional staff should pay more attention to DF supplementation in critically ill patients.

Innovative point

1. Using the latent class trajectory modelling (LCTM) determined the fitting trajectories of DF supplement.

2. Early, consistent and sufficient dose of DF supplementation significantly reduced the risk of the incidence of AGI and one-month mortality in critically ill patients.

Table 1 Summary of model fits for DFS trajectory

| Trajectories | BIC | Log-Likelihood | AIC | Relative Entropy | Percentage of persons in groups |
|--------------|---------|----------------|---------|------------------|----------------------------------|
| 1 | 5012.29 | -2487.99 | 4989.98 | — | 100.0 |
| 2 | 4904.09 | -2420.92 | 4865.83 | 0.84 | 45.8; 54.2 |
| 3 | 4833.62 | -2372.72 | 4779.44 | 0.84 | 47.5; 36.9; 15.6 |
| 4 | 4829.92 | -2357.90 | 4759.80 | 0.91 | 35.7; 31.3; 17.9; 15.1 |
| 5 | 4834.61 | -2347.28 | 4748.55 | 0.85 | 33.5; 15.1; 15.6; 19.0; 16.8 |
| 6 | 4860.47 | -2347.24 | 4758.48 | 0.73 | 34.1; 12.3; 8.9; 4.5; 20.7; 19.6 |

Notes: DFS, dietary fiber supplement; AIC, akaike information criterion; BIC, bayesian information criterion.

Table 2 Status of daily dietary fiber intake in the groups with different DFS trajectories

| Variable (n) | D1 (g/d), mean ± SD | D2 (g/d), mean ± SD | D3 (g/d), mean ± SD | D4 (g/d), mean ± SD | D5 (g/d), mean ± SD |
|------------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Sustained low group (64) | 0.37±0.90 | 0.62±1.32 | 0.79±1.52 | 2.22±3.23 | 3.40±3.75 |
| Slowly rising group (32) | 0.39±1.57 | 0.48±1.84 | 3.18±4.07 | 7.00±5.17 | 11.64±4.34 |
| ESR group (56) | 4.14±3.41 | 7.53±4.02 | 9.75±4.25 | 10.43±5.86 | 9.42±5.49 |
| Rapidly rising group (27) | 0.24±0.99 | 7.69±3.32 | 12.67±3.46 | 14.86±0.72 | 15.00±0.00 |

Notes: DFS, dietary fiber supplement; D1, D2, D3, D4, and D5: the first, second, third, fourth and fifth days of admission, respectively; ESR, early supplement and slowly rising.

Table 3 Incidence of AGI on the D5 and D7 in the groups with different DFS trajectory

| Variable | D5 AGI (n=179, n, %) | | | χ^2 | <i>P</i> value | D7 AGI (n=135, n, %) | | | χ^2 | <i>P</i> value |
|----------------------|----------------------|------------|--------------|----------|----------------|----------------------|------------|--------------|----------|----------------|
| | Grade 0 | Grade I/II | Grade III/IV | | | Grade 0 | Grade I/II | Grade III/IV | | |
| Sustained low group | 28 (43.75) | 30 (46.87) | 6 (9.38) | 9.644 | 0.140 | 13 (32.50) | 21 (52.50) | 6 (15.00) | 18.173 | <0.001** |
| Slowly rising group | 12 (37.50) | 18 (56.25) | 2 (6.25) | | | 22 (78.57) | 4 (14.29) | 2 (7.14) | | |
| ESR group | 34 (60.71) | 21 (37.50) | 1 (1.79) | | | 28 (70.00) | 9 (22.50) | 3 (7.50) | | |
| Rapidly rising group | 13 (48.15) | 14 (51.85) | 0 (0.00) | | | 18 (66.67) | 9 (33.33) | 0 (0.00) | | |

Notes: D5, D7: the fifth and seventh days of admission; AGI, acute gastrointestinal injury; DFS, dietary fiber supplement; ESR, early supplement and slowly rising; ***P* < 0.001.

Table 4 Characteristics of the patients by AGI on the D7 of admission

| Variable | D7 AGI | | | F/ χ^2 | P value |
|---|-------------------|-------------------|-------------------|-------------|----------|
| | Grade 0 | Grade I/II | Grade III/IV | | |
| Age (year), mean \pm SD | 64.94 \pm 17.56 | 60.93 \pm 22.39 | 62.27 \pm 17.16 | 0.634 | 0.532 |
| Sex (male), n (%) | 57 (59.37) | 30 (31.25) | 9 (9.38) | 0.673 | 0.714 |
| BMI (kg/m ²), mean \pm SD | 22.24 \pm 3.01 | 22.97 \pm 3.01 | 24.32 \pm 3.50 | 2.573 | 0.080 |
| MVT (day), mean \pm SD | 4.95 \pm 8.14 | 10.42 \pm 16.79 | 12.18 \pm 7.01 | 4.222 | 0.017* |
| APACHE-II, mean \pm SD | 12.57 \pm 6.80 | 13.16 \pm 7.29 | 21.09 \pm 9.45 | 6.859 | 0.001* |
| Vasopressor (yes), n (%) | 31 (44.93) | 29 (42.03) | 9 (13.04) | 14.084 | <0.001** |
| Sedative (yes), n (%) | 30 (46.15) | 25 (38.46) | 10 (15.39) | 13.781 | 0.001* |
| D1AGI (yes), n (%) | 78 (60.94) | 39 (30.46) | 11 (8.60) | 2.446 | 0.294 |
| PN (yes), n (%) | 0 (0.00) | 2 (66.70) | 1 (33.30) | 5.724 | 0.060 |
| CRP (mg/L), mean \pm SD | 39.72 \pm 59.61 | 48.41 \pm 82.84 | 53.05 \pm 94.04 | 0.314 | 0.731 |

Notes: D7: the seventh days of admission; AGI, acute gastrointestinal injury; AGI D1, AGI at the admission day; BMI, body mass index; MVT, mechanical ventilation time; APACHE-II, acute physiology, and chronic health evaluation-II; PN, parenteral nutrition at the admission day; CRP, C reaction protein at the admission day; *, $P < 0.05$; **, $P < 0.001$.

Table 5 ordinal logistic regression analysis for the grade of AGI on D5 and D7 of admission

| Variable | D5 AGI | | D7 AGI | |
|----------------------|--------------------|---------|---------------------|----------|
| | OR (95% CI) | P value | OR (95% CI) | P value |
| DFS trajectories | | | | |
| Rapidly rising group | Ref. | — | Ref. | — |
| Sustained low group | 4.51 (1.78, 11.42) | 0.001* | 11.40 (3.70, 35.06) | <0.001** |
| Slowly rising group | 3.40 (1.24, 9.32) | 0.018* | 1.12 (0.30, 4.19) | 0.862 |
| ESR group | 1.30 (0.52, 3.27) | 0.580 | 1.72 (0.56, 5.27) | 0.341 |
| APACHE-II | 1.04 (0.99, 1.09) | 0.087 | 1.08 (1.02, 1.14) | 0.011* |
| MVT (day) | 1.02 (0.99, 1.04) | 0.577 | 1.01 (0.99, 1.04) | 0.356 |
| Vasopressor (yes) | 2.05 (1.05, 4.01) | 0.036* | 1.94 (0.82, 4.61) | 0.131 |
| Sedative (yes) | 2.96 (1.54, 5.71) | 0.001* | 3.25 (1.42, 7.43) | 0.005* |

Notes: AGI, acute gastrointestinal injury; CI, confidence interval; OR, odds ratio; ESR, early supplement and slowly rising; APACHE-II, acute physiology and chronic health evaluation-II; MVT, mechanical ventilation time; *, $P < 0.05$; **, $P < 0.001$

Table S1 Demographic characteristics in the groups with different DFS trajectories

| Variable | All | Sustained low group | Slowly rising group | ESR group | rapidly rising group | <i>P</i> value |
|---|-------------------|---------------------|---------------------|-------------------|----------------------|----------------|
| Age (year), mean \pm SD | 62.46 \pm 19.01 | 59.31 \pm 21.10 | 61.22 \pm 19.01 | 64.14 \pm 18.56 | 67.93 \pm 18.56 | 0.207 |
| Sex (male), n (%) | 121 (67.60) | 39 (21.79) | 21 (11.73) | 43 (24.02) | 18 (10.06) | 0.318 |
| BMI (kg/m ²), mean \pm SD | 22.97 \pm 3.84 | 23.35 \pm 3.89 | 22.80 \pm 4.09 | 22.62 \pm 3.04 | 22.99 \pm 2.51 | 0.704 |
| MVT (day), mean \pm SD | 2.00 \pm 10.63 | 3.80 \pm 8.71 | 5.41 \pm 6.24 | 5.38 \pm 10.53 | 12.00 \pm 16.05 | 0.008* |
| APACHE-II, mean \pm SD | 12.68 \pm 7.54 | 11.06 \pm 7.61 | 15.34 \pm 8.37 | 12.50 \pm 7.26 | 13.74 \pm 16.11 | 0.056 |
| ICU stay (day), mean \pm SD | 13.91 \pm 12.16 | 11.08 \pm 10.00 | 15.47 \pm 9.50 | 11.85 \pm 1.59 | 18.67 \pm 17.88 | 0.042* |
| Vasopressor (yes), n (%) | 79 (44.14) | 25 (13.97) | 14 (7.82) | 24 (13.41) | 16 (8.94) | 0.360 |
| Sedative (yes), n (%) | 81 (45.25) | 24 (13.41) | 14 (7.82) | 27 (15.08) | 16 (8.94) | 0.270 |
| PN (yes), n (%) | 4 (2.23) | 4 (2.23) | 0 (0) | 0 (0) | 0 (0) | 0.032* |

Notes: DFS: dietary fiber supplement; ESR, early supplement and slowly rising; BMI, body mass index; MVT, mechanical ventilation time; APACHE-II, acute physiology, and chronic health evaluation-II; PN, parenteral nutrition; *, $P < 0.05$.

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