

Original Article

Dysbiosis of intestinal microbiota in critically ill patients and risk of in-hospital mortality

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Abstract: Background: Despite the essential functions of the intestinal microbiota in human physiology, little research was reported on gut microbiota alterations in intensive care patients. This investigation examined the dysbacteriosis of intestinal flora in critically ill patients and evaluated the prognostic performance of this dysbiosis to predict in-hospital mortality. Methods: A prospective cohort of patients were consecutively recruited in the Intensive Care Units (ICUs) in Guangdong Provincial People's Hospital from March 2017 through October 2017. Acute Physiology and Chronic Health Evaluation (APACHE) II score and Sequential Organ Failure Assessment (SOFA) score were assessed, and fecal samples were taken for examination within 24 hours of ICU admission. The taxonomic composition of the intestinal microbiome was determined using 16S rDNA gene sequencing. Patients were divided into survival and death groups based on hospital outcomes. The two groups were statistically compared using the Wilcoxon test and Metastats analysis. The genera of bacteria showing significantly different abundance between groups were assessed as predictors of in-hospital death. The prognostic value of bacterial abundance alone and in combination with APACHE II or SOFA score was evaluated using the area under the receiver operating characteristic curve (AUROC). Results: Among the 61 patients examined, 12 patients (19.7%) died during their hospital stay. *Bifidobacterium* abundance was higher in the survival group than the death group ($P = 0.031$). The AUROC of *Bifidobacterium* abundance in identifying in-hospital death at a cut-off probability of 0.0041 was 0.718 (95% confidence interval [CI], 0.588-0.826). The panel of *Bifidobacterium* abundance plus SOFA (AUROC, 0.882; 95% CI, 0.774-0.950) outperformed SOFA (AUROC, 0.649; 95% CI, 0.516-0.767; $P = 0.012$) and *Bifidobacterium* abundance alone ($P = 0.007$). The panel of *Bifidobacterium* abundance plus APACHE II (AUROC, 0.876; 95% CI, 0.766-0.946) outperformed APACHE II (AUROC, 0.724; 95% CI, 0.595-0.831; $P = 0.035$) and *Bifidobacterium* abundance alone ($P = 0.012$). Conclusions: Dysbiosis of intestinal microbiota with variable degrees of reduction in *Bifidobacterium* abundance exhibited promising performance in the predicting of in-hospital mortality and provides incremental prognostic value to existing scoring systems in the adult intensive care unit (ICU) setting.

Keywords: Intestinal dysbiosis, *bifidobacterium*, in-hospital mortality, prognostic value, intensive care unit, scoring system

Introduction

Intestinal microbiota diversity plays a vital role in maintaining intestinal homeostasis, human nutrition and health [1]. However, this diversity

is highly vulnerable to diseases, especially critical illnesses with high mortality rates [2, 3]. Critical illnesses frequently cause gastrointestinal motility disorder, intestinal mucosal ischemia, and impaired intestinal barrier function

Gut dysbiosis predicts in-hospital death in intensive care units

[4, 5], which lead to dramatically altered intestinal microbiota [3, 6]. Dysbiosis of gut microbiota is widely viewed as a potential marker for many diseases [7]. Therefore, it may be a new mortality predictor in critically ill patients [5, 7]. Xu et al. indicated that gut microbiota dysbiosis was associated with patients' 180-day mortality in a neurological intensive care unit [6]. However, the prognostic ability of this potential marker in predicting in-hospital mortality in intensive care unit patients was not determined.

The present prospective observational cohort study investigated intestinal dysbiosis in critically ill patients at admission and detected that the altered abundance of some bacterial genera were associated with in-hospital mortality. Further assessments of the prognostic performance of this dysbiosis with existing scoring systems (APACHE II/SOFA score) were also performed to obtain an optimal clinical model to predict in-hospital mortality.

Materials and methods

Study design and population

A prospective cohort of patients was consecutively recruited in Intensive Care Units (ICUs) in Guangdong Provincial People's Hospital from March 2017 through October 2017. Patients were admitted from general or emergency wards. Participants were excluded if any of the following criteria were met: (1) the participant was under the age of 18 years; (2) the participant received systematic antibiotic treatment within 48 hours before ICU admission; (3) the participant was admitted to the ICU for an end-stage chronic disease; or (4) the participant died within 24 hours of ICU admission. The local ethics committee approved the study. All patients provided informed consent form before participating in the study.

Data collection

Demographic, laboratory and clinical variables were recorded at admission to the ICU. SOFA and APACHE II scores were assessed twice within 24 hours of ICU admission, and the worst value was chosen. Stool samples or rectal swabs (if stool was unavailable) were collected at ICU admission and immediately frozen at -80°C. Taxonomic compositions of the intestinal

microbiome were determined using 16S rDNA gene sequencing of the stool sample.

Intestinal microbiota analysis

Intestinal flora analysis was performed using the 16S rDNA amplicon sequencing method, which is commonly used for bacterial phylogeny and classification identification [8-10]. The genomic DNA of the sample was extracted using the sodium dodecyl sulphate (SDS) method. A sample without genomic DNA extraction was used as the blank control. The purity and concentration of the DNA were detected using 1% agarose gel electrophoresis. The DNA was diluted to 1 ng/ml with sterile water depending on the concentration. Specific primers (e.g., 16S V4: 515F-806R, 18S V4: 528F-706R, 18S V9: 1380F-1510R, et al.) with barcodes were used to amplify the 16S rDNA gene in different regions (16S V4/16S V3/16S V3-V4/16S V4-V5, 18S V4/18S V9, ITS1/ITS2, and Arc V4). All PCR reactions were performed using Phusion® High-Fidelity PCR Master Mix (New England Biolabs, Ipswich, MA, USA). The same volume of 1X loading buffer (containing SYB green) was mixed with the PCR product and electrophoresed on a 2% agarose gel. Samples with a bright master band between 400-450 base pairs were selected for further experiments. A sample without template was used as the PCR negative control. The mixed PCR products were purified using a Qiagen Gel Extraction Kit (Qiagen, Duesseldorf, Germany). The TruSeq® DNA PCR-Free Sample Preparation Kit (Illumina, San Diego, CA, USA) was used to generate sequencing libraries, according to the manufacturer's recommendations, and index codes were added. A Qubit 2.0 fluorometer (Thermo Scientific, Waltham, MA, USA) and Agilent Bioanalyzer 2100 system (Agilent Technologies, Beijing, China) were used to evaluate the library quality [11]. The library was sequenced using an Illumina HiSeq2500 (Illumina, San Diego, CA, USA) platform, and 250 base-pair paired-end reads were generated [12].

Sequences analysis was performed using Uparse software (Uparse v7.0.1001, <http://drive5.com/uparse/>) [13]. By default, the sequences were clustered into operational taxonomic units (OTUs) with 97% identity. A representative sequence of OTUs was selected. According to the algorithm principle, the sequence with the highest frequency in OTUs was

Gut dysbiosis predicts in-hospital death in intensive care units

Table 1. Clinical and demographic characteristics of patients

Variables	Total (n = 61)	Death (n = 12)	Survival (n = 49)	P value
Age, y	60.2 ± 19.0	61.1 ± 20.2	60.0 ± 18.9	0.871
Male, n (%)	42 (68.8)	10 (83.3)	32 (65.3)	0.186
Admission Type, n (%)				0.541
Neurologic	25 (41.0)	3 (25.0)	22 (44.9)	0.209
Respiratory	9 (14.8)	2 (16.7)	7 (14.3)	0.836
Digestive	10 (16.4)	3 (25.0)	7 (14.3)	0.369
Sepsis	5 (8.2)	3 (25.0)	2 (4.0)	0.018
Others	12 (19.6)	1 (8.3)	11 (22.5)	0.270
CRP, mg/L	67.3 ± 65.6	97.8 ± 81.9	59.4 ± 59.2	0.149
PCT, ng/L	10.5 ± 4.6	13.3 ± 5.1	8.5 ± 9.0	0.127
ICU stay, days	26.6 ± 43.7	14.7 ± 11.9	29.5 ± 48.1	0.057
SOFA score	9.8 ± 3.7	13.4 ± 3.4	8.9 ± 3.1	0.001
APACHE II score	20.4 ± 7.1	27.5 ± 6.6	18.7 ± 6.0	0.001

Continuous variables are presented as mean ± SD and categorical variables as number (percentage). APACHE II, Acute Physiology and Chronic Health Evaluation II; CRP, C reactive protein; ICU, intensive care unit; PCT, procalcitonin; SD, standard deviation; SOFA, sequential organ failure assessment.

selected as the representative of OTUs. The Mothur method (with a cut-off value of 0.8) and Silva database (version 128, <https://www.arb-silva.de>) were used to annotate OTU representative sequences and analyze species annotations to obtain classification information at each classification level: kingdom, phylum, taxa, order, family, genus and species [13-15]. Fast multi-sequence alignments were performed using MUSCLE (Version 3.8.31, <http://www.drive5.com/muscle/>) software to obtain phylogenetic relationships for all OTU representative sequences [15]. The data of each sample were homogenized, and the sample was homogenized according to the minimum amount of data in the sample.

Data analysis

Patients participating in the study were categorized into two groups according to their survival status in the hospital, i.e., survival and death groups. All baseline data between groups were assessed. Based on the OTU clustering results, the abundance analysis of OTUs was carried out to examine differences in the community structure between groups. The difference between the beta diversity index groups was analyzed. Metastats analysis was performed at each classification level (phylum,

class, order, family, genus, and species). *P* values were obtained by performing permutation tests between groups, and abundance distribution boxes of different species between groups were plotted.

The prognosis prediction models for *Bifidobacterium* abundance, APACHE II score, and SOFA score was established using univariate logistic regression. The prognosis prediction models for APACHE II score plus *Bifidobacterium* abundance and SOFA score plus *Bifidobacterium* abundance were established using multivariate logistic regression. All prediction models were evaluated as the area under the receiver operating characteristic curves (AUROC). To avoid an overfitting effect due to relatively small sample size, the bootstrap method was used with 1000 resamples, and the bootstrap-corrected AUROCs and 95% CI are reported.

The Youden index [16] was used to determine the optimal cut-off points. Comparisons between groups of AUROCs were performed using the DeLong [17] and bootstrapping methods [19].

Continuous variables are presented as means ± standard deviation (SD) and were compared using the Wilcoxon test. Categorical variables are presented as numbers (percentage) and were compared using Pearson's χ^2 test or Fisher's exact test, where appropriate. The significance level was set at $P < 0.05$. The analyses were performed using SPSS 24.0 software (SPSS, Chicago, IL, USA), MedCalc 12.5.0 software (MedCalc Software, Ostend, Belgium), and R 3.3.1 software (R Foundation for Statistical Computing, Vienna, Austria) using RStudio v1.0.136 (RStudio Inc., Boston, MA, USA).

Results

Sixty-one critically ill patients with a mean age 60.2 years were included in this study. Forty-nine patients (80.3%) survived, and 12 patients (19.7%) died in the hospital. The patients' clinical and laboratory characteristics are shown in **Table 1**. Notably, the SOFA and APACHE II scores were markedly higher in the death group than the survival group ($P = 0.001$).

Gut dysbiosis predicts in-hospital death in intensive care units

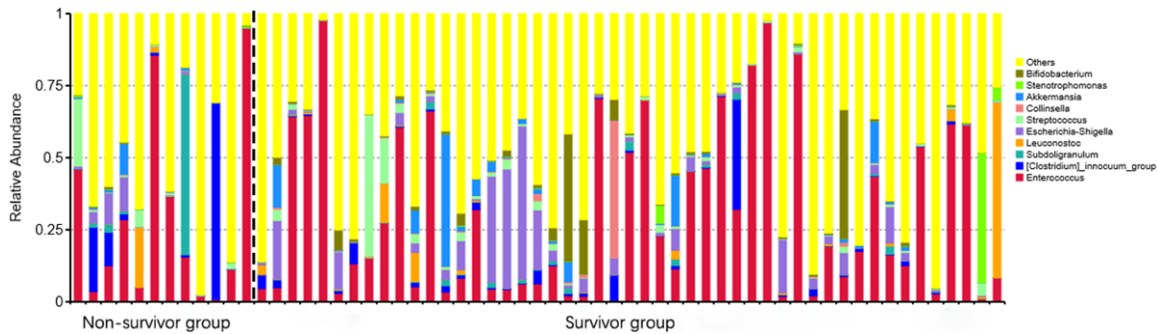


Figure 1. TOP 10 species relative abundance histogram at the genus level of the personal sample. The abscissa is the sample name; the ordinate is the relative abundance; the others represented the sum of the relative abundances of all the other genus except the 10 genera.

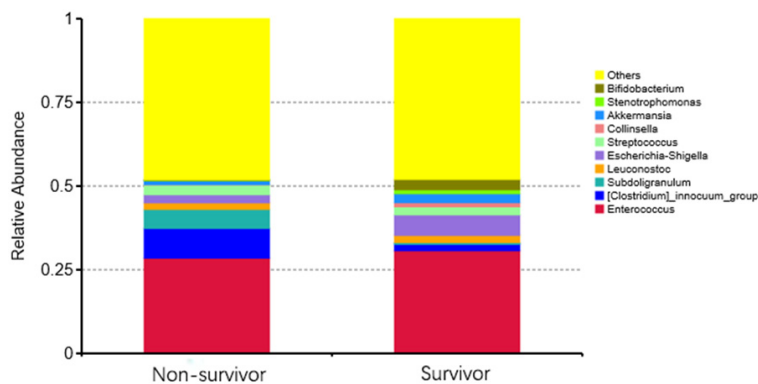


Figure 2. TOP 10 species relative abundance histogram at the genus level of the groups. The abscissa is the group name; the ordinate is the relative abundance; the others represent the sum of the relative abundances of all the other genus except the 10 genera.

After paired-end read merging and error correction of 16S rDNA sequencing, a total of 4,592,443 effective tags were obtained from 61 stool samples, for a mean of 75,286 tags. Based on 97% sequence identity, amplicons were clustered into 4954 OTUs. A total of 837 genera were identified in gut microbiomes in this study. OTU richness of the intestinal microbiota showed no significant difference between groups. According to the results of species annotation at the genus level, 10 genera exhibited a higher level of abundance in the two groups and accounted for greater than 50% of the total. The top 10 genera with the highest abundance at the genus classification level were enrolled to generate a columnar accumulation plot of relative abundance. The top 10 genera were *Enterococcus*, *Clostridiuminnocuum*, *Subdoligranulum*, *Leuconostoc*, *Stenotrophomonas*, *Escherichia-Shigella*, *Streptococcus*, *Collinsella*, *Akkermansia*, and *Bifidobacterium*, and did not include some of the most

common organisms that are typically seen in the human gut, such as *Bacteroides* and *Lachnospiraceae*. **Figure 1** shows the composition in each sample, and **Figure 2** describes the relative abundance between groups. To identify different species in the 10 genera, we performed a *t* test to analyze the intestinal flora and identify species with a significant difference ($P < 0.05$).

Table 2 shows that only *Bifidobacterium* abundance exhibited a significant difference between groups, with a larger reduction in the death group

than the survival group ($P = 0.031$). Notably, the abundance of *Bifidobacterium* in both groups was not relatively low, which may be related to the relative old age of the patients we included (the average age was approximately 60 years old). In general, *Bifidobacterium*, as a probiotic bacterium, decreases slowly with age. The abundance distribution of different species between groups was also mapped (**Figure 3**). Notably, there was a trend of a lower abundance of *Escherichia-Shigella* in the patients who died compared with patients who survived, which should be investigated in future studies using a larger sample size.

AUROC analysis was used to assess the predictive accuracy of APACHE II, SOFA, and *Bifidobacterium* abundance for the prognosis of hospital death in critically ill patients. The AUROC analysis of the three univariate models (APACHE II, SOFA, and *Bifidobacterium* abundance) indicated that APACHE II (AUROC, 0.724; 95%

Gut dysbiosis predicts in-hospital death in intensive care units

Table 2. Mean abundance of gut microbiome taxa in patients

Taxa	Death	Survival	P value
<i>Enterococcus</i>	0.1397 (0.0387-0.4347)	0.1628 (0.0473-0.6092)	0.830
<i>Clostridium innocuum</i>	0.0050 (0.0004-0.0924)	0.0050 (0.0019-0.0119)	0.253
<i>Subdoligranulum</i>	0.0007 (<0.0001-0.01451)	0.0013 (0.0002-0.0059)	0.342
<i>Leuconostoc</i>	0.0004 (<0.0001-0.0017)	0.0010 (<0.0001-0.0055)	0.933
<i>Escherichia-Shigella</i>	0.0023 (0.0007-0.0317)	0.0170 (0.0035-0.0538)	0.072
<i>Streptococcus</i>	0.0063 (0.0023-0.0188)	0.0073 (0.0030-0.0205)	0.810
<i>Collinsella</i>	0.0001 (<0.0001-0.0009)	0.0010 (0.0001-0.0031)	0.242
<i>Akkermansia</i>	0.0009 (<0.0001-0.0080)	0.0021 (<0.0001-0.0128)	0.268
<i>Stenotrophomonas</i>	0.0004 (<0.0001-0.0017)	0.0002 (<0.0001-0.0013)	0.261
<i>Bifidobacterium</i>	0.0009 (0.0002-0.0031)	0.0047 (0.0009-0.0115)	0.031

Abundance of gut microbiome are presented as median (IQR). IQR, interquartile range.

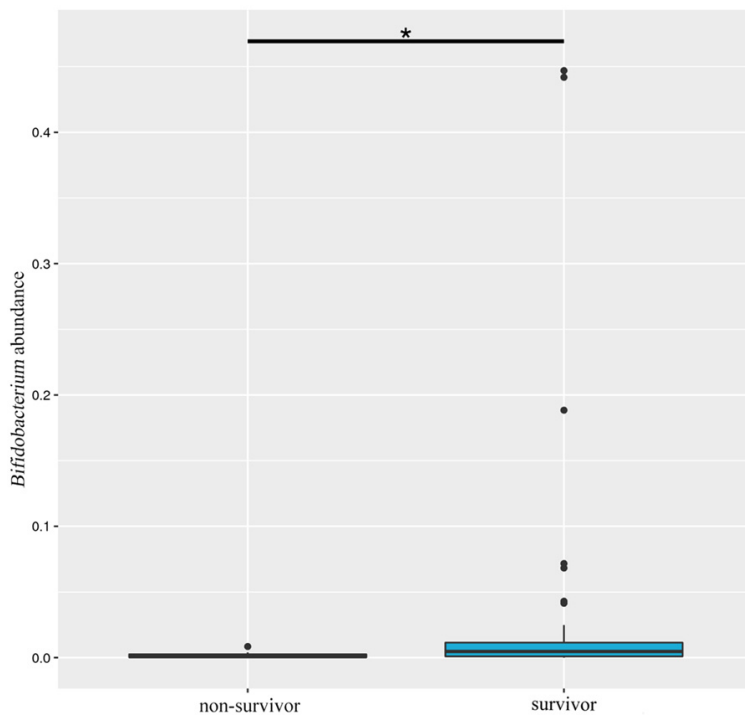


Figure 3. Box analysis of the abundance distribution of *Bifidobacterium* between groups. The horizontal axis is the sample grouping; the vertical direction is the relative abundance of *Bifidobacterium*; the horizontal lines represent two groups with significant differences. * $P < 0.05$.

CI, 0.595-0.831) had a slightly better discrimination than SOFA (AUROC, 0.649; 95% CI, 0.516-0.767) and *Bifidobacterium* abundance (AUROC, 0.718; 95% CI, 0.588-0.826) (**Figure 4A** and **Table 3**). However, the pairwise comparative analysis showed no significant difference (**Table 4**).

To assess the performance of combinations of these predictors, we performed logistic regression using two panels of predictors (APACHE II

score plus *Bifidobacterium* abundance and SOFA score plus *Bifidobacterium* abundance). The ROC curve analysis showed that the panel of *Bifidobacterium* abundance and APACHE II score had the largest AUROC of 0.876 (95% CI, 0.766-0.946) (**Figure 4B** and **Table 3**) with no significant difference ($P = 0.9274$). Further comparison of AUROCs between individual and combined predictors revealed that APACHE II score plus *Bifidobacterium* abundance significantly outperformed *Bifidobacterium* abundance ($P = 0.018$) and APACHE II score ($P = 0.035$) alone (**Table 3**). The AUROC of SOFA was 0.649 (95% CI, 0.516-0.767), and the AUROC of SOFA plus *Bifidobacterium* abundance was 0.882 (95% CI, 0.774-0.950). The combination of *Bifidobacterium* abundance and SOFA had higher specificity (85.71%)

but lower sensitivity (75%) (**Figure 4C**). We compared the AUROC of SOFA versus SOFA plus *Bifidobacterium* abundance, and *Bifidobacterium* abundance versus SOFA plus *Bifidobacterium* abundance, and both comparisons showed significant differences with P values of 0.007 and 0.012, respectively (**Table 3**).

Discussion

The results of our study suggest that dysbiosis of intestinal microbiota with variable degrees

Gut dysbiosis predicts in-hospital death in intensive care units

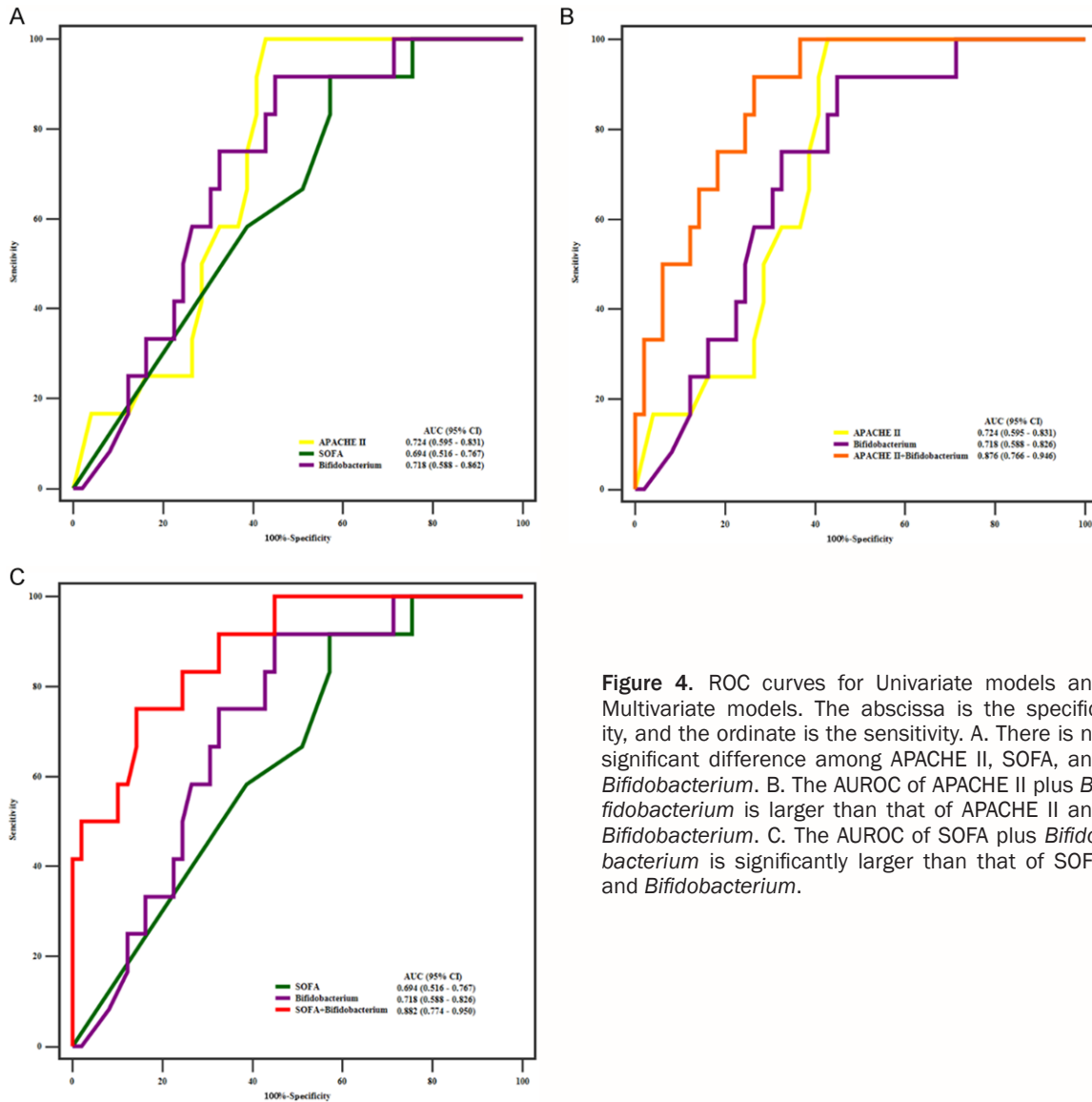


Figure 4. ROC curves for Univariate models and Multivariate models. The abscissa is the specificity, and the ordinate is the sensitivity. A. There is no significant difference among APACHE II, SOFA, and *Bifidobacterium*. B. The AUROC of APACHE II plus *Bifidobacterium* is larger than that of APACHE II and *Bifidobacterium*. C. The AUROC of SOFA plus *Bifidobacterium* is significantly larger than that of SOFA and *Bifidobacterium*.

Table 3. Predictive characteristics of admission indicator and their combinations for ICU mortality

Logistic regression model	AUROC (95% CI)	Youden index	Cut-off	OR (95% CI)	P
Univariate models					
APACHE II	0.724 (0.595-0.831)	0.5714	27.00	1.261 (1.091-1.458)	0.002
SOFA	0.649 (0.516-0.767)	0.3452	10.00	1.436 (1.159-1.777)	0.001
<i>Bifidobacterium</i>	0.718 (0.588-0.826)	0.4677	0.0041	0.800 (0.622-1.029)	0.082
Multivariate models					
APACHE II plus <i>Bifidobacterium</i>	0.876 (0.766-0.946)	0.6514	1.82	2.716 (1.435-5.141)	0.002
SOFA plus <i>Bifidobacterium</i>	0.882 (0.774-0.950)	0.6071	1.07	2.720 (1.488-4.973)	0.001

Optimal cut-off value is determined by Youden's index. Cut-off points of the multivariate indicator models were the predicted probability generated by the multiple logistic regression model. AUROC, area under the receiver operating characteristic curve. OR, odds ratio. CI, confidence interval.

of reduction in *Bifidobacterium* abundance is associated with critically ill patients' risk of death in the hospital. The abundance of intesti-

nal *Bifidobacterium* distribution was markedly lower in the death group than the survival group. Therefore, this abundance exhibited

Gut dysbiosis predicts in-hospital death in intensive care units

Table 4. Comparisons of AUROCs among prediction models

Comparison pairs	P value
AUROC comparison among univariate models	
APACHE II vs SOFA	0.419
APACHE II vs <i>Bifidobacterium</i>	0.927
SOFA vs <i>Bifidobacterium</i>	0.463
AUROC comparison between multivariate and univariate model	
APACHE II plus <i>Bifidobacterium</i> vs APACHE II	0.035
APACHE II plus <i>Bifidobacterium</i> vs <i>Bifidobacterium</i>	0.012
SOFA plus <i>Bifidobacterium</i> vs SOFA	0.012
SOFA plus <i>Bifidobacterium</i> vs <i>Bifidobacterium</i>	0.007

APACHE II, Acute Physiology and Chronic Health Evaluation II; AUROC, area under receiver operating characteristic curve; CI, Confidence Interval; SOFA, sequential organ failure assessment.

good prognostic values for in-hospital mortality. It also provided incremental prognostic value to existing scoring systems in the ICU.

Bifidobacterium is a genus of Gram-positive, non-motile, often branched anaerobic bacteria that were first discovered and isolated by Tissier et al. in 1899 from breastfeeding infant feces [18]. *Bifidobacterium* are a major genera of bacteria that make up the gut flora in humans, and its physiological functions include the promoting of nutrient absorption [19], maintaining intestinal micro-ecological balance [20], immune regulation [21], and anti-tumor activity [22-24]. However, *bifidobacteria* are susceptible to some adverse conditions, like aging and disease [25], and are likely reduced in intensive care patients [3, 26]. The pathophysiological effects of critical illness (e.g., decreased oral intake, intestinal dysmotility, gut hypoperfusion, reperfusion injury, and impaired mucosal integrity) and the clinical interventions of intensive care (e.g., supine positioning, gastric-acid suppression, sedatives, opiates and neuromuscular blockade, and systemic antibiotics) cause ecological imbalances that substantially alter the gut microbiome.

The advent of culture-independent microbiology and high-throughput sequencing methods has enabled researchers to identify specific features of the microbiome that promote and disrupt homeostasis in critically ill patients. The present study used 16S rDNA amplicon sequencing for bacterial phylogeny and classification identification. Notably, our study found that *Bifidobacterium* abundance was associated the severity of illness. Patients with a lower

Bifidobacterium content in gut had a higher risk for death in the hospital. Subsequent statistical analyses of logistic regression determined that *Bifidobacterium* abundance was a predictor for in-hospital mortality with an AUROC of 0.718. These findings are consistent with previous findings that the reduction of *Bifidobacterium* abundance is a sign of disorders [10, 26, 27].

Notably, the results of our study conflict with Xu et al. [6] who investigated the dysbiosis of gut microbiota in patients in a neuro-

critical care unit. Rather than *Bifidobacterium*, Xu et al. discovered that the gut genera with significantly decreased abundance longitudinally over time were *Ruminococcaceae* and *Lachnospiraceae* using the same 16S rRNA gene sequence analysis. This inconsistency may be attributed to several factors. First, participants in our study were consisted critically ill patients in a medical ICU rather than a neuro-surgical ICU. Second, in contrast to healthy volunteers as the control cohort in the previous study, our control cohort was composed of patients who survived in the hospital. We also focused on the outcome of in-hospital death as a binomial variable for the logistic regression analysis rather than 180-day death as a time-dependent covariate for COX regression analysis. Despite these differences in designs and results, the two studies effectively enhance our common understanding that intestinal microbiota dysbiosis is associated with patients' adverse outcomes and may be a predictor for death risk in critically ill patients.

As new diagnostic, therapeutic and prognostic techniques become available and ICU populations change, the scoring systems used in ICUs may not be very closely relevant to each patient population. This evolving situation calls for fresh biological or clinical markers to reflect current practice patterns and treatments for critical illness. Notably, we found that *Bifidobacterium* abundance was a promising prognosis factor for in-hospital mortality, and it added to the prognostic value of existing scoring systems, including SOFA and APACHE II scores. *Bifidobacterium* abundance exhibited a prognostic value that was slightly lower than the

Gut dysbiosis predicts in-hospital death in intensive care units

APACHE II score but higher than the SOFA score for in-hospital death in critically ill patients. When combined with *Bifidobacterium* abundance, the APACHE II score and SOFA score performed better in the prognosis prediction of critically ill patients. The reason for this result may be that indicators with different characteristics have different sensitivities and specificities, and a reasonable combination may improve the diagnostic performance. This result shares a similar mechanism with Deng [28], who combined a functional marker (sCysC) and a tubular injury marker (uNAG) to predict outcomes in patients with severe AKI, and the combination demonstrated superior discriminating performance compared to sCysC and uNAG alone.

To the best of our knowledge, there are few reports in the literature on gut microbiota dysbiosis in ICU patients. We demonstrated that the reduction of gut *Bifidobacterium* content was an independent risk factor for the prognosis of critically ill patients. Some *Bifidobacterium* strains [29] are important probiotics that show promise in the treatment of ulcerative colitis [30] and infection reduction, including ventilator-associated pneumonia (VAP), which is common in critical illness [31]. Therefore, we suggest that some pharmaceutical probiotic products containing *Bifidobacterium* may facilitate the maintenance or restoration of the homeostatic balance of infected intestine and improve the survival prognosis of patients in the ICU. However, further prospective clinical trials are required to confirm this proposal.

Our study has some limitations. First, the relatively small sample size as a result of the implementation of rigorous inclusion criteria and avoiding the use of too many resources (e.g., subjects, time, and financial costs), may cause an overestimation of the predictability of *Bifidobacterium* abundance. However, we used bootstrapping methods with 1000 resamples to avoid an overfitting effect in logistic regression, and we reported the bootstrap-corrected AUROC and 95% CI. Our findings are limited to a single-center study, and center-specific effects cannot be excluded. Further multicenter studies with larger sample sizes are required to verify the present results. The PCR and 16S rRNA amplicon sequencing methods are based on DNA and RNA extraction, respectively, and exhibit high accuracy but are cumbersome and

time-consuming, and cannot quickly quantify the intestinal flora [8, 32, 33]. Therefore, it is especially important to develop a method that can quickly and accurately quantify the abundance of intestinal flora.

Conclusion

Dysbiosis of intestinal microbiota with variable degrees of reduction in *Bifidobacterium* abundance exhibited promising performance in the predicting of in-hospital mortality and provided incremental prognostic value to existing scoring systems in an intensive care unit (ICU) setting.

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Informed consent was obtained from all individual participants included in the study.

Disclosure of conflict of interest

None.

Abbreviations

APACHE-II, Acute Physiology and Chronic Health Evaluation-II; AUROC, area under receiver operating characteristic curve; CI, Confidence interval; ICU, Intensive care unit; IQR, Interquartile range; OUT, Operational taxonomic unit; PCR, polymerase chain reaction; ROC, receiver operating characteristic curve; SD, Standard deviation; SOFA, Sequential Organ Failure Assessment.

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Gut dysbiosis predicts in-hospital death in intensive care units

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Gut dysbiosis predicts in-hospital death in intensive care units

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