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Analiza lipidomiczna w diagnostyce transplantacyjnej

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

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Streszczenie w języku angielskim

Lipidomic analysis in transplant diagnostics

The number of patients placed on kidney transplant waiting lists continues to rise, resulting in a growing disproportion between organ demand and availability. Consequently, transplant centers are increasingly challenged to optimize the utilization of available organ resources and to expand the donor pool to mitigate this gap. Standard criteria donors are typically preferred in kidney transplantation, as grafts from these donors are associated with more favorable outcomes. However, the ongoing shortage of donor kidneys has necessitated the inclusion of marginal organs from expanded criteria donors to increase transplant rates and reduce patient wait times. It is well established that donor organ quality significantly influences long-term transplant outcomes, with expanded criteria donor kidneys being associated with poorer prognoses, an increased risk of delayed graft function, and a higher incidence of primary non-function. Accordingly, there is an urgent need for innovative strategies that enable early graft quality assessment, prediction of post-transplant complications, and improved management of high-risk recipients. Additionally, effective preservation strategies are required to minimize ischemic injury, enhance organ quality, and ultimately improve transplant success rates.

In response to these challenges, the primary aim of this study was to address the limitations of current peri-transplant diagnostics by demonstrating the potential of solid-phase microextraction (SPME) for kidney quality assessment. The study was designed to evaluate a novel analytical approach involving direct *in vivo* tissue analysis through chemical biopsy, combined with lipidomic profiling. In the initial phase, an animal model was used to assess the impact of ischemia on organ quality based on two donor types, and to compare different preservation techniques with respect to their effects on the kidney lipidome. Subsequently, the SPME technique was applied in a clinical setting to predict the risk of complications and to identify a panel of metabolites and lipids with potential diagnostic relevance.

The use of SPME—characterized by a minimally invasive sampling probe (~200 µm in diameter) that does not require tissue excision—enabled repeated, non-destructive sampling from the same organ. This facilitated monitoring of biochemical alterations throughout the transplantation process, from organ retrieval and preservation to reperfusion, while also

enabling the detection of a wide range of compounds with diverse polarities. Moreover, comparative analysis of different preservation methods revealed that storage temperature exerted a greater influence on the kidney's lipidomic profile than the mechanical nature of the preservation technique. Notably, normothermic perfusion was associated with reduced accumulation of lipids linked to ischemia-reperfusion injury, mitochondrial dysfunction, pro-inflammatory responses, and oxidative stress, suggesting a potential protective effect on graft function.

In the final stage of the study, SPME was implemented clinically to perform metabolomic and lipidomic analyses at multiple time points using both donor kidney tissue and recipient plasma samples, with the aim of detecting changes associated with delayed graft function. The identified compounds with potential predictive value included amino acids and their derivatives, nucleotides, organic acids, peptides, and lipids—particularly phospholipids and triacylglycerols. These findings highlight the translational potential of chemical biopsy and plasma metabolite profiling for non-invasive risk assessment and monitoring of post-transplant complications. The identified metabolites may form the basis for the development of a comprehensive tool for the evaluation and prediction of delayed graft function and for managing high-risk transplant recipients. Importantly, the application of chemical biopsy in a clinical setting did not prolong cold ischemia time or disrupt the transplantation workflow, thereby further supporting its clinical feasibility and potential for integration into routine diagnostic practice.

Keywords: solid-phase microextraction (SPME); kidney transplantation; lipidomics; graft quality assessment; delayed graft function (DGF)