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ORIGINAL RESEARCH

Gut Microbiome and Short-Chain Fatty Acid Alterations After Cardiopulmonary Bypass are Associated with Nutritional and Functional Impairment in Young Children with Congenital Heart Defects

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Background: Cardiac surgery with cardiopulmonary bypass (CPB) in young children is associated with systemic stress, gastrointestinal dysfunction, and impaired nutritional recovery. The role of gut microbiome disruption and short-chain fatty acid (SCFA) metabolism in these processes remains insufficiently studied.

Objective: To evaluate changes in gut microbiome composition, SCFA profiles, and nutritional status in children aged 0–3 years after CPB, and to assess their association with postoperative feeding intolerance and impaired growth.

Methods: This prospective observational study included 20 children undergoing cardiac surgery with CPB. Stool samples were collected preoperatively and during the early postoperative period. Microbiota composition was assessed using culture-based microbiological methods, and fecal SCFA concentrations were measured by gas chromatography. Clinical, anthropometric, and laboratory parameters were assessed, and their associations with CPB characteristics and microbiome alterations were analyzed.

Results: The postoperative period was characterized by significant intestinal dysbiosis, including reduced abundance of beneficial bacteria (Bifidobacterium, Lactobacillus, Bacteroides) and decreased SCFA-producing taxa. Fecal butyrate and propionate levels were significantly reduced. These changes were associated with increased intestinal inflammation, feeding intolerance, impaired nutrient absorption, and insufficient weight gain. The severity of dysbiosis correlated with CPB duration.

Conclusion: CPB in early childhood is associated with disruption of gut microbiota and reduced SCFA production, which are linked to postoperative feeding intolerance and impaired nutritional recovery. Targeted monitoring and modulation of the gut microbiome may improve clinical outcomes in pediatric cardiac surgery patients.

Keywords: congenital heart defects, cardiopulmonary bypass, gut microbiome, short-chain fatty acids, feeding intolerance, nutritional status, early childhood, intestinal dysbiosis, microbial metabolism

Introduction

Congenital heart defects (CHD) remain one of the leading causes of morbidity and mortality in early childhood and frequently require surgical correction within the first months of life.[1–3] Despite substantial advances in pediatric cardiac surgery, anesthesiology, and intensive care, the early postoperative period in young children continues to be associated with a high incidence of metabolic, nutritional, and functional complications.[2] A critical factor influencing postoperative outcomes is the use of cardiopulmonary bypass (CPB), which, while enabling definitive surgical correction, also triggers systemic inflammatory responses, ischemia–reperfusion injury, and disturbances in microcirculation.[4]

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Under conditions of surgical stress, the gastrointestinal tract represents one of the most vulnerable target organs of systemic inflammation. Impaired intestinal perfusion, hypoxia, exposure to perioperative medications, and alterations in enteral feeding during the postoperative period contribute to destabilization of the intestinal microbiome and a reduction in its metabolic capacity.[5,6] In recent years, the gut microbiome has been increasingly recognized not only as a component of digestive function but also as a key regulator of immune homeostasis, metabolic processes, and intestinal barrier integrity—particularly in early childhood, when the microbiota is still developing and highly susceptible to external influences. A central indicator of intestinal microbial function is the production of short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate. These metabolites play a pivotal role in maintaining energy balance, supporting enterocyte nutrition, preserving epithelial barrier integrity, and modulating immune responses. Reduced SCFA availability has been associated with increased intestinal permeability, disruption of barrier function, bacterial translocation, and amplification of systemic inflammation, all of which may adversely affect recovery during the early postoperative phase.[7,8]

These mechanisms are of particular clinical relevance in infants and young children, for whom adequate nutritional status is directly linked to physical growth, neurodevelopment, adaptive capacity, and immune competence. Postoperative feeding intolerance, insufficient weight gain, loss of muscle and fat mass, and delays in motor development remain common yet often underestimated complications following cardiac surgery for CHD.[9,10] Although growing evidence highlights the importance of the gut microbiome in cardiovascular and surgical outcomes, data regarding its composition and metabolic activity in young children during the early postoperative period after cardiac surgery remain limited. The interactions between cardiopulmonary bypass, microbiome alterations, and SCFA changes remain insufficiently characterized. This knowledge gap underscores the need for comprehensive investigations aimed at elucidating the pathophysiological mechanisms of postoperative intestinal dysfunction and identifying potential therapeutic targets to optimize nutritional strategies and modulate the gut microbiome.[2,3,11–14] Therefore, investigation of the intestinal microbiome and its metabolic activity represents a clinically important and promising area of research in pediatric cardiac surgery.[15,16] Despite growing evidence on the role of the gut microbiome in surgical and cardiovascular outcomes, data on microbiome composition and SCFA metabolism in young children after cardiopulmonary bypass remain limited. This highlights the clinical importance of investigating microbiome-related mechanisms to improve postoperative nutritional recovery.

The aim of this study was to evaluate gut microbiome composition, short-chain fatty acid (SCFA) profiles, and nutritional status in children aged 0–3 years after cardiopulmonary bypass, and to assess their association with post-operative feeding intolerance and impaired growth.

Materials and Methods

Study Design and Participants

This was an exploratory prospective observational study. The sample size reflected the total number of eligible children undergoing cardiac surgery with cardiopulmonary bypass (CPB) during the defined recruitment period at a single regional center. Therefore, no formal a prior sample size calculation was performed.

The study was conducted between August and October 2025 and included children aged 0–3 years who underwent cardiac surgery with CPB. It was performed at the Specialized Scientific and Practical Medical Center of Cardiology and Cardiac Surgery of the Aral Sea region in the pediatric intensive care unit.

The study population comprised 20 children with congenital heart defects (CHD). The main group included 12 children who underwent cardiac surgery with CPB, while the control group consisted of 8 children with CHD assessed prior to surgical intervention. The groups were comparable in terms of age and sex distribution, with a mean age of 15.6 ± 12.9 months.

The control group consisted of children with CHD rather than healthy individuals. This approach was chosen to provide a clinically comparable population; however, potential baseline differences in gut microbiome composition cannot be excluded.

For age-specific analyses, the main group was stratified into three subgroups: subgroup A (0–6 months), subgroup B (6–12 months), and subgroup C (1–3 years).

Children with acute infectious diseases, severe concomitant somatic conditions, or those requiring prolonged preoperative antibiotic therapy were excluded. The study protocol complied with institutional ethical standards, and written informed consent was obtained from the parents or legal guardians of all participants prior to inclusion.

Ethical Considerations

The study was approved by the Ethics Committee of the Ministry of Health of the Republic of Uzbekistan under protocol no. 6/15-2107, dated 27 May 2025, and was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and applicable national regulations of the Republic of Uzbekistan.

Clinical Research

Parents or legal guardians received detailed information about the study both orally and in writing from the study physicians and nursing staff. Written and dated informed consent was obtained from the parents or legal guardians of all participating children prior to enrollment and before any study-related procedures, including blood and stool sampling.

Microbiome and Short-Chain Fatty Acid Analysis

Stool samples were collected from all participants before surgery (control group and preoperative sampling) and during the early postoperative period in the CPB group. Biological material was obtained using sterile stool collection devices with rectal cannulas, immediately frozen and stored at −22 °C according to the standard protocol of the certified laboratory, which is considered acceptable for short-term preservation prior to microbiological and SCFA analysis. Samples were transported under controlled conditions to the certified private laboratory "Genscreen" (Uzbekistan), where all microbiological and SCFA analyses were performed. Intestinal microbiota composition was assessed using culture-based microbiological methods with quantitative evaluation of key commensal and opportunistic taxa. Although this approach allows assessment of clinically relevant bacterial groups, it provides lower taxonomic resolution compared with 16S rRNA gene sequencing or metagenomic approaches. This limitation was considered when interpreting the findings.

The intestinal dysbiosis (ID) index was calculated based on quantitative deviations of key microbial taxa from age-specific reference values using standard microbiological criteria.

Fecal concentrations of short-chain fatty acids (SCFAs), including acetic, propionic, and butyric acids, were determined by gas chromatography using a Chromos GH-1000 system (Chromos, Moscow, Russia). SCFA profiles were used as indicators of microbial metabolic activity.

Potential confounding factors, including antibiotic exposure, feeding regimens, and perioperative management, were not fully controlled due to the exploratory design of the study and were considered when interpreting the results.

Clinical and Nutritional Assessment

Clinical and nutritional assessments were performed during the early postoperative period (1–5 days after surgery). Anthropometric measurements included body weight, length/height, body mass index (BMI), and body circumferences. Nutritional status was evaluated using BMI-for-age z-scores in accordance with the World Health Organization (WHO) Growth Standards for children under five years of age and established principles of malnutrition screening and assessment.[17] A BMI z-score < -2 was classified as underweight, and < -3 as severe undernutrition. In infants and young children, body weight below 90% of the age- and height-specific median was considered insufficient.

Laboratory evaluation included routine blood, urine, and stool analyses.[18] Blood tests assessed total protein, albumin, hemoglobin, iron parameters, and electrolyte balance. Urinalysis was used to evaluate hydration status and renal function. Stool examination was performed to identify signs of malabsorption, including steatorrhea, and to support microbiological assessment.

Functional status was assessed using standardized clinical observation, including feeding tolerance, gastrointestinal symptoms, urine output, and general activity level. Instrumental investigations (echocardiography, electrocardiography, and chest imaging) were performed as part of routine postoperative monitoring to assess cardiac and pulmonary status.

Outcomes

Primary outcomes

The primary outcomes were: alterations in intestinal microbiome composition during the early postoperative period after CPB; changes in fecal SCFA concentrations as markers of microbial metabolic activity.

Secondary Outcomes

Secondary outcomes included: the association between microbiome dysbiosis and postoperative feeding intolerance; indicators of impaired nutritional status, including insufficient weight gain, reduced BMI-for-age z-scores, and laboratory markers of protein and micronutrient deficiency; correlations between CPB parameters (duration and intensity) and the severity of intestinal dysbiosis and SCFA depletion.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 30.0 (IBM Corp., Armonk, NY, USA).[19] Data distribution was assessed using the Shapiro–Wilk test. Normally distributed variables are presented as mean ± SD and were compared using the Student's *t*-test. Non-normally distributed variables are presented as median (IQR) and were compared using the Mann–Whitney *U*-test.

For comparisons across more than two age-based subgroups, one-way ANOVA (for normally distributed data) or the Kruskal–Wallis test (for non-normal data) with Dunn's post-hoc testing was applied.[19,20] Paired preoperative–postoperative comparisons were analyzed using the paired *t*-test or Wilcoxon signed-rank test, as appropriate. Categorical variables were compared using Fisher's exact test.

Associations between CPB parameters, microbiome indices, SCFA concentrations, and clinical outcomes were evaluated using Spearman's rank correlation coefficient (ρ).[21] Relative risk (RR) with 95% confidence intervals (CI) was calculated for binary outcomes.

A two-sided p-value < 0.05 was considered statistically significant. Where multiple comparisons were performed, p-values were adjusted using the Benjamini–Hochberg false discovery rate (FDR) method.

Given the exploratory nature and small sample size of the study, the statistical analyses were interpreted cautiously. The results were considered hypothesis-generating, and associations were not interpreted as evidence of causality. These considerations were taken into account when interpreting the results.

Results

Study Population and Subgroup Stratification

Children undergoing cardiac surgery with cardiopulmonary bypass (CPB) were stratified into three age-based subgroups: subgroup A (0–6 months), subgroup B (6–12 months), and subgroup C (1–3 years). A control group included children with congenital heart defects prior to surgical intervention. Groups were comparable in age and sex distribution, with no significant differences observed ($p > 0.05$).

Intestinal Microbiome Alterations and Dysbiosis

Compared with preoperative controls, children in the early postoperative period after CPB showed a significant reduction in beneficial commensal taxa, including Bifidobacterium, Lactobacillus, and Bacteroides (FDR-adjusted $p < 0.05$).

A relative increase in opportunistic microorganisms, including Enterobacteriaceae and Clostridium spp., was also observed (FDR-adjusted $p < 0.05$).

The severity of dysbiosis, expressed as the intestinal dysbiosis (ID) index, showed a moderate positive correlation with CPB duration ($\rho = 0.42$, $p = 0.038$). Dysbiosis severity reflects the degree of deviation from age-specific reference microbiota composition.

These findings indicate alterations in selected culturable bacterial taxa and should be interpreted within the limitations of culture-based microbiological methods.

SCFA Profiles and Metabolic Activity

Butyric and propionic acid concentrations were significantly lower in postoperative children compared with controls ($p = 0.012$ and $p = 0.018$, respectively).

Acetic acid concentrations differed significantly across study groups ($p < 0.001$), with higher levels observed in postoperative subgroups. Acetate levels increased progressively across postoperative age strata.

Reduced fecal butyrate and propionate concentrations were moderately associated with higher dysbiosis index values ($\rho = 0.38–0.42$, $p < 0.05$).

Markers of Intestinal Barrier Function and Inflammation

Circulating markers of intestinal barrier dysfunction were significantly higher in postoperative children compared with controls (claudin-2: $p = 0.031$; claudin-3: $p = 0.008$; I-FABP: $p = 0.006$).

Fecal calprotectin concentrations were also elevated in postoperative children and differed significantly across age-based subgroups ($p = 0.041$).

Nutritional and Functional Outcomes

Children undergoing CPB demonstrated impaired nutritional recovery during the early postoperative period, including reduced weight gain velocity and biochemical indicators of protein deficiency.

Postoperative feeding intolerance was significantly associated with severe dysbiosis ($p = 0.022$). The relative risk of feeding intolerance in children with SCFA depletion was 2.1 (95% CI: 1.1–4.0).

Reduced fecal butyrate concentrations were moderately associated with lower weight gain velocity ($\rho = 0.39$, $p = 0.044$) and reduced serum albumin levels ($\rho = 0.41$, $p = 0.036$).

Decreased abundance of SCFA-producing taxa, including Bifidobacterium spp. and Bacteroides spp., was also associated with feeding intolerance (FDR-adjusted $p < 0.05$).

These findings indicate an association between microbial metabolic alterations and impaired postoperative nutritional recovery. Given the small sample size, these findings should be interpreted with caution and considered exploratory.

Discussion

This prospective exploratory study suggests that cardiac surgery with cardiopulmonary bypass (CPB) in early childhood is associated with substantial alterations in the intestinal microbiome and its metabolic activity during the early postoperative period.[2,11,13] The observed dysbiosis was characterized not only by taxonomic shifts but also by a functional reduction in short-chain fatty acid (SCFA) production, particularly butyrate and propionate, metabolites known to support enterocyte energy supply, mucosal immune regulation, and epithelial barrier integrity.[3,7,8]

The correlation between CPB duration and dysbiosis severity supports the concept that extracorporeal circulation represents a major systemic stressor affecting gut microbial ecology.[4,5] Reduced abundance of obligate anaerobic butyrate producers, including Faecalibacterium prausnitzii, Roseburia spp., and Clostridium clusters IV and XIVa, may be associated with impaired epithelial nutrition and increased intestinal permeability, as reflected by elevated barrier dysfunction markers.[3,7,8] The identification of obligate anaerobic taxa should be interpreted with caution, as culture-based microbiological methods provide limited taxonomic resolution compared with sequencing-based approaches.

Altered SCFA profiles, characterized by relative acetate predominance and reduced butyrate availability, may be associated with postoperative feeding intolerance.[3,12,14] Butyrate deficiency has been shown to impair intestinal motility, digestive enzyme secretion, and nutrient absorption, which may explain the observed associations with inadequate weight gain and biochemical signs of undernutrition.[3,9,10,14] These mechanisms are based on findings from previous studies and should be considered speculative in the context of the present data.[11–13]

Importantly, these findings highlight the clinical relevance of assessing not only microbial composition but also microbial metabolic capacity in pediatric cardiac surgery patients.[2,6,12] Although limited by sample size, this study provides evidence supporting potential mechanisms and emphasizes microbiome-focused strategies, including targeted nutritional support and microbiota modulation, as potential approaches to improve postoperative nutritional recovery and functional outcomes in this vulnerable population.[6,9]

These findings are consistent with emerging evidence on the role of the gut microbiome in postoperative recovery in pediatric populations.

These findings should be interpreted as associations rather than causal relationships due to the observational design of the study.

Limitations

This study has several limitations. First, the relatively small sample size (n=20) limits statistical power and generalizability. The sample reflected the number of eligible children treated during the defined recruitment period in a single regional center. Second, microbiome assessment was based on culture-based techniques, which provide limited taxonomic resolution compared with contemporary sequencing-based methods. Third, the use of preoperative CHD patients as controls may introduce baseline bias, as children with congenital heart defects may already have altered microbiome profiles before surgery. Fourth, the short follow-up period of 1–5 days restricts interpretation of longer-term nutritional, growth, and developmental outcomes. Finally, because of the observational design, the reported relationships should be interpreted as associations rather than causal effects. Larger multicenter studies using sequencing-based microbiome analysis and longer follow-up are needed to confirm these findings.

Conclusion

This prospective study suggests that young children in the early postoperative period after cardiac surgery with cardiopulmonary bypass exhibit significant alterations in the intestinal microbiome, including a reduction in commensal bacteria and decreased production of short-chain fatty acids (SCFAs). These microbiome disturbances were closely associated with impaired intestinal barrier integrity and an increased risk of postoperative feeding intolerance.

Functional and metabolic shifts in gut microbiota, particularly reduced butyric and propionic acid levels and elevated markers of intestinal inflammation, were associated with impaired physical development, including slowed weight gain, loss of muscle and fat mass, and deficiencies in protein, albumin, vitamins, and trace elements. The severity of dysbiosis was positively associated with the duration and intensity of cardiopulmonary bypass, indicating a potential association between surgical stress and microbiome disruption.

These findings highlight the importance of maintaining a balanced intestinal ecosystem and preserving microbial metabolic activity for optimal nutritional recovery. Targeted monitoring and modulation of the gut microbiome and nutritional status may represent potential approaches for improving postoperative outcomes in pediatric cardiac surgery patients. These findings support the potential role of microbiome-targeted strategies in improving postoperative recovery in this population.

Abbreviations

CPB, cardiopulmonary bypass; CHD, congenital heart defects; SCFA, hort-chain fatty acids; BMI, body mass index; WHO, World Health Organization; ID, intestinal dysbiosis; I-FABP, intestinal fatty acid-binding protein; RR, relative risk; CI, confidence interval; FDR, false discovery rate.

Data Sharing Statement

Due to the nature of the data, which include personal clinical information of pediatric patients, the full dataset cannot be made publicly available in order to protect patient privacy. All data supporting the results and analyses presented in this manuscript are stored in our institutional archive (urgfil.tma.uz) and are available from the corresponding author upon reasonable request. Researchers or the journal editorial office may contact the corresponding author at babadjanovafaniya@gmail.com to obtain access to the data in accordance with ethical considerations and confidentiality principles.

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Disclosure

No potential conflict of interest was reported by the authors.

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