Plasma lipid profiling and identification of diagnostic lipid biomarkers for glioma patients

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ABSTRACT

Introduction: Gliomas are the most aggressive primary brain cancers, frequently result in fatal outcomes and carry the poorest prognosis. Dysregulation in lipid metabolism was one of the factors contributing to the development and aggressiveness of glioma. Screening of plasma lipidome may alleviate the diagnosis of glioma and further improve prognosis and patient survival. **Objective:** This study aims to characterise the lipid composition in the plasma of glioma patients and identify potential lipid biomarkers that can differentiate glioma from other brain diseases. **Materials and Methods:** Plasma lipid compositions from 11 control individuals and 72 patients diagnosed with varying grades of glioma (comprising 26 low-grade gliomas, LGG, and 46 high-grade gliomas, HGG) were examined via liquid chromatography-mass spectrometry (LC-MS). The univariate and multivariate analysis techniques were employed to identify the differentially abundant lipids in plasma (significance $p<0.05$). A receiver operating characteristic (ROC) analysis was performed with values larger than 0.75, which were identified as potential lipid biomarkers. **Results:** The lipidomic analysis revealed elevated lipid composition, with 1171 and 1208 detected in LGG and HGG, respectively. Bioinformatics analysis revealed reduced in individual lipid subclasses, including fatty acyls, glycerolipids and phosphatidylcholine derivatives, whereas carnitine, ceramide and sphingomyelin were elevated in the plasma of glioma patients. Partial least squares-discriminant analysis (PLSDA) and heatmap demonstrated that glioma patient and control populations were visually separated by identified lipid biomarkers. Lipid metabolites, phosphatidylethanolamine (PE 21:3, AUC=0.862), ceramide-1-phosphate (CerP 26:1, AUC=0.861) and sphingomyelin (SM 24:3, AUC=0.858) were among the best lipids biomarkers in the plasma of glioma patients. **Conclusion:** Collectively, these lipidomic results unveil the aberrant and heterogeneous multiple lipid classes in the plasma of glioma patients. This research demonstrates that 11 lipid biomarkers show great potential for the non-invasive diagnosis of glioma with high throughput.

Keywords: Glioma, plasma lipidome, lipidomic, lipid biomarkers, mass spectrometry