Addressing patient mortality in hemodialysis via AI applied to metabolomics and material science

Abstract: Patients undergoing hemodialysis (HD) exhibit significantly higher mortality rates compared to those who had kidney transplants. This disparity is largely attributed to the accumulation of uremic toxins that standard HD treatments fail to completely remove. Despite this acknowledged issue, systematic identification of specific uremic toxins impacting mortality in patients receiving maintenance HD has not been effectively addressed. This project integrates AI, metabolomics, and biomedical materials science to accelerate the identification of key metabolites and biological pathways involved in the mortality of dialysis patients and to discover biocompatible filtering materials that could enhance HD efficacy in toxin removal. By leveraging data from existing literature and collaborations, this synergistic approach seeks to elucidate the mechanisms behind elevated mortality in HD patients and develop solutions to mitigate these risks, with the ultimate goal of reducing patient mortality.

Introduction

Approximately 2 million individuals globally suffer from kidney failure, necessitating treatment options such as transplantation and dialysis. Transplantation is limited by donor availability, forcing many to rely on HD. Whereas transplant recipients exhibit approximately 80% survival rates five years post-procedure, those undergoing HD have less than a 50% chance of surviving the same period due to what's known as “residual uremic syndrome.” This condition results from the incomplete removal of certain uremic toxins during HD, significantly contributing to the higher mortality observed in these patients [1]. Current HD technologies rely on membranes which are limited by size, thus unable to effectively eliminate larger uremic toxins from the patient's bloodstream. This approach lacks precision and effectiveness as it is designed on small molecules like urea and fails to address other, more harmful toxins.

Research Challenge:

Achieving more effective HD treatment and reducing current mortality rates is a complex challenge that requires a multidisciplinary approach. The first crucial step is to clearly identify the metabolites associated with adverse effects. This task can be addressed using a combination of metabolomics and AI. Metabolomics can detect a wide range of metabolites, some of which may play critical roles in the health outcomes of patients with kidney failure. Three studies have investigated the link between serum metabolites and mortality in patients with kidney disease, but they have yielded inconsistent results regarding which metabolites are implicated, underscoring the need for further research. The integration of metabolomics with AI may also enhance our understanding of the mechanisms: this deeper insight is essential for developing more effective HD treatments that can mitigate the adverse effects. [2-4]. A comprehensive AI-based analysis of the existing data is essential, laying the groundwork for future large-scale metabolomics research.

However, identifying these metabolites is just the initial step. The ultimate goal is to leverage this information to enhance dialysis treatments by developing materials capable of efficiently capturing the most toxic molecules. AI has the potential to expedite the exploration of the vast materials space.

Achieving both the identification of harmful metabolites and the development of effective materials is an ambitious task, given the multitude of toxins and materials involved. Fortunately, AI technologies can greatly accelerate progress towards these dual objectives.

Data & Methodology:

Data for the AI-metabolomics study will be those coming from studies carried out in the literature, in particular from three previous metabolomics studies focusing on mortality in HD patients in 2013, 2019 and 2024 [2-4]. The possibility to validate results with target tests using the from NURTuRE biobank of the Kidney Research UK charity, that will serve as our external collaborator, will be evaluated if necessary [5].

The identified metabolites will be then addressed using molecular simulations and several materials will be considered in order to remove them from the patient blood. In particular we will consider around 600 materials including several Covalent Organic Frameworks, coming from the CoreCOF and other literature databases. **Data will come from molecular simulations** using a method, previously used by our group to address the binding strength of materials towards uremic toxins such as urea [6]. Once built the database, several different types of supervised ML regressions will be considered to perform a large-scale screening of suitable materials, using a methodology currently being developed in the Engineering group for small toxins within the project REDIAL. [7].

Such study will allow to correlate specific materials features (e.g. chemical composition and porosity descriptors) to the ability of the filtering materials of removing toxic molecules correlated to mortality. This work will provide guidelines for material synthesis and/or selection in the design of more efficient and tailored HD treatment which can reduce patients' mortality.

Responsible AI/Ethical Considerations: This research will strictly adhere to ethical guidelines, ensuring responsible use of AI and data privacy, focusing particularly on the implications of implementing AI in healthcare environments.

Expected Outcome & Impact: this is clearly an ambitious project where different disciplines are involved, linked by the way they use AI to accelerate the understanding of adverse clinical outcomes in dialysis patients, and find material solutions to improve the HD treatment. We expect this project to lie the basis for interdisciplinary research between the involved groups and provide evidence for larger studies.

External collaborators: Kidney Research UK, https://www.kidneyresearchuk.org/ , providing in-kind contribution via patients involvement, the Nurture Biobank, advertisement of the project on social media, time of the research support team.

References

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