THE BILE ACID METABOLISM PATHWAY IS A SIGNIFICANT METABOLIC CHARACTERISTIC OF POSTOPERATIVE RECURRENCE OF HEPATOCELLULAR CARCINOMA UNDERGOING LIVER TRANSPLANTATION BEYOND MILAN CRITERIA

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Purpose Liver transplantation is one of the most important treatments for hepatocellular carcinoma (HCC), especially advanced HCC. But the prediction and prevention of postoperative recurrence of hepatocellular carcinoma undergoing liver transplantation beyond Milan criteria are still unknown. More and more evidence showed that metabolic biological progress plays a vital role in initial carcinogenesis and recurrence of HCC. Due to the high risk and lack of donor liver, it is urgent to reveal the mechanism of postoperative recurrence of HCC undergoing liver transplantation beyond Milan criteria. In our research, we used bioinformatics methods to find the metabolic characteristic of postoperative recurrence of hepatocellular carcinoma undergoing liver transplantation beyond Milan criteria.

Method We downloaded the data from Gene Expression Omnibus, TCGA, and normal liver tissues in the GTEx database, and we focused on the biological functions of metabolism-related genes. Firstly, we ran the Limma algorithm to find differential expression genes between recurrence and non-recurrence cancerous tissue of hepatocellular carcinoma undergoing liver transplantation beyond Milan criteria. Secondly, Gene Set Enrichment Analysis (GSEA) and Gene Set Variant Analysis (GSVA) were utilized to calculate the scores of the differential expression metabolism-related genes and gene sets. Finally, Kaplan-Meier analysis and Cox regression analysis were used to verify the clinical significance of the result. Bioinformatics methods are used to analyze the genomics, transcriptomics, and clinical data.

Results By analyzing the data from GEO, TCGA, and normal liver tissues of GTEx, metabolism-related gene sets were selected for further research. We ran the GSEA algorithm, and we found ‘HALLMARK_BILE_ACID_METABOLISM’ had the highest enrichment score. And we ran GSVA to confirm the importance of the ‘HALLMARK_BILE_ACID_METABOLISM’ gene set in HCC. Moreover, it’s obvious the higher score of ‘HALLMARK_BILE_ACID_METABOLISM’ is relevant to the worse overall survival (P<0.01) and median survival (P<0.01).

Conclusion Our work revealed the importance of the bile acid metabolism pathway in postoperative recurrence of hepatocellular carcinoma undergoing liver transplantation beyond Milan criteria. It helps us to understand the mechanism of the bile acid metabolism pathway of hepatocellular carcinoma recurrence. It also helps us to predict the recurrence of HCC undergoing liver transplantation beyond Milan criteria. Targeting the bile acid metabolism pathway will be a hopeful strategy to predict and prevent the recurrence of hepatocellular carcinoma after liver transplantation.