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SUPPLEMENT

# The role of microbiome and metabolomics in personalized ICU nutrition

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## Abstract

### Introduction

Emerging research highlights the essential influence of the gut microbiome and metabolic profiling in managing critically ill patients. In contemporary intensive care units, nutritional support transcends traditional caloric and protein matching; it demands a responsive, multifactorial approach that acknowledges microbial ecology and dynamic metabolic states. These scientific advancements hold promise for redefining nutritional protocols and enhancing patient outcomes in critical care.

The gut microbiome, often termed "the forgotten organ," significantly impacts immune function, energy metabolism, and mucosal health. Similarly, metabolomics—the study of small molecular byproducts of cellular processes—provides real-time insight into patient physiology. Combined, these tools are propelling a revolution in personalized nutritional interventions in the ICU.

### Dysbiosis in Critical Illness

Critical illnesses disrupt numerous physiological systems, including the gut microbiota. In stable health, the intestinal microbiota maintains homeostasis, but this balance is severely compromised in ICU patients due to systemic inflammation, medication exposure, nutritional deprivation, and physiological stress.

Common features of ICU-associated dysbiosis include diminished microbial diversity, depletion of beneficial organisms such as Lactobacillus and Bifidobacterium, and overgrowth of opportunistic pathogens. These alterations contribute to impaired nutrient absorption, compromised gut barrier function, and heightened systemic inflammation. Consequently, dysbiosis exacerbates the progression to organ dysfunction and sepsis.

Addressing gut microbiota health is thus increasingly recognized as a critical component of comprehensive ICU care, particularly through nutritional strategies aimed at mitigating dysbiosis-induced complications.

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**Metabolomics: Mapping the Biochemical Landscape**

Metabolomics provides clinicians with a snapshot of the metabolic environment within critically ill Specific metabolomic signatures, such as elevated lactate or altered branched-chain amino acid levels, indicate underlying issues like tissue hypoxia or Utilizing metabolomic profiles, healthcare providers can tailor nutrition plans that address identified metabolic deficiencies, thereby promoting more efficient recovery and reducing the risk of metabolic complications.

**Microbiome-Metabolome Interactions**

There is a dynamic relationship between gut microbes and host metabolism. Gut bacteria ferment dietary substrates, generating metabolites such as short-chain fatty acids (SCFAs) that play key roles in modulating inflammation and supporting epithelial health.

Conversely, host factors—including bile acids and immune mediators—influence the composition and function of the microbiota. In critically ill patients, disruptions to this bidirectional interaction impair nutrient utilization, compromise gut integrity, and enhance systemic inflammatory responses.

Metabolomics enables the detection of these disruptions by identifying changes in concentrations of microbial

metabolites, offering targets for nutritional and therapeutic interventions aimed at restoring homeostasis.

**Nutritional Strategies Based on Microbiome and Metabolomics**

Personalizing nutrition in the ICU can benefit from interventions informed by microbiome and metabolomic data:

1. Prebiotics and Fibers: Supplementation with fermentable fibers supports beneficial bacteria, fostering SCFA production and promoting gut barrier resilience.
2. Probiotics: Administering selected strains may enhance immune regulation, reduce infection rates, and support gut homeostasis, though careful patient selection is vital.
3. Postbiotics: Delivering microbial metabolites directly offers a promising strategy for modulating host responses without introducing live organisms.
4. Amino Acid Supplementation: Adjusting amino acid delivery based on observed metabolic needs, particularly concerning

patients. Analyzing biological fluids allows for the identification of disruptions in pathways related to energy production, protein turnover, and immune response.

accelerated muscle breakdown. Variations in the tryptophan-kynurenine axis, for instance, reveal shifts in immune system activation and tolerance.

pathways like the kynurenine-tryptophan axis, may optimize immune and metabolic balance.

5. Tailored Macronutrient Formulations: Real-time metabolic data can guide adjustments to energy, carbohydrate, and lipid provision, minimizing risks associated with metabolic instability.

**Clinical Applications**

Examples of personalized interventions based on these insights include:

1. Sepsis Management: Supporting gut barrier function with fibers and SCFA supplementation, while moderating glucose loads to avoid immune suppression.
2. Acute Respiratory Distress Syndrome (ARDS): Providing anti-inflammatory nutrients and high-protein support to preserve lean body mass and pulmonary function.
3. Renal Dysfunction: Modulating protein intake and enhancing fiber delivery to mitigate toxin accumulation and support gut-derived nitrogen disposal.

**Challenges and Future Directions**

The integration of microbiome and metabolomic information into ICU nutrition faces several challenges:

1. Technical Limitations: High-throughput sequencing and mass spectrometry require specialized resources and expertise.
2. Lack of Standardization: Variability in methodologies complicates data comparison and generalization.
3. Need for Validation: Large-scale, multicenter trials are necessary to establish the clinical efficacy of these personalized approaches.
4. Economic Considerations: Ensuring cost-effective and accessible technologies is vital for widespread adoption. Future prospects include developing artificial intelligence platforms that synthesize multi-omic data to generate actionable nutrition plans and integrating point-of-care testing into ICU workflows.

**Conclusion**
Personalized ICU nutrition based on microbiome integrity and metabolic profiling represents a significant advancement in critical care. Recognizing the interconnectedness of microbial health, systemic metabolism, and nutritional needs allows for more nuanced and effective therapeutic strategies. As technologies advance and become more accessible, incorporating microbiome and metabolomic analyses into everyday ICU practice has the potential to transform patient outcomes, shifting the paradigm toward truly individualized metabolic support and recovery.

**Keywords :** critical care nutrition, dysbiosis, gut microbiome, metabolomics, personalized nutrition

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