

Metabolomic Profiling of Plasma Bile Acids in Resectable Gastric Cancer

Ștefan Ursu^{1,2}, Răzvan Alexandru Ciocan¹, Cristina-Paula Ursu^{1,2}, Radu-Cristian Moldovan³, Florin Zaharie^{2,4}, Zeno Spârchez⁵, Tudor Moisoiu⁶, Alexandra-Iulia Băraian³, Rodica Sorina Pop⁷, Cătălin Ioan Bodea², Cristina-Adela Iuga^{3,8}, Claudia Diana Gherman¹, Nadim Al Hajjar^{2,4}

¹Department of Surgery – Practical Skills, Iuliu Hațieganu University of Medicine and Pharmacy Cluj-Napoca, Romania

²Department of Surgery, Octavian Fodor Regional Institute of Gastroenterology and Hepatology Cluj-Napoca, Romania

³Department of Personalized Medicine and Rare Diseases, MedFuture Institute for Biomedical Research, Iuliu Hațieganu University of Medicine and Pharmacy Cluj-Napoca, Romania

⁴Department of Surgery – Surgery III, Iuliu Hațieganu University of Medicine and Pharmacy Cluj-Napoca, Romania

⁵Department of Internal Medicine – Medical III, Iuliu Hațieganu University of Medicine and Pharmacy Cluj-Napoca, Romania

⁶Department of Urology, Clinical Institute of Urology and Renal Transplantation, Cluj-Napoca, Romania

⁷Department of Community Medicine, Iuliu Hațieganu University of Medicine and Pharmacy Cluj-Napoca, Romania

⁸Department for Drug Analysis, Faculty of Pharmacy, Iuliu Hațieganu University of Medicine and Pharmacy Cluj-Napoca, Romania

Abstract

Background: Gastric cancer (GC) is characterized by late-stage diagnosis and a lack of reliable non-invasive biomarkers. This study aims to investigate the plasma bile acid (BA) profile to enhance the understanding of GC metabolism and identify potential diagnostic and prognostic tools.

Methods: In a case-control design, 62 GC patients (stages I–III) and 70 matched controls were recruited. Using liquid chromatography-tandem mass spectrometry (LC-MS/MS), the concentrations of 48 metabolites in plasma were measured. Statistical analysis included univariate tests, principal component analysis, and linear discriminant analysis (LDA).

Results: GC patients showed a significantly lower CA/CDCA ratio and alterations in secondary and conjugated bile acids, including TLCA, GLCA, TDCA, GDCA, and GUDCA, suggesting involvement of the gut–liver–microbiome axis. The ability to distinguish between groups was moderate (AUC = 0.731). Furthermore, BA levels were negatively correlated with tumor stage, tumor size, and systemic inflammatory markers (CRP, mGPS), while they were positively correlated with nutritional and hematological markers such as albumin and hemoglobin.

Conclusions: Gastric cancer is associated with a distinct circulating BA profile that reflects not only tumor-related metabolic remodeling, but also systemic inflammation, nutritional status, and disease burden. The reduced CA/CDCA ratio and alterations in secondary and conjugated

bile acids support the involvement of the gut-liver-microbiome axis in GC biology. Although BA profiling alone showed moderate diagnostic performance, its integration with conventional tumor markers, inflammatory indices, and clinico-pathological parameters may improve multimodal biomarker panels for non-invasive patient stratification, disease assessment, and future prognostic evaluation.

Keywords: gastric cancer, bile acids, metabolomics, LC-MS/MS, gut-liver-microbiome axis