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Comparison Of The Tissue And Gut Microbiome In Extrahepatic Cholangiocarcinoma Patients And Healthy Liver Donors

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Background : Biliary tract cancer (BTC) is an aggressive malignancy associated with a poor prognosis. Recently, there has been growing evidence that gut microbial dysbiosis is related to multiple diseases, including biliary disease and cancer. However, the association between tumor and gut microbiome environments and BTC, especially extrahepatic cholangiocarcinoma (EH-CCA), remains unclear. In the present study, we compared the microbiome from the tissue and stool samples of EH-CCA patients and healthy living liver donors (controls).

Methods : A total of 21 people (11 EH-CCA patients and ten healthy controls) were included. We collected fecal and swab samples, which were obtained from the EH-CCA tissues of the patients and normal gallbladder tissues of the controls during the operation. The bacterial 16S rRNA gene (V3 and V4 region) was amplified using PCR and sequenced on the Illumina MiSeq platform. The QIIME 2 pipelines were used to analyze the raw data.

Results : The swab samples from EH-CCA patients showed significantly lower alpha diversity than those from the controls (pShannon < 0.001). Proteobacteria was the most commonly found phylum (53%) in the EH-CCA patients; Firmicutes (79%) and Actinobacteria (13%) were the common phyla in the controls. The genera Enterobacter (19%), Enterococcus (17%), Escherichia_Shigella (16%), Streptococcus (15%), and Clostridium_sensu_stricto_1 (10%) were found in the patient samples, whereas Blautia (12%), Limosilactobacillus (12%), and Bifidobacterium (19%) were observed in the controls. The Principal Coordinate Analysis (PCoA) plot of the weighted UniFrac distances showed that the patient and control groups formed separate clusters, except for three patients. Streptococcus (10%), Enterococcus (8%), and Faecalibacterium (8%) were the most abundant genera in the fecal samples from the patients, whereas Blautia (17%), Faecalibacterium (10%), and Bifidobacterium (8%) were the commonly observed genera in the control samples. The PCoA plot of the fecal samples showed no significant differences in microbiota composition between the EH-CCA patients and healthy controls. The patient-swab samples formed distinct clusters in the beta diversity analysis of all samples (swab plus fecal). In contrast, the patient-fecal, control-swab, and control-fecal samples showed overlapping clusters.

Conclusions : To the best of our knowledge, this study is the first that compares the microbiome of tissues and stools from EH-CCA patients and healthy controls; the EH-CCA patients and healthy controls showed different microbiota profiles.

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