

INTESTINAL MICROBIOTA CHANGES FOLLOWING CHOLECYSTECTOMY: MECHANISMS OF DYSBIOSIS DEVELOPMENT AND METHODS OF ITS CORRECTION

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Annotation: *The article provides a detailed analysis of the pathogenesis underlying intestinal microbiota transformation in post-cholecystectomy patients. The role of gallbladder reservoir function loss, continuous bile acid influx into the duodenum, and accelerated enterohepatic circulation is thoroughly reviewed. Key taxonomic shifts at the phylum and genus levels, as well as the mechanisms behind the accumulation of cytotoxic secondary bile acids, are described. Modern therapeutic strategies for correcting post-cholecystectomy dysbiosis, including dietary modifications, synbiotics, and targeted pharmacotherapy, are highlighted.*

Key words: cholecystectomy, gut microbiota, dysbiosis, bile acids, deoxycholic acid, post-cholecystectomy syndrome, ursodeoxycholic acid, probiotics.

Cholecystectomy (CE) remains one of the most frequently performed elective and emergency abdominal surgeries worldwide. Despite its technical refinement, the removal of the gallbladder does not always lead to complete clinical recovery. Approximately 15% to 40% of patients experience a cluster of post-operative dyspeptic and motor-evacuation disorders collectively termed "post-cholecystectomy syndrome" (PCS) or bile acid diarrhea (BAD). Modern metagenomic sequencing has demonstrated that the driving force behind PCS is a profound rearrangement of the intestinal microbiome, induced by the loss of physiological regulation over the bile acid (BA) pool. Mechanisms of Post-Cholecystectomy Dysbiosis Physiologically, the gallbladder ensures the timed and concentrated delivery of bile into the duodenum in response to dietary triggers. Following CE, this controlled rhythm is replaced by a continuous, uncoordinated flow of hepatic bile into the intestinal lumen. Three primary pathogenic pathways drive subsequent dysbiosis: Direct Antimicrobial Pressure. Bile acids exhibit robust detergent-like properties. By acting as surfactants, they disrupt the phospholipid bilayer of bacterial membranes, induce protein denaturation, and trigger intracellular oxidative stress. The unremitting presence of free BAs in the lumen selectively suppresses bile-sensitive, predominantly Gram-positive commensal bacteria. Activation of 7 α -Dehydroxylation. The continuous transit of primary BAs—

cholic acid (CA) and chenodeoxycholic acid (CDCA)—provides a selective growth advantage to bile-resistant obligate anaerobes. Species possessing the 7 α -dehydroxylation enzyme (chiefly belonging to Clostridium clusters XIVa and IV) proliferate rapidly. They transform primary BAs into secondary BAs: deoxycholic acid (DCA) and lithocholic acid (LCA). Elevated concentrations of DCA are highly cytotoxic, causing apoptosis of normal colonic epithelium and further driving structural dysbiosis. Accelerated Motility and Metabolic Shift. An excess of free BAs reaching the colon overstimulates smooth muscle receptors, significantly accelerating intestinal transit time. This shortens the window available for the fermentation of dietary fibers by short-chain fatty acid (SCFA)-producing bacteria, precipitating a localized energy deficiency in colonocytes.

Taxonomic Alterations in the Microbiota

Based on 16S rRNA gene sequencing data, post-CE patients display reproducible taxonomic shifts:

- **Phylum-Level Shifts:** Studies reveal a characteristic distortion in the **Bacteroidetes-to-Firmicutes** ratio, typically leaning toward an expansion of Bacteroidetes, alongside a significant enrichment of opportunistic **Proteobacteria**.
- **Genus-Level Shifts:** There is a severe depletion of beneficial *Bifidobacterium*, *Lactobacillus*, and key indigenous butyrate producers, such as *Faecalibacterium prausnitzii*. Conversely, populations of *Bacteroides*, *Escherichia*, and *Bilophila wadsworthia* (a sulfite-reducing pathobiont associated with intestinal inflammation) show marked increases.

Methods of Therapeutic Correction

A comprehensive therapeutic approach is required to target the core pathogenic links of the condition:

1. **Dietary Modification and Mucoprotection.** The administration of soluble dietary fibers (e.g., psyllium, pectin) is essential. These fibers physically adsorb excess hydrophobic BAs, neutralizing their cytotoxic potential. Restricting saturated animal fats reduces hepatic choleresis and minimizes the substrate for toxic secondary BA conversion.
2. **Targeted Probiotic and Prebiotic Support.** Multi-strain probiotics containing bile-resistant *Bifidobacterium* and *Lactobacillus* strains are utilized alongside

prebiotics (inulin, fructooligosaccharides) to stimulate indigenous SCFA production and restore epithelial barrier integrity.

3. **Bile Acid Pool Modification.** Ursodeoxycholic acid (UDCA) represents the primary pharmacological intervention. As a hydrophilic, non-toxic BA, UDCA integrates into the general BA pool, displaces toxic hydrophobic DCA, and mitigates mucosal inflammation. In severe cases of refractory secretory diarrhea, anion-exchange bile acid sequestrants (e.g., cholestyramine, colesevelam) are indicated.

Conclusion

Cholecystectomy acts as a distinct trigger for persistent structural and functional alterations in the gut microbiota, dictated by disrupted bile acid kinetics. Timely nutritional and pharmacological correction stabilizes the intestinal ecosystem, prevents severe dysbiosis, restores metabolic homeostasis, and substantially improves the post-operative quality of life for patients.

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