UNIWERSYTET
MIKOŁAJA KOPERNIKA
W TORUNIU
Wydział Lekarski
Collegium Medicum w Bydgoszczy

Kamil Mateusz Łuczykowski

Nowe możliwości diagnostyczne w monitorowaniu funkcji wątroby od pobrania narządu do przeszczepienia

Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu
Streszczenie w języku angielskim

Promotor:
Prof. dr hab. Barbara Bojko

Bydgoszcz, 2025 r.

Streszczenie w języku angielskim

New diagnostic capabilities for monitoring liver function from organ procurement to transplantation.

Liver transplantation currently represents one of the most effective treatments for end-stage liver failure. Significant advances in surgical techniques, immunosuppression, and patient care have led to a steadily increasing number of recipients qualifying for the procedure. Unfortunately, the number of available organs cannot meet the growing demand, resulting in high mortality rates among patients awaiting transplantation. In response to this disparity, transplant centers are expanding the donor pool by utilizing organs from extended criteria donors. However, such organs are associated with a higher risk of postoperative complications, and the lack of unequivocal and reliable methods hinders the assessment of their quality prior to transplantation. Therefore, the greatest challenge in modern transplantology lies in developing and improving organ preservation techniques and analytical tools to identify parameters or compounds that could enable more effective evaluation of transplanted organs.

The aim of this dissertation was to assess the impact of various liver preservation methods and the degree of organ ischemia on changes in the metabolomic profile of bile using a porcine animal model. This approach aimed to identify potential biomarkers of changes occurring in preserved organs during the peri-transplant period. Bile samples were prepared using solid-phase microextraction (SPME), and metabolomic analyses were performed using liquid chromatography coupled with mass spectrometry (LC-MS).

The results showed that both the preservation method and ischemia time influenced the bile metabolome. Unlike normothermic machine perfusion, bile samples from livers previously subjected to static cold storage exhibited higher levels of specific bile acids—such as chenodeoxycholic acid, tauroursodeoxycholic acid, and glycohyocholic acid—as well as various lipids, including lysophosphatidylcholines and lysophosphatidylethanolamines. These metabolites have already been described in the literature in the context of liver diseases and primary sclerosing cholangitis. Furthermore, normothermic machine perfusion mitigated the negative effects of ischemia on organ function, confirming its benefits for organs obtained from extended criteria donors. Given that ischemia impacts the levels of bile acids—key components of bile—further experiments focused on developing targeted methods for

quantifying metabolites from this group. Analyses conducted using a fully validated LC-MS method demonstrated that organ ischemia significantly affected taurocholic, glycocholic, and glycochenodeoxycholic acid levels in samples collected during perfusion. Moreover, these findings correlated with results from analyses of bile acid isomers obtained using a newly developed method that combines SPME directly with mass spectrometry via a microfluidic open interface (MOI).

In summary, this doctoral dissertation successfully proposed high-throughput sample analysis protocols based on SPME and applied them to the preparation of bile samples. The study identified metabolites worth considering as potential markers of changes occurring in preserved grafts, which could be further evaluated in future studies involving human liver grafts. The proposed SPME-MOI-MS method enables near real-time results, offering a promising tool for assessing organ function and predicting potential post-transplant complications at an early stage.

Keywords: liver transplantation, machine perfusion, bile, solid-phase microextraction (SPME), metabolomics.