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Gastrointestinal tract microbiome changes in intensive care units patients: review

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ABSTRACT

Hospitalization in the intensive care unit (ICU) changes the adaptive mechanisms of the patient, which affects his microbiome. Important triggers of microbiome disorders are the severity of the patient's condition, the lack of oral nutrition and/or artificial nutrition, as well as the duration of stay in the ICU. Intestinal dysbiosis with the development of pathobionts increases the risk of complications and the outcome of the disease. The review includes articles describing changes in the microbiome of the gastrointestinal tract in patients hospitalized in ICU departments. The main changes in the microbiome occurring in different parts of the gastrointestinal tract in patients hospitalized in the ICU are analyzed. Changes in the intestinal microbiome of the oral cavity were detected in patients from the first day of stay in the ICU with an increase in microbial contamination and the release of pathogens of nosocomial infections in the plaque. A direct relationship has been established between the duration of the patient's stay in the ICU and the depth of changes in the microbiome with the development of pathobiont dominance, regardless of the age and pathology profile of patients. An established risk factor for the development of complications and the onset of an unfavorable outcome is a decrease in the diversity of *Firmicutes* and the ratio of *Firmicutes* and *Bacteroidetes*. The influence of disorders of the functional activity of the intestinal microbiome and metabolism of certain bacterial species on the severity and prognosis of the disease has been determined. The factors influencing changes in the microbiota of newborns and their clinical significance are described. The positive effect of pre-, pro-, synbiotics, and fecal transplantation on the correction of microbiome disorders has been shown. In patients hospitalized in the ICU, pronounced changes in the gastrointestinal microbiome are diagnosed, while there is a relationship between the severity of the condition and a decrease in bacterial diversity and an increased risk of developing multiple organ failure and nosocomial infection. The greatest clinical significance in predicting a fatal outcome is the depletion of Firmicutes and a decrease in the ratio of Firmicutes/Bacteroidetes. The study of changes in the microbiome can be useful in the early diagnosis of nosocomial infection in critically ill patients and in predicting the risk of outcome.

Keywords: microbiome, gastrointestinal tract, intensive care units

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Изменения микробиома желудочно-кишечного тракта у пациентов реанимационных отделений: обзор литературы

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АННОТАЦИЯ

Госпитализация в отделение реанимации и интенсивной терапии (ОРИТ) изменяет адаптационные механизмы пациента, что влияет на его микробиом. Важными триггерами нарушения микробиома являются тяжесть состояния пациента, отсутствие перорального питания и/или проведение искусственного питания, а также длительность пребывания в ОРИТ. Дисбиоз кишечника с развитием патобионтов повышает риск развития осложнений и исход заболевания. Обзор базируется на научных статьях, описывающих изменения микробиома желудочно-кишечного тракта у пациентов, госпитализированных в отделения ОРИТ. Проанализированы основные изменения микробиома, происходящие в разных отделах желудочно-кишечного тракта (ЖКТ) у пациентов, госпитализированных в ОРИТ. Изменения кишечного микробиома ротовой полости выявлены у пациентов с первых суток нахождения в ОРИТ с увеличением микробной обсемененности и выделением в налете возбудителей внутрибольничных инфекций. Установлена прямая связь между длительностью пребывания пациента в ОРИТ и глубиной изменений микробиома с развитием доминирования патобионтов вне зависимости от возраста и профиля патологии пациентов. Установленным фактором риска развития осложнений и наступления неблагоприятного исхода является снижение разнообразия *Firmicutes* и соотношения *Firmicutes* и *Bacteroidetes*. Определено влияние нарушений функциональной активности микробиома кишечника и метаболизма отдельных видов бактерий на тяжесть и прогноз заболевания. Описаны факторы, влияющие на изменение микробиоты новорожденных, и клиническое значение этих факторов. Показано положительное влияние пре-, про-, синбиотиков, фекальной трансплантации на коррекцию нарушений микробиома. У пациентов, госпитализированных в ОРИТ, диагностируют выраженные изменения микробиома ЖКТ, при этом прослеживается зависимость между тяжестью состояния, снижением бактериального разнообразия, повышением рисков развития полиорганной недостаточности и внутрибольничного инфицирования. Наибольшее клиническое значение в прогнозировании летального исхода имеет истощение численности *Firmicutes* и уменьшение соотношения *Firmicutes/Bacteroidetes*. Изучение изменений микробиома может быть полезным в ранней диагностике внутрибольничного инфицирования у пациентов в критическом состоянии и прогнозировании риска неблагоприятного исхода.

Ключевые слова: желудочно-кишечный тракт, микробиом, отделения интенсивной терапии

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INTRODUCTION

Hospitalization of a patient to an intensive care unit (ICU) alters the body's adaptive mechanisms and directly or indirectly affects the microbiome. The onset of any critical condition leads to significant alterations in the microbiota across all organ systems [1, 2, 10, 15, 19]. The complex interactions between the gut microbial flora and the human host substantially impact patient health. The inability to maintain a regular oral diet in ICU patients alters the oral microflora, irrespective of the quality of general and specialized care [10]. Enteral nutrition, administered via a feeding tube or gastrostomy, alters the microbial profile throughout the entire digestive tract [4, 6–10, 15, 38].

For the gut microbiota, interaction axes such as the "gut–lung", "gut–brain", "gut–muscle", and "gut–kidney" axes, among others, have been described [5, 15–17, 20, 26]. The role of the gut microbiota as a modulator of disease is particularly important in critically ill patients. The mucous membrane of the digestive tract serves as the interface between the external environment and the body. It has been established that the gut is exposed not only to a flow of nutrients but also to massive stimuli and signals from the microbiota; furthermore, the pathways of interaction between gut microbes and nutrients, as well as among the microbes themselves, have been identified. Evidence indicates that the overgrowth of pathogenic flora in the gut influences the risk of complications and disease outcomes. To date, the relationships between the microbiome and the severity of condition in ICU patients remain insufficiently studied. Moreover, the mechanisms of modulating the microbiome through dietary changes and therapeutic strategies employed in intensive care also require further investigation.

This review analyzes current scientific literature on alterations in the gastrointestinal (GI) tract microbiome in patients of various ages hospitalized in the ICU.

The majority of publications focus on changes in the gut microbiome of critically ill patients, with only one study addressing the microbial diversity of dental plaque. The identification of pathogens, particularly when diagnosis is challenging with culture-based methods, is significantly enhanced by the use of 16S rRNA sequencing and its modifications [33, 51, 56]. Despite the difficulties in differentiating some closely related species within the same prokaryotic phylum due to pronounced intra-genomic heterogeneity, this method is used for determining the taxonomic profile of bacteria [32, 39, 47].

ORAL CAVITY MICROBIOME

The majority of ICU patients receive enteral nutrition via a nasogastric tube or gastrostomy, which eliminates the natural cleansing effect of food in the oral cavity. Within the first 24 hours of ICU admission, the oral microbiota load reaches 4.40×10^5 CFU/mL, with a tendency to increase to 3.44×10^6 CFU/mL by the end of the first week [50]. Pathogens associated with healthcare-associated infections (HAIs) are detected in 26% of patient samples. Therefore, a significant increase in microbial colonization of dental plaque and the presence of HAI pathogens in plaque represent a risk factor for complications [50].

A study of the oral microbiome (16S rRNA) in gastrostomy patients revealed early colonization by pathogens following the cessation of oral feeding, as well as substantial differences compared to healthy volunteers [6, 8, 10, 13, 15, 38].

Most studies focus on the gut luminal microbiota, the dynamics of its biodiversity reduction, and the potential use of changes in the Shannon index and microbiome composition ratios for the development of prognostic models for survival.

CHARACTERISTICS AND DYNAMICS OF THE GUT MICROBIOME

Numerous studies focus on investigating alterations in the *Firmicutes/Bacteroidetes* ratio (hereinafter referred to as the F/B ratio) in critically ill patients, driven by the crucial role these bacterial phyla play in gastrointestinal function. While *Firmicutes* convert lactic acid into butyrate, which stimulates mucin production, *Bacteroidetes* metabolize lactic acid into other short-chain fatty acids (acetate, formate, propionate) that may adversely affect the gut microbiome [15, 18]. Studies have confirmed the viability of using not only stool samples (luminal microbiota) but also rectal swabs (mucosa-associated microbiota) as biological materials for assessing gut microbiota in critically ill patients [15, 23].

The gut microbiome undergoes alterations within hours of patient admission to the ICU [63]. This transformation of the microbial pool is driven by several factors, including nutritional disruptions and impaired intestinal transit (constipation/diarrhea), administration of broad-spectrum antibiotics, proton pump inhibitors, morphine, local or systemic inflammatory changes in the intestinal wall, and compromised intestinal epithelial perfusion [63]. A direct correlation has been established between marked *Firmicutes/Bacteroidetes* microbiota imbalance (decreased *F/B* ratio) and the development of infectious complications along with multiple organ dysfunction syndrome [45].

A dynamic study of patients hospitalized in the ICU revealed a statistically significant reduction in *Firmicutes* abundance along with a decreased *F/B* ratio. Additionally, a negative correlation was found between patient condition severity (assessed by APACHE — Acute Physiology and Chronic Health Evaluation scores) and the *F/B* ratio [32].

Patients with prolonged critical illness exhibited marked alterations in gut microbiota species composition. After short-

term ICU stays, the microbiome recovered shortly following patient discharge [22].

Reduced gut microbial diversity, accompanied by the absence or loss of gut commensals, develops in two-thirds of ICU patients by day 5 of hospitalization [48]. In 75% of these patients, episodes of opportunistic pathogen dominance in the gut (*E. faecium, Kl. pneumoniae, E. cloacae, E. coli, Kl. oxytoca, P. mirabilis, Candida albicans*) with signs of nosocomial infection were recorded. Meropenem was shown to negatively affect gut microbial diversity, whereas no statistically significant changes were observed with piperacillin/tazobactam use. Some patients demonstrated an increased relative abundance of *Methanobrevibacter smithii*, an intestinal commensal. No significant correlations were detected between stool consistency, microbial diversity, and SOFA (Sequential Organ Failure Assessment) scores [48]. Thus, prolonged ICU stay reduces microbial diversity and decreases commensal flora dominance in the gut microbiome of most critically ill patients.

Similar conclusions have been reached by other authors. In a study of microbiomes from three biotopes (feces, oral cavity, and skin), a significant decrease in bacterial phylogenetic diversity was observed by day 10 following ICU admission [43]. Notably, stool samples and oral swabs collected at patient admission showed greater similarity to each other than to samples obtained at discharge, indicating a direct influence of ICU stay duration and associated disruptions to normal lifestyle on microbiome composition.

Alterations in fecal microbiota are characteristic of adult patients across various clinical specialties.

Within 72 hours, patients with severe traumatic injuries develop changes in the phylogenetic composition of the gut microbiome and relative taxon abundance, marked by depletion of *Bacteroidales, Fusobacteriales,* and *Verrucomicrobiales* alongside an increase in *Clostridiales* and *Enterococcus*. This represents a risk factor for ventilator-associated pneumonia (VAP), acute respiratory distress syndrome (ARDS), and multiple organ failure. Thus, patients with severe trauma demonstrate a characteristic reduction in non-pathogenic microorganisms and an increase in opportunistic pathogens, which may elevate the risk of unfavorable outcomes [36].

Cardiac surgery patients demonstrate significant alterations in bacterial diversity (Shannon index) during the postoperative period. Specifically, they exhibit a reduction in abundance of strict anaerobic gut bacteria producing short-chain fatty acids (*Faecalibacterium, Anaerostipes, Blautia,* and *Roseburia*) alongside an increase in pathobionts (*Enterococcus*, *Eggerthella*, *Peptococcus*, *Rothia*), including mucin-degrading *Akkermansia, Bifidobacterium*, and *Methanobrevibacter* [21]. Bacterial diversity recovers in these patients by the time of hospital discharge [44].

Patients with acute neurological pathology experiencing prolonged ICU stays showed reduced α-diversity of *Ruminococcaceae* and *Lachnospiraceae*. A direct positive correlation was identified between *Enterobacteriaceae* abundance and modified Rankin Scale scores at discharge, as well as between the detection of *Christensenellaceae* and *Erysipelotrichaceae* and increased mortality risk [60, 61].

In summary, gut microbiome alterations occur within the first 24 hours of hospitalization and progressively worsen throughout the ICU stay. Following brief ICU admissions, gut flora biodiversity recovers rapidly. A direct relationship exists between the extent of microbiome alterations and mortality. Rapid shifts in the quantitative and qualitative composition of gut microbiota can affect outcomes in severe somatic diseases, traumatic conditions, and the postoperative course [22, 36, 44]. Hospitalization duration correlates with low bacterial diversity identified during the preoperative period. According to study authors, changes in α-diversity during hospitalization influence 180-day patient mortality [60].

PROGNOSTIC SIGNIFICANCE OF GUT MICROBIOME ALTERATIONS

The dynamics of the microbial landscape were analyzed in patients with various diseases during a two-week ICU hospitalization. A *Bacteroidetes/Firmicutes* ratio exceeding 10% is associated with increased mortality [42, 45]. Conversely, in septic patients, despite reduced bacterial diversity, no association was found between microbiota diversity, the *Firmicutes/Bacteroidetes* ratio, or the gram-positive/gram-negative bacterial ratio and either complication rates or survival outcomes [37, 40].

The prognostic significance of gut flora dysbiosis for the prediction of in-hospital mortality in critically ill patients has been demonstrated. A direct relationship exists between reduced *Bifidobacterium* diversity and an increased risk of in-hospital death [57]. Furthermore, mortality risk probability based on the combination of *Bifidobacterium* concentration and SOFA scores was higher than that calculated using SOFA scores or bacterial counts alone [1, 57]. Enterococcus dominance in the gut microbiome has been linked to the development of multiple organ failure and unfavorable clinical outcomes [32, 37].

Reduced α-diversity in the microbiota of rectal swabs from ICU patients exhibits an inverse correlation with plasma concentrations of interleukin-6 (IL-6), C-C motif ligand-2 (CCL-2), and tumor necrosis factor (TNF), suggesting the potential for predicting complication risks [23].

Thus, gut microbiome disruption may contribute to risk stratification and early infection diagnosis in the ICU, correlates with various infectious and inflammatory diseases,

and is frequently observed in critically ill patients. Mortality has been associated with an increase in *Bacteroidetes* and a decrease in *Firmicutes*, phyla that play crucial roles in metabolism.

ENTEROTYPES: TOWARD A CLASSIFICATION OF MICROBIOME ALTERATIONS IN ICU PATIENTS

Studies attempting to classify dysbiosis in critically ill patients hospitalized in the ICU are of significant importance. An analysis of the relationship between the gut microbiome, clinical data (SOFA, APACHE II), and laboratory parameters (serum lactate concentration) in septic patients identified two distinct enterotypes that differed significantly in their taxonomic distribution [42]. Patients with lower microbial species diversity (enriched in *Bacteroidetes, Parabacteroides,* and *Enterobacteriaceae*) were assigned to the first enterotype, which was characterized by higher APACHE II scores and elevated serum lactate concentrations [42]. In patients with this enterotype, a *Bacteroidetes/Firmicutes* ratio greater than 10 correlated with higher in-hospital mortality, suggesting its potential as a marker for critical illness progression. A second enterotype is defined by the predominance of *Enterococcus, Vagococcus,* and *Lactobacillus*. Among ICU patients classified into this second enterotype, an increase in enterococcal abundance was associated with a lower incidence of septic shock [34]. Thus, ICU enterotypes may serve as independent clinical markers for characterizing a patient's gut microbiota in the intensive care setting and as indicators of disease severity.

SELECTIVE DECONTAMINATION OF THE DIGESTIVE TRACT IN ICU PATIENTS: IS IT ALWAYS BENEFICIAL?

The absence of a patient's regular oral nutrition leads to an increased proportion of opportunistic pathogens in the gut, which can cause infectious complications during ICU stay. To suppress intestinal colonization by opportunistic microorganisms, some countries employ prophylactic antibiotic therapy (selective decontamination of the digestive tract — SDD), which improves clinical outcomes in ICU patients [25]. However, prolonged and aggressive antibiotic therapy can exacerbate alterations in the patient's microbiome. The choice of antimicrobial agent, duration, dosage, and route of administration all influence the microbiome [53].

Studies demonstrate that SDD regimens cause rapid biodiversity loss during the initial days of ICU stay, while healthy individuals maintain stable microbial ratios [25]. ICU patients (based on 16S rRNA analysis) show higher abundance of *Bacteroidetes* and *Bacillus*, and lower levels of *Clostridium* clusters IV and XIVa, anaerobic gram-positive butyrate-producing bacteria, and *E. coli*. This pattern indicates recolonization of the intestinal tract with coliform flora and other aerobic gram-negative bacteria [25]. Therefore, preventive decontamination of gut flora does not always promote recovery in ICU patients.

The negative consequences of antibiotic therapy for the gut microbiome are particularly significant in critically ill patients. Reduced microbiota α-diversity combined with an imbalanced *Bacteroidetes/Firmicutes* ratio (exceeding 8 or below 1/8) during the first week of ICU hospitalization is associated with higher mortality (odds ratio: 5.54, 95% CI: 1.39–22.18, p=0.015) [46].

In mechanically ventilated critically ill patients with *Enterobacteriaceae spp*. dominance, early use of intravenous anti-anaerobic antibacterial agents is associated with reduced ventilator- and infection-free survival rates, along with increased mortality [27]. Thus, early administration of anti-anaerobic antibacterial agents has been linked to elevated mortality.

ALTERATIONS IN THE GUT MICROBIOME OF CHILDREN IN THE ICU

Given distinct anatomical, physiological, and functional characteristics, alterations in the gut microbiome of pediatric patients warrant specific consideration. The development of the gastrointestinal microbiota is known to significantly impact infant health and postnatal physiological adaptation, particularly due to differences between the microbiomes of full-term and preterm infants [1, 2, 14]. Whereas healthy full-term infants initially show predominance of gram-positive cocci, *Enterobacteriaceae*, and *Bifidobacteriaceae,* with a sequential progression toward *Bifidobacterium dominance*, preterm infants in the ICU demonstrate abundant staphylococci immediately after birth, with delayed bifidobacterial colonization [55]. Infants with dominant bifidobacterial flora exhibited higher acetate and short-chain fatty acid concentrations, along with lower pH.

Exposure to stress factors in newborns, including very low birth weight preterm infants, alters gut microbiota structure. Stress exposure in the ICU during the first 1–2 days of life significantly affects *Proteus* and *Veillonella* populations. Antibacterial use significantly influences colonization dynamics of *Proteus, Citrobacter,* and *C. perfringens*, with gender-specific differences identified in *Proteus colonization* [30]. Thus, stress factors during the neonatal period substantially impact the developing gut microbiome. Furthermore, preterm infants demonstrated a distinct panel of amino acid metabolites and central metabolism intermediates that significantly correlated with the relative abundance of eight bacterial species [30]. Early-life factors (gestational age, birth weight) and ICU stay duration exert a sustained influence on gut microbial composition dynamics and metabolism in neonates and infants [62].

Antibacterial agents administered at birth alter both the quantitative and qualitative composition of the microbiome, whereas later courses of antimicrobial therapy do not lead to profound alterations. A direct positive correlation has been established between antibacterial therapy initiated from birth and reduced folate biosynthesis in children, particularly when accompanied by decreased abundance of *Bifidobacterium breve* and *E. coli*. Simultaneously, these children show increased abundance of *Klebsiella* and *Bacteroides*, resulting in enhanced glycerolipid metabolism, fatty acid biosynthesis, and glycolysis [24]. Thus, antibacterial agent usage affects both the formation and subsequent modification of the gut microbiome in newborns.

Total parenteral nutrition (TPN) adversely affects the gut microbiome of children. By the fourth week, fecal α-diversity becomes significantly reduced in TPN patients compared to those receiving enteral nutrition [31]. Patients on TPN exhibited low abundance of *Bacteroides* and *Bifidobacterium* alongside high abundance of *Akkermansia* muciniphila throughout all observation weeks. Additionally, TPN patients showed decreased *Bacteroidetes* and increased *Verrucomicrobia* abundance, with a trend toward growing divergence from control group patients [31]. The authors acknowledge TPN's potential contribution to unfavorable clinical outcomes in children.

Therefore, the key triggers for microbiome alterations in pediatric ICU patients include early gestational age, low birth weight, complete absence of enteral (breast) nutrition, and early-course antibacterial therapy (prior to physiological gut colonization). The general patterns and interindividual variations in gut microbiome developmental dynamics represent an important step toward controlling disease risks in preterm infants.

THE GUT MICROBIOME AND ITS METABOLITES

Alterations in the gut microbiome can be evaluated not only through culture-based or genetic methods but also indirectly via metabolite levels in biological fluids. Bacterial metabolites and bioactive compounds can be detected in both stool and urine, serving as markers of intestinal microbiome homeostasis/imbalance. The presence of short-chain fatty acids (SCFAs) in urine or stool represents an indicator of intestinal health.

Persistent differences in global metabolic profiles of urine samples (1H-NMR) have been identified between critically ill ICU patients and healthy children, including reduced urinary excretion of hippurate, 4-cresol sulfate, and formate. These alterations reflect disparities in both endogenous metabolites and gut microbiome-derived metabolites [58]. The critically ill children exhibited distinct overall metabolic profiles, notably decreased fecal excretion of SCFAs (including butyrate, propionate, and acetate). Fecal butyrate levels correlated with the number of intensive care-free days at 30 days, while urinary formate was inversely correlated with the need for vasopressor support [58]. Thus, a direct relationship has been established between impaired functional activity of the gut microbiome and progressive organ failure in critically ill children, potentially increasing the risk of adverse outcomes.

Pediatric ICU patients receiving antibacterial therapy exhibit reduced anaerobic communities against a background of overall decreased gut microbiota α-diversity [35]. The loss of anaerobic microbiota directly correlates with overgrowth of aerobic pathobionts and their corresponding bacteriophages, along with absolute enrichment of opportunistic yeasts capable of causing invasive diseases. An elevated fungi-to-bacteria ratio is associated with marked SCFA depletion, demonstrating a strong correlation with propionate concentration ($p < 0.0001$) [35]. Consequently, critically ill patients undergoing antibacterial therapy show a significantly increased risk of opportunistic invasive mycoses, resulting not only from reduced gut microbiota biodiversity but also from functional alterations in remaining bacterial communities. Diminished SCFA production may yield long-term negative consequences, including contribution to dysphagia development in ICU patients [4, 11, 12].

In patients with diagnosed neuroinfections, SCFA analysis from fecal extracts revealed decreased *Bacteroidetes*, *Proteobacteria*, and *Bacilli*. These patients demonstrated positive correlation between cerebrospinal fluid-to-serum albumin ratio and α-diversity, but negative correlation with fecal butyrate concentration. Encephalitis patients exhibited increased fecal acetate, propionate, and butyrate concentrations [60]. These findings confirm a potential direct relationship between gut microbiome alteration severity and brain injury extent, thereby validating functional activity of the "gut-brain microbiota" axis [20].

Thus, the complexity of transcriptional changes following gut microbiome disruption has been demonstrated. Clinical profiling of bacterial metabolites in stool and urine samples could aid in the diagnosis and treatment of intestinal dysbiosis in critically ill patients. Utilizing anaerobic bacteria and SCFAs to suppress fungal overgrowth following antibacterial exposure may positively impact clinical outcomes in ICU patients.

CORRECTION OF MICROBIOME DISORDERS

Growing interest in microbial dysbiosis development during critical illness against the backdrop of evolving antibacterial strategies has prompted investigation into the therapeutic potential of microbiome modification using

probiotics [15]. Recommended therapeutic strategies for ICU patients with microbiota alterations include pro-, pre-, and synbiotics, along with fecal microbiota transplantation. Collectively, these interventions may not only maintain intestinal microbiota integrity but also restore homeostasis [3, 15, 41, 59, 63].

Administration of synbiotics (*Bifidobacterium breve* strain *Yakult, Lactobacillus casei* strain *Shirota*, and galactooligosaccharides) initiated within 3 days of admission in septic patients who were in the ICU and receiving mechanical ventilation led to reduced incidence of enteritis and VAP. However, no significant survival difference was observed between patients receiving synbiotics and controls. Thus, a positive association has been established between synbiotic administration and gut microbiota modulation, enteritis prevention, and VAP reduction in septic patients [54].

Eight studies have evaluated the effects of dietary fiber on gut microbiota status, ICU length of stay, and time to mortality in hemodynamically stable ICU patients receiving enteral nutrition via nasogastric tube who presented with gastrointestinal symptoms (abdominal distension, diarrhea, vomiting, constipation, and high gastric residual volume). Diarrhea and constipation occurred significantly less frequently in children receiving fiber supplementation [18, 49]. Soluble fiber administration in all hemodynamically stable critically ill patients was established as safe and beneficial for reducing gastrointestinal symptoms, particularly diarrhea [18, 49].

Of 15 conducted studies, 14 failed to demonstrate beneficial effects of pre-, pro-, or synbiotic administration on enteral nutrition tolerance or duration of hospital and ICU stay [52]. Opioid analgesic use may affect gastrointestinal motility disorder frequency in critically ill patients without exerting direct effects on the microbiome [28]. Further research is needed to determine the roles of gut dysfunction and microbiome alterations as markers of disease severity, critical illness duration, or mortality. Challenges in establishing potential relationships stem from the absence of standardized methods for identifying and quantifying disturbances in microbiome phylum ratios. The investigated biomarkers (intestinal fatty acid-binding protein, citrulline) show promise but require additional study [29].

Critical illness leads to impaired intestinal barrier function and affects the development and severity of multiple organ dysfunction. Patients with sepsis or acute respiratory distress syndrome demonstrate substantially disrupted gut microbiota composition, resulting in intestinal dysbiosis. Identification of potential strategies for the maintenance of normal microbiota is warranted, complemented by modern therapeutic approaches including pre-, pro-, and synbiotics, along with fecal microbiota transplantation [43].

Current evidence indicates that ICU patients exhibit marked alterations in the gastrointestinal microbiome, where prolonged hospitalization induces substantial microbial community shifts toward pathobiont dominance. Reduced gastrointestinal bacterial diversity in critically ill patients correlates with elevated risks of multiple organ dysfunction and nosocomial infection. Established risk factors for microbiome alterations in pediatric ICU patients include low gestational age, low birth weight, complete absence of enteral (breast) nutrition, and early-course antibacterial therapy. Depletion of *Firmicutes* and decreased *Firmicutes/Bacteroidetes* ratio hold the greatest clinical significance for mortality prediction. Comprehensive analysis of qualitative and quantitative GI microbiome alterations, combined with bacterial metabolite profiling, will facilitate timely diagnosis of nosocomial infections and treatment outcome prognostication in ICU patients. Gut microbiota restoration in critically ill patients should incorporate modern therapeutic modalities (pre-, pro-, synbiotics, fecal transplantation) while restricting early administration of anti-anaerobic antibacterial agents.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

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Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

REFERENCES

1. Aleksandrovich Yu.S., Ivanov D.O., Pavlovskaya E.Yu., Pshenisnov K.V., Savicheva A.M., Shalepo K.V., Akimenko T.I., Zemlyanoy D.A. Features of microbiota in newborns in critical condition at admission to the intensive care unit of a specialized hospital. *Messenger of Anesthesiology and Resuscitation*.. 2022;19(2):56–63. (In Russian). DOI: 10.21292/2078-5658-2022-19-2-56-63.
2. Ahmedov V.A., Kasheva K.A., Gaus O.V. Intestinal microbiota and critical conditions] *Medical alphabet*. 2020;(37):16-20. (In Russian). DOI: 10.33667/2078-5631-2020-37-16-20.

3. Beloborodova N.V., Chernevskaja E.A. Prospects for Microbiota-Oriented Therapy in Neurorehabilitology] *Physical and rehabilitation medicine, medical rehabilitation.* 2020;2(1):79–85. (In Russian). DOI: 10.36425/rehab19432.
4. Gostimskij A.V., Gavshchuk M.V., Zav'yalova A.N., Barsukova I.M., Najdenov A.A., Karpatskij I.V., Petrosyan A.A., Lisovskij O.V. Features of nutritional support and care for patients with gastrostoma. *Medicine: Theory and Practice*. 2018;3(2):3–10. (In Russian).
5. Zavyalova A.N., Novikova V.P., Ignatova P.D. Axis "microbiota — muscle". *Experimental and Clinical Gastroenterology*. 2022;207(11):60–69. (In Russian). DOI: 10.31146/1682-8658-ecg-207-11-60-69.
6. Zavyalova A.N., Novikova V.P., Kuznetsova Yu.V. et al. Atabase "Sequencing of 16SrRNK microbiome from three biotopes in a gastrostomized pediatric patient". Application № 2023620378 from 13.02.2023. Date of state registration in the Register of databases 22.03.2023. (In Russian).
7. Zavyalova A.N., Novikova V.P., Orel V.I. et al. Organization of the stomy patient nutrition. Choice of food substrate. *Pediatrician (St. Petersburg).* 2023;14(2):93–104. (In Russian). DOI: 10.17816/PED14293-104.
8. Kuznetsova Yu.V., Zavyalova A.N., Davletova L.A. et al. Oral microbiome in children fed through a gastrostomy. *Forcipe*. 2022;5(S2):285–286. (In Russian).
9. Kuznetsova Ju.V., Zavyalova A.N., Lisovskii O.V. et al. Oral microbiome in patients feeding through a gastrostomy. *Preventive and clinical medicine*. 2023;87(2):68–76. (In Russian). DOI: 10.47843/2074-9120_2023_2_68.
10. Kuznetsova Yu.V., Zavyalova A.N., Lisovskii O.V. et al. Features of the microbial landscape of the stomach in children, feeding through the gastrostomy or nasogastric tube. *Pediatrician (St. Petersburg).* 2023;14(2):17–27. (In Russian). DOI: 10.17816/PED14217-27.
11. Lisitsa I.A., Aleksandrovich Yu.S., Zavyalova A.N. et al. Dysphagia in pediatric intensive care unit patients (review). *Messenger of anesthesiology and resuscitation*. 2023;20(6):97–105. (In Russian). DOI: 10.24884/2078-5658-2023-20-6-97-105.
12. Lisica I.A., Zavyalova A.N., Ignatova P.D., Makarova T.Yu. Microbiome of patients in the intensive care unit. Literature review. *University Therapeutic Journal*. 2024;6(3):5–18. (In Russian). DOI: 10.56871/UTJ.2024.67.59.001.
13. Markovskaja I.N. Microbiome of a child of the first year of life, long-term stay in ORIT, according to 16S rRNA sequencing. Theses of the X All-Russian Conference with International Participation *"FLORES VITAE. Polyclinic Pediatrics"*. 2022:16–17. (In Russian).
14. Naboka Y.L., Rymashevskiy A.N., Svirava E.G., Vasilyeva L.I., Bragina L.Y., Chernitskaya M.L., Dzhalagoniya K.T. Development of microbiota in the large intestine of newborns depending on various delivery methods. *Pediatrician (St. Petersburg).* 2014;5(3):22–29. (In Russian). DOI: 10.17816/PED5322-29.
15. Novikova V.P., Gurova M.M., Havkin A.I. Intestinal microbiota as a regulator of the work of human organs and systems: a guide for doctors. Moscow: GEOTAR-Media; 2024. (In Russian). DOI: 10.33029/9704-8174-5-IMR-2024-1-352.
16. Novikova V.P., Havkin A.I., Gorelov A.V. et al. The lung-gut axis and COVID-19. *Infectious diseases*. 2021;19(1):91–96. (In Russian). DOI: 10.20953/1729-9225-2021-1-91-96.
17. Prokop'eva N.Je., Novikova V.P., Havkin A.I. Gut microbiota — kidney axis. features in diseases of the urinary system and urogenital tract. *Medicine: Theory and Practice*. 2022;7(4):68–77. (In Russian). DOI: 10.56871/MTP.2022.51.41.008.
18. Havkin A.I., Zavyalova A.N., Novikova V.P. Impact of nutrients on gut microbiota. *Pediatric Nutrition*. 2023;21(1):66–75. 2023. (In Russian). DOI: 10.20953/1727-5784-2023-1-66-75.
19. Chernevskaja E.A., Beloborodova N.V. Gut Microbiome in Critical Illness (Review). *General Reanimatology.* 2018;14(5):96–119. (In Russian). DOI: 10.15360/1813-9779-2018-5-96-119.
20. Shapovalova N.S., Novikova V.P. The role of the gut-brain axis in functional gastrointestinal disorders. *Children's Medicine of the North-West.* 2021;9(4):33–50. (In Russian).
21. Aardema H., Lisotto P., Kurilshikov A. et al. Marked changes in gut microbiota in cardio-surgical intensive care patients: a longitudinal cohort study. *Front Cell Infect Microbiol*. 2020;9:467. DOI: 10.3389/fcimb.2019.00467.
22. Akrami K., Sweeney D.A. The microbiome of the critically ill patient. *Curr Opin Crit Care*. 2018;24(1):49–54. DOI: 10.1097/MCC.0000000000000469.
23. Bansal S., Nguyen J.P., Leligdowicz A. et al. Rectal and naris swabs: practical and informative samples for analyzing the microbiota of critically ill patients. *mSphere*. 2018;3(3):e00219-18. DOI: 10.1128/mSphere.00219-18.
24. Bender J.M., Li F., Purswani H. et al. Early exposure to antibiotics in the neonatal intensive care unit alters the taxonomic and functional infant gut microbiome. *J Matern Fetal Neonatal Med*. 2021;34(20):3335–3343. DOI: 10.1080/14767058.2019.1684466.
25. Buelow E., Bello González T.D.J., Fuentes S. et al. Comparative gut microbiota and resistome profiling of intensive care patients receiving selective digestive tract decontamination and healthy subjects. *Microbiome*. 2017;5(1):88. DOI: 10.1186/s40168-017-0309-z.
26. Caldarelli M., Franza L., Rio P. et al. Gut-kidney-heart: a novel trilogy. *Biomedicines*. 2023;11(11):3063. DOI: 10.3390/biomedicines11113063.
27. Chanderraj R., Baker J.M., Kay S.G. et al. In critically ill patients, anti-anaerobic antibiotics increase risk of adverse clinical outcomes. *Eur Respir J*. 2023;61(2):2200910. DOI: 10.1183/13993003.00910-2022.
28. Chapple L.A., Deane A. From dysmotility to virulent pathogens: implications of opioid use in the ICU. *Curr Opin Crit Care*. 2018;24(2):118–123. DOI: 10.1097/MCC.0000000000000487.
29. Chapple L.S., Plummer M.P., Chapman M.J. Gut dysfunction in the ICU: diagnosis and management. *Curr Opin Crit Care*. 2021;27(2):141–146. DOI: 10.1097/MCC.0000000000000813.
30. D'Agata A.L., Wu J., Welandawe M.K.V. et al. Effects of early life NICU stress on the developing gut microbiome. *Dev Psychobiol*. 2019;61(5):650–660. DOI: 10.1002/dev.21826.

31. Dahlgren A.F., Pan A., Lam V. et al. Longitudinal changes in the gut microbiome of infants on total parenteral nutrition. *Pediatr Res.* 2019;86(1):107–114. DOI: 10.1038/s41390-019-0391-y.

32. Elfiky S.A., Mahmoud Ahmed S., Elmenshawy A.M. et al. Study of the gut microbiome as a novel target for prevention of hospital-associated infections in intensive care unit patients. *Acute Crit Care*. 2023;38(1):76–85. DOI: 10.4266/acc.2022.01116.

33. Fida M., Wolf M.J., Hamdi A. et al. Detection of pathogenic bacteria from septic patients using 16S ribosomal RNA gene-targeted metagenomic sequencing. *Clin Infect Dis*. 2021;73(7):1165–1172. DOI: 10.1093/cid/ciab349.

34. Freedberg D.E., Zhou M.J., Cohen M.E. et al. Pathogen colonization of the gastrointestinal microbiome at intensive care unit admission and risk for subsequent death or infection. *Intensive Care Med*. 2018;44(8):1203–1211. DOI: 10.1007/s00134-018-5268-8.

35. Haak B.W., Argelaguet R., Kinsella C.M. et al. Integrative Transkingdom analysis of the gut microbiome in antibiotic perturbation and critical illness. *mSystems*. 2021;6(2):e01148–20. DOI: 10.1128/mSystems.01148-20.

36. Howard B.M., Kornblith L.Z., Christie S.A. et al. Characterizing the gut microbiome in trauma: significant changes in microbial diversity occur early after severe injury. *Trauma Surg Acute Care Open*. 2017;2(1):e000108. DOI: 10.1136/tsaco-2017-000108.

37. Iapichino G., Callegari M.L., Marzorati S. et al. Impact of antibiotics on the gut microbiota of critically ill patients. *J Med Microbiol*. 2008;57(Pt 8):1007–1014. DOI: 10.1099/jmm.0.47387-0.

38. Kuznetsova Yu.V., Zavyalova A.N., Dudurich V.V. The microbiome of the stomach in children fed through a gastrostomy. World of Microbiome. Vienna: Kenes group; 2022: 104.

39. Lamoureux C., Surgers L., Fihman V. et al. Prospective comparison between shotgun metagenomics and sanger sequencing of the 16S rRNA gene for the etiological diagnosis of infections. *Front Microbiol*. 2022;13:761873. DOI: 10.3389/fmicb.2022.761873.

40. Lankelma J.M., van Vught L.A., Belzer C. et al. Critically ill patients demonstrate large interpersonal variation in intestinal microbiota dysregulation: a pilot study. *Intensive Care Med*. 2017;43(1):59–68. DOI: 10.1007/s00134-016-4613-z.

41. Limketkai B.N., Hendler S., Ting P.S. et al. Fecal microbiota transplantation for the critically ill patient. *Nutr Clin Pract*. 2019;34(1):73–79. DOI: 10.1002/ncp.10228.

42. Liu W., Cheng M., Li J. et al. Classification of the gut microbiota of patients in intensive care units during development of sepsis and septic shock. *Genomics Proteomics Bioinformatics*. 2020;18(6):696–707. DOI: 10.1016/j.gpb.2020.06.011.

43. McDonald D., Ackermann G., Khailova L. et al. Extreme dysbiosis of the microbiome in critical illness. *mSphere*. 2016;1(4):e00199-16. DOI: 10.1128/mSphere.00199-16.

44. Mustansir Dawoodbhoy F., Patel B.K., Patel K. et al. Gut microbiota dysbiosis as a target for improved post-surgical outcomes and improved patient care: a review of current literature. *Shock*. 2021;55(4):441–454. DOI: 10.1097/SHK.0000000000001654.

45. Ojima M., Motooka D., Shimizu K. et al. Metagenomic analysis reveals dynamic changes of whole gut microbiota in the acute phase of intensive care unit patients. *Dig Dis Sci*. 2016;61(6):1628–1634. DOI: 10.1007/s10620-015-4011-3.

46. Ojima M., Shimizu K., Motooka D. et al. Gut dysbiosis associated with antibiotics and disease severity and its relation to mortality in critically ill patients. *Dig Dis Sci*. 2022;67(6):2420–2432. DOI: 10.1007/s10620-021-07000-7.

47. Paul B. Concatenated 16S rRNA sequence analysis improves bacterial taxonomy. *F1000Res*. 2023;11:1530. DOI: 10.12688/f1000research.128320.3.

48. Ravi A., Halstead F.D., Bamford A. et al. Loss of microbial diversity and pathogen domination of the gut microbiota in critically ill patients. *Microb Genom*. 2019;5(9):e000293. DOI: 10.1099/mgen.0.000293.

49. Reis A.M.D., Fruchtenicht A.V., Loss S.H. et al. Use of dietary fibers in enteral nutrition of critically ill patients: a systematic review. *Rev Bras Ter Intensiva*. 2018;30(3):358–365. DOI: 10.5935/0103-507X.20180050.

50. Sachdev M., Ready D., Brealey D. et al. Changes in dental plaque following hospitalisation in a critical care unit: an observational study. *Crit Care*. 2013;17(5):R189. DOI: 10.1186/cc12878.

51. Sanschagrin S., Yergeau E. Next-generation sequencing of 16S ribosomal RNA gene amplicons. *J Vis Exp*. 2014;90:51709. DOI: 10.3791/51709.

52. Seifi N., Jafarzadeh Esfahani A., Sedaghat A. et al. Effect of gut microbiota modulation on feeding tolerance of enterally fed critically ill adult patients: a systematic review. *Syst Rev*. 2021;10(1):95. DOI: 10.1186/s13643-021-01633-5.

53. de Sire A., de Sire R., Curci C. et al. Role of dietary supplements and probiotics in modulating microbiota and bone health: the gut-bone axis. *Cells*. 2022;11(4):743. DOI: 10.3390/cells11040743.

54. Shimizu K., Yamada T., Ogura H. et al. Synbiotics modulate gut microbiota and reduce enteritis and ventilator-associated pneumonia in patients with sepsis: a randomized controlled trial. *Crit Care*. 2018;22(1):239. DOI: 10.1186/s13054-018-2167-x.

55. Tauchi H., Yahagi K., Yamauchi T. et al. Gut microbiota development of preterm infants hospitalised in intensive care units. *Benef Microbes*. 2019;10(6):641–651. DOI: 10.3920/BM2019.0003.

56. Watts G.S., Youens-Clark K., Slepian M.J. et al. 16S rRNA gene sequencing on a benchtop sequencer: accuracy for identification of clinically important bacteria. *J Appl Microbiol*. 2017;123(6):1584–1596. DOI: 10.1111/jam.13590.

57. Wei R., Chen X., Hu L. et al. Dysbiosis of intestinal microbiota in critically ill patients and risk of in-hospital mortality. *Am J Transl Res*. 2021;13(3):1548–1557.

58. Wijeyesekera A., Wagner J., De Goffau M. et al. Multi-compartment profiling of bacterial and host metabolites identifies intestinal dysbiosis and its functional consequences in the critically ill child. *Crit Care Med*. 2019;47(9):e727–e734. DOI: 10.1097/CCM.0000000000003841.

59. Wischmeyer P.E., McDonald D., Knight R. Role of the microbiome, probiotics, and 'dysbiosis therapy' in critical illness.

Curr Opin Crit Care. 2016;22(4):347–353. DOI: 10.1097/MCC.0000000000000321.

60. Xu R., Tan C., He Y. et al. Dysbiosis of gut microbiota and short-chain fatty acids in encephalitis: a chinese pilot study. *Front Immunol*. 2020;11:1994. DOI: 10.3389/fimmu.2020.01994.

61. Xu R., Tan C., Zhu J. et al. Dysbiosis of the intestinal microbiota in neurocritically ill patients and the risk for death. *Crit Care*. 2019;23(1):195. DOI: 10.1186/s13054-019-2488-4.

62. Yap P.S.X., Chong C.W., Ahmad Kamar A. et al. Neonatal intensive care unit (NICU) exposures exert a sustained influence on the progression of gut microbiota and metabolome in the first year of life. *Sci Rep*. 2021;11(1):1353. DOI: 10.1038/s41598-020-80278-1.

63. Zanza C., Romenskaya T., Thangathurai D. et al. Microbiome in critical illness: an unconventional and unknown ally. *Curr Med Chem*. 2021;29(18):3179–3188. DOI: 10.2174/0929867328666210915115056.

ЛИТЕРАТУРА

1. Александрович Ю.С., Иванов Д.О., Павловская Е.Ю. и др. Особенности микробиоты у новорожденных в критическом состоянии при поступлении в ОРИТ специализированного стационара. *Вестник анестезиологии и реаниматологии*. 2022;19(2):56–63. DOI: 10.21292/2078-5658-2022-19-2-56-63.

2. Ахмедов В.А., Кашева К.А., Гаус О.В. Микробиота кишечника и критические состояния. *Медицинский алфавит*. 2020;(37):16–20. DOI: 10.33667/2078-5631-2020-37-16-20.

3. Белобородова Н.В., Черневская Е.А. Перспективы микробиота-ориентированной терапии в нейрореабилитологии. *Физическая и реабилитационная медицина, медицинская реабилитация*. 2020;2(1):79–85. DOI: 10.36425/rehab19432.

4. Гостимский А.В., Гавщук М.В., Завьялова А.Н., Барсукова И.М., Найденов А.А., Карпатский И.В., Петросян А.А., Лисовский О.В. Особенности нутритивной поддержки и ухода за пациентами с гастростомой. *Медицина: теория и практика*. 2018;3(2):3–10.

5. Завьялова А.Н., Новикова В.П., Игнатова П.Д. Ось «микробиота–мышцы». *Экспериментальная и клиническая гастроэнтерология*. 2022;207(11):60–69. DOI: 10.31146/1682-8658-ecg-207-11-60-69.

6. Завьялова А.Н., Новикова В.П., Кузнецова Ю.В. и др. База данных «Секвенирование 16SrRNK микробиома из трех биотопов у гастростомированного пациента детского возраста». Заявка № 2023620378 от 13.02.2023. Дата государственной регистрации в Реестре баз данных 22.03.2023.

7. Завьялова А.Н., Новикова В.П., Орел В.И. и др. Организация питания стомированного пациента. Выбор пищевого субстрата. *Педиатр*. 2023;14(2);93–104. DOI: 10.17816/PED14293-104.

8. Кузнецова Ю.В., Завьялова А.Н., Давлетова Л.А. и др. Микробиом ротовой полости у детей, питающихся через гастростому. *Forcipe*. 2022;5(S2):285–286.

9. Кузнецова Ю.В., Завьялова А.Н., Лисовский О.В. и др. Микробиом ротовой полости у пациентов, питающихся через гастростому. *Профилактическая и клиническая медицина*. 2023;87(2):68–76. DOI: 10.47843/2074-9120_2023_2_68.

10. Кузнецова Ю.В., Завьялова А.Н., Лисовский О.В. и др. Особенности микробного пейзажа желудка у детей, питающихся через гастростому или назогастральный зонд. *Педиатр*. 2023;14(2):17–27. DOI: 10.17816/PED14217-27.

11. Лисица И.А., Александрович Ю.С., Завьялова А.Н. и др. Дисфагия у пациентов педиатрических отделений реанимации и интенсивной терапии (обзор литературы). *Вестник анестезиологии и реаниматологии*. 2023;20(6):97–105. DOI: 10.24884/2078-5658-2022-20-6-97-105.

12. Лисица И.А., Завьялова А.Н., Игнатова П.Д., Макарова Т.Ю. Микробиом пациентов в отделении реанимации и интенсивной терапии. Обзор литературы. *Университетский терапевтический вестник*. 2024;6(3):5–18. DOI: 10.56871/UTJ.2024.67.59.001

13. Марковская И.Н. Микробиом ребенка первого года жизни, длительно находящегося в условиях ОРИТ, по данным секвенирования 16S rRNA. Тезисы X общеросс. конф. с междунар. участием «FLORES VITAE. Поликлиническая педиатрия». 2022:16–17.

14. Набока Ю.Л., Рымашевский А.Н., Свирава Э.Г. и др. Становление микробиоты толстого кишечника новорожденных при различных способах родоразрешения. *Педиатр*. 2014;5(3):22–29. DOI: 10.17816/PED5322-29.

15. Новикова В.П., Гурова М.М., Хавкин А.И. Кишечная микробиота как регулятор работы органов и систем человека. М.: ГЭОТАР-Медиа; 2024. DOI: 10.33029/9704-8174-5-IMR-2024-1-352.

16. Новикова В.П., Хавкин А.И., Горелов А.В. и др. Ось «легкие–кишечник» и COVID- инфекция. *Инфекционные болезни*. 2021;19(1):91–96. DOI: 10.20953/1729-9225-2021-1-91-96.

17. Прокопьева Н.Э., Новикова В.П., Хавкин А.И. Ось «кишечная микробиота–почки». Особенности при заболеваниях мочевыделительной системы и урогенитального тракта. *Медицина: теория и практика*. 2022;7(4):68–77. DOI: 10.56871/MTP.2022.51.41.008.

18. Хавкин А.И., Завьялова А.Н., Новикова В.П. Влияние нутриентов на микробиоту кишечника. *Вопросы детской диетологии*. 2023;21(1):66–75. DOI: 10.20953/1727-5784-2023-1-66-75.

19. Черневская Е.А., Белобородова Н.В. Микробиота кишечника при критических состояниях (обзор). *Общая реаниматология*. 2018;14(5):96–119. DOI: 10.15360/1813-9779-2018-5-96-119.

20. Шаповалова Н.С., Новикова В.П. Ось «кишечник–мозг» и ее роль в развитии функциональных гастроинтестинальных расстройств. *Children's Medicine of the North-West*. 2021;9(4):33–51.

21. Aardema H., Lisotto P., Kurilshikov A. et al. Marked changes in gut microbiota in cardio-surgical intensive care patients: a longitudinal cohort study. *Front. Cell. Infect. Microbiol*. 2020;9:467. DOI: 10.3389/fcimb.2019.00467.

22. Akrami K., Sweeney D.A. The microbiome of the critically ill patient. *Curr. Opin. Crit. Care*. 2018;24(1):49–54. DOI: 10.1097/MCC.0000000000000469.

23. Bansal S., Nguyen J.P., Leligdowicz A. et al. Rectal and naris swabs: practical and informative samples for analyzing the microbiota of critically ill patients. *mSphere*. 2018;3(3):e00219-18. DOI: 10.1128/mSphere.00219-18.

24. Bender J.M., Li F., Purswani H. et al. Early exposure to antibiotics in the neonatal intensive care unit alters the taxonomic and functional infant gut microbiome. *J Matern Fetal Neonatal Med*. 2021;34(20):3335–3343. DOI: 10.1080/14767058.2019.1684466.

25. Buelow E., Bello González T.D.J., Fuentes S. et al. Comparative gut microbiota and resistome profiling of intensive care patients receiving selective digestive tract decontamination and healthy subjects. *Microbiome*. 2017;5(1):88. DOI: 10.1186/s40168-017-0309-z.

26. Caldarelli M., Franza L., Rio P. et al. Gut-kidney-heart: a novel trilogy. *Biomedicines*. 2023;11(11):3063. DOI: 10.3390/biomedicines11113063.

27. Chanderraj R., Baker J.M., Kay S.G. et al. In critically ill patients, anti-anaerobic antibiotics increase risk of adverse clinical outcomes. *Eur Respir J*. 2023;61(2):2200910. DOI: 10.1183/13993003.00910-2022.

28. Chapple L.A., Deane A. From dysmotility to virulent pathogens: implications of opioid use in the ICU. *Curr Opin Crit Care*. 2018;24(2):118–123. DOI: 10.1097/MCC.0000000000000487.

29. Chapple L.S., Plummer M.P., Chapman M.J. Gut dysfunction in the ICU: diagnosis and management. *Curr Opin Crit Care*. 2021;27(2):141–146. DOI: 10.1097/MCC.0000000000000813.

30. D'Agata A.L., Wu J., Welandawe M.K.V. et al. Effects of early life NICU stress on the developing gut microbiome. *Dev Psychobiol*. 2019;61(5):650–660. DOI: 10.1002/dev.21826.

31. Dahlgren A.F., Pan A., Lam V. et al. Longitudinal changes in the gut microbiome of infants on total parenteral nutrition. *Pediatr Res*. 2019;86(1):107–114. DOI: 10.1038/s41390-019-0391-y.

32. Elfiky S.A., Mahmoud Ahmed S., Elmenshawy A.M. et al. Study of the gut microbiome as a novel target for prevention of hospital-associated infections in intensive care unit patients. *Acute Crit Care*. 2023;38(1):76–85. DOI: 10.4266/acc.2022.01116.

33. Fida M., Wolf M.J., Hamdi A. et al. Detection of pathogenic bacteria from septic patients using 16S ribosomal RNA gene-targeted metagenomic sequencing. *Clin Infect Dis*. 2021;73(7):1165–1172. DOI: 10.1093/cid/ciab349.

34. Freedberg D.E., Zhou M.J., Cohen M.E. et al. Pathogen colonization of the gastrointestinal microbiome at intensive care unit admission and risk for subsequent death or infection. *Intensive Care Med*. 2018;44(8):1203–1211. DOI: 10.1007/s00134-018-5268-8.

35. Haak B.W., Argelaguet R., Kinsella C.M. et al. Integrative Transkingdom analysis of the gut microbiome in antibiotic perturbation and critical illness. *mSystems*. 2021;6(2):e01148–20. DOI: 10.1128/mSystems.01148-20.

36. Howard B.M., Kornblith L.Z., Christie S.A. et al. Characterizing the gut microbiome in trauma: significant changes in microbial diversity occur early after severe injury. *Trauma Surg Acute Care Open*. 2017;2(1):e000108. DOI: 10.1136/tsaco-2017-000108.

37. Iapichino G., Callegari M.L., Marzorati S. et al. Impact of antibiotics on the gut microbiota of critically ill patients. *J Med Microbiol*. 2008;57(Pt 8):1007–1014. DOI: 10.1099/jmm.0.47387-0.

38. Kuznetsova Yu.V., Zavyalova A.N., Dudurich V.V. The microbiome of the stomach in children fed through a gastrostomy. World of Microbiome. Vienna: Kenes group; 2022: 104.

39. Lamoureux C., Surgers L., Fihman V. et al. Prospective comparison between shotgun metagenomics and sanger sequencing of the 16S rRNA gene for the etiological diagnosis of infections. *Front Microbiol*. 2022;13:761873. DOI: 10.3389/fmicb.2022.761873.

40. Lankelma J.M., van Vught L.A., Belzer C. et al. Critically ill patients demonstrate large interpersonal variation in intestinal microbiota dysregulation: a pilot study. *Intensive Care Med*. 2017;43(1):59-68. DOI: 10.1007/s00134-016-4613-z.

41. Limketkai B.N., Hendler S., Ting P.S. et al. Fecal microbiota transplantation for the critically ill patient. *Nutr Clin Pract*. 2019;34(1):73–79. DOI: 10.1002/ncp.10228.

42. Liu W., Cheng M., Li J. et al. Classification of the gut microbiota of patients in intensive care units during development of sepsis and septic shock. *Genomics Proteomics Bioinformatics*. 2020;18(6):696–707. DOI: 10.1016/j.gpb.2020.06.011.

43. McDonald D., Ackermann G., Khailova L. et al. Extreme dysbiosis of the microbiome in critical illness. *mSphere*. 2016;1(4):e00199-16. DOI: 10.1128/mSphere.00199-16.

44. Mustansir Dawoodbhoy F., Patel B.K., Patel K. et al. Gut microbiota dysbiosis as a target for improved post-surgical outcomes and improved patient care: a review of current literature. *Shock*. 2021;55(4):441–454. DOI: 10.1097/SHK.0000000000001654.

45. Ojima M., Motooka D., Shimizu K. et al. Metagenomic analysis reveals dynamic changes of whole gut microbiota in the acute phase of intensive care unit patients. *Dig Dis Sci*. 2016;61(6):1628–1634. DOI: 10.1007/s10620-015-4011-3.

46. Ojima M., Shimizu K., Motooka D. et al. Gut dysbiosis associated with antibiotics and disease severity and its relation to mortality in critically ill patients. *Dig Dis Sci*. 2022;67(6):2420–2432. DOI: 10.1007/s10620-021-07000-7.

47. Paul B. Concatenated 16S rRNA sequence analysis improves bacterial taxonomy. *F1000Res*. 2023;11:1530. DOI: 10.12688/f1000research.128320.3.

48. Ravi A., Halstead F.D., Bamford A. et al. Loss of microbial diversity and pathogen domination of the gut microbiota in critically ill patients. *Microb Genom*. 2019;5(9):e000293. DOI: 10.1099/mgen.0.000293.

49. Reis A.M.D., Fruchtenicht A.V., Loss S.H. et al. Use of dietary fibers in enteral nutrition of critically ill patients: a systematic review. *Rev Bras Ter Intensiva*. 2018;30(3):358–365. DOI: 10.5935/0103-507X.20180050.

50. Sachdev M., Ready D., Brealey D. et al. Changes in dental plaque following hospitalisation in a critical care unit: an observational study. *Crit Care*. 2013;17(5):R189. DOI: 10.1186/cc12878.

51. Sanschagrin S., Yergeau E. Next-generation sequencing of 16S ribosomal RNA gene amplicons. *J Vis Exp*. 2014;90:51709. DOI: 10.3791/51709.

52. Seifi N., Jafarzadeh Esfahani A., Sedaghat A. et al. Effect of gut microbiota modulation on feeding tolerance of enterally fed critically ill adult patients: a systematic review. *Syst Rev*. 2021;10(1):95. DOI: 10.1186/s13643-021-01633-5.
53. de Sire A., de Sire R., Curci C. et al. Role of dietary supplements and probiotics in modulating microbiota and bone health: the gut-bone axis. *Cells*. 2022;11(4):743. DOI: 10.3390/cells11040743.
54. Shimizu K., Yamada T., Ogura H. et al. Synbiotics modulate gut microbiota and reduce enteritis and ventilator-associated pneumonia in patients with sepsis: a randomized controlled trial. *Crit Care*. 2018;22(1):239. DOI: 10.1186/s13054-018-2167-x.
55. Tauchi H., Yahagi K., Yamauchi T. et al. Gut microbiota development of preterm infants hospitalised in intensive care units. *Benef Microbes*. 2019;10(6):641–651. DOI: 10.3920/BM2019.0003.
56. Watts G.S., Youens-Clark K., Slepian M.J. et al. 16S rRNA gene sequencing on a benchtop sequencer: accuracy for identification of clinically important bacteria. *J Appl Microbiol*. 2017;123(6):1584–1596. DOI: 10.1111/jam.13590.
57. Wei R., Chen X., Hu L. et al. Dysbiosis of intestinal microbiota in critically ill patients and risk of in-hospital mortality. *Am J Transl Res*. 2021;13(3):1548–1557.
58. Wijeyesekera A., Wagner J., De Goffau M. et al. Multi-compartment profiling of bacterial and host metabolites identifies intestinal dysbiosis and its functional consequences in the critically ill child. *Crit Care Med*. 2019;47(9):e727–e734. DOI: 10.1097/CCM.0000000000003841.
59. Wischmeyer P.E., McDonald D., Knight R. Role of the microbiome, probiotics, and 'dysbiosis therapy' in critical illness. *Curr Opin Crit Care*. 2016;22(4):347–353. DOI: 10.1097/MCC.0000000000000321.
60. Xu R., Tan C., He Y. et al. Dysbiosis of gut microbiota and short-chain fatty acids in encephalitis: a chinese pilot study. *Front Immunol*. 2020;11:1994. DOI: 10.3389/fimmu.2020.01994.
61. Xu R., Tan C., Zhu J. et al. Dysbiosis of the intestinal microbiota in neurocritically ill patients and the risk for death. *Crit Care*. 2019;23(1):195. DOI: 10.1186/s13054-019-2488-4.
62. Yap P.S.X., Chong C.W., Ahmad Kamar A. et al. Neonatal intensive care unit (NICU) exposures exert a sustained influence on the progression of gut microbiota and metabolome in the first year of life. *Sci Rep*. 2021;11(1):1353. DOI: 10.1038/s41598-020-80278-1.
63. Zanza C., Romenskaya T., Thangathurai D. et al. Microbiome in critical illness: an unconventional and unknown ally. *Curr Med Chem*. 2021;29(18):3179–3188. DOI: 10.2174/0929867328666210915115056.

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