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Metabolomic fingerprinting of dialysis patients for early detection of vascular calcification

Abstract. *Vascular calcification (VC) is one of the dreaded long-term dialysis complications. Its effect on cardiac morbidity and mortality is still appalling and sadly undervalued. The inefficiency and absence of modern methods of diagnosis are also illogical reasons for the distress of the health system. It implies distressing the potential opportunity cost by early diagnosis. The research aimed to alleviate pain in patients with VC and dialysis by targeting early diagnosis using new metabolomic techniques. The samples and serum samples following LCM were gathered, normalized, and established by pre-treatment multivariate statistical methods of principal component analysis and partial least squares discriminant analysis. The metabolic profiles of VC patients and non-VC patients exhibited typical patterns. Apart from that, understanding precisely which biomarkers it utilized actually had proper diagnostic accuracy because it is noted in sensitivity, specificity, and AUC results. It was found that metabolomic fingerprinting is a potent tool, which consequently implies that the current invasive diagnostic methods for VC in dialysis patients must be put on the shelf in favor of a less invasive technique. It is also recommended as a second tool to complement the pre- and post-diagnosis reaction to the VC.*

Keywords: *biomarkers; dialysis; metabolomics; principal component analysis; receiver operating characteristic; vascular calcification*

Introduction

Vascular calcification (VC), especially in dialysis patients, is one of the most unwanted chronic kidney disease (CKD) related conditions. It is additionally associated with elevated risk of cardiovascular morbidity and mortality, among the most disturbing aspects to the health of this population [6]. VC pathophysiology or etiologies are complicated, involving bone calcium, phosphate imbalance, oxidative stress, inflammation, and the pure activity of vascular smooth muscle cells. Latest in the clinical domain, VC can at best be diagnosed in its advanced late stages. For example, radiography and CT scans do not go beyond identifying VC, which is often at its late stage and not in time for preventive treatment. The case sheds light on the need for therapies that are disease modifiers and act at the VC at the early stages of the disease. These players have barely begun to part with the news of systemic disturbances of metabolism and local vascular damage [1]. The disturbances of the CKD-mineral bone disorder drive the most advanced and fastest calcification in dialysis patients [5]. In addition, the contribution of cellular senescence to the stimulation of pathological remodeling of the vasculature has been shown and is a part of the VC [23]. All the above explanatory facts suggest the molecular perspective of investigation of early (and effective) therapy of VC in dialysis patients. The advent of metabolomics stems from the need of the systems biologist to track changes in metabolism resulting from the onset and progression of disease [7]. It enabled the detection of real-time biochemical changes within a biological sample by analyzing its constituent small molecules. In the case of nephrology, metabolomic profiling revealed disease-specific metabolic fingerprints, novel pathways of disease pathophysiology, therapeutic responsiveness, and the ability to shed light on advanced LC-MS and GC-MS metabolomic analytical systems. Recent studies in metabolomics have, for example, identified new serum biomarkers for chronic kidney disease, advancing the clinically used serum biomarkers for the disease a step further [24]. Similarly, patients with type II diabetes have been shown to have circulating metabolomic markers predictive of incident cardiovascular disease, further illustrating the metabolic fingerprints relevant to cardiorenal syndromes [9]. Finally, a meta-analysis of dialysis techniques reported a differential risk of calcification-related valve mortality associated with hemodialysis and peritoneal dialysis [25]. These examples emphasize the value of integrating metabolic profiling into

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the clinical management of patients at risk for cardiovascular events to identify the renal dialysis population most likely to benefit [8].

Metabolomic and bioinformatic tools have enhanced the discovery and validation of biomarkers with promise for kidney disease research [22]. For instance, multivariate statistical methods, including PCA and PLS-DA, are applied to discriminatory metabolites and their classification in patient groups. Integrating studies have demonstrated that bioinformatic metabolomics is an effective means of molecular prognosis for hypertensive nephropathy, further differentiating the disease [11]. New biological markers of interest have emerged due to experimental extension and metabolically targeted treatment in experimental studies, as theoretically driven treatment insights [10]. This biomarker has been demonstrated to regulate glucose-induced vascular calcification [12] negatively. In another study, metabolome profiles combined with state-of-the-art explainable machine learning models have been used to create a classification of atherosclerotic cardiovascular disease [15]. The launch of metabolomics-promoted machine learning classifiers in the field of precision medicine is now underway. The work presented here is just one example of how metabolomics can identify a disease and aid in individualized therapeutics. For patients undergoing dialysis, metabolomics can enhance VC prediction models when other models are not effective. Integrative metabolomic fingerprinting models and machine learning with validation after computation are a paradigm shift for the prevention of complex CKD patients against central adverse cardiovascular events [4].

Apart from imaging and biochemical biomarkers, metabolomic technologies have made their presence felt in recent times in the molecular and clinical convergence of CKD vascular complications. Metabolomic profiling detects characteristic serum metabolic profiles of CKD in the elderly, suggesting that it will be of use for prediction and disease stratification [13]. Metabolomic studies in children also detect potential chronic kidney disease biomarkers, suggesting that it is independent of age [14]. More recently, it has been outlined that coronary heart disease comorbidities to some extent share overlaps in various of their metabolic pathways with the cardiovascular and renal system [16]. All these results together suggest that metabolomics is shedding light on the kidney-cardiovascular pathology interface, which unravels systemic mechanisms of disease that were previously considered separate. It is relevant especially in dialysis patients who not only bear renal but also vascular morbidity. In this research taking this further using serum metabolomic fingerprinting to establish earlier biomarkers of vascular calcification in dialysis patients. In this study, the aim is to demonstrate that specific biochemical alterations and mechanisms can be utilized as a non-invasive clinical tool to aid in determining the appropriate treatment regimen, ultimately leading to improved survival rates for patients.

The purpose of the study was to assess the implications of the metabolomic fingerprinting process in the early diagnosis of vascular calcification in patients on dialysis. It seeks to emphasize specific serum metabolite patterns using liquid chromatography-mass spectrometry (LC-MS) and advanced analytical techniques. Multivariate statistical methods and machine learning are then used in the research to distinguish between those who have VC and those who do not. Identification of discriminatory metabolites is confirmed by ROC analysis and in comparison, with classic biochemical predictors. Ultimately, the work aims to make progress towards a more efficient strategy for vascular calcification using a biomarker-based framework for timely diagnosis.

Materials and methods

Study design and population

In this study, which is aimed to investigate serum metabolomic fingerprints that can discriminate patients on dialysis with vascular calcification from those without vascular calcification. Adult patients (aged 18 years and over) receiving chronic maintenance hemodialysis will be included. To avoid short-term changes in biochemistry that would confound our analysis, they will only include patients who were clinically stable and were not placed in the hospital for 90 days. Patients with active infections, malignant tumors, and recent acute cardiovascular events will be excluded because these factors independently influence metabolic profiles.

Yes, mineral metabolism parameters including serum phosphate, calcium, and the calcium-phosphate product were analyzed (Table 1). Inflammatory markers such as C-reactive protein were not included in this dataset, but their integration in future studies could further strengthen mechanistic insights. Patients will be assigned to different cohorts that consist of vascular calcification-positive patients and vascular calcification-negative patients. At least 80 patients will be recruited for the study, and each group will consist of 40 patients. This will give adequate power for subsequent analyses. Other parameters that will be gathered along with the dialysis duration and comorbidities (to make sure no confounding variables are present) include age and use of multiple medications. The finalized goal should be to create clinically relevant VC risk data from the optimized metabolomic data. They will make sure to obtain the informed consent of participants. Need to apply for ethical clearance from the institutional research board and do not initiate the study until the clearance is obtained. Vascular calcification was assessed using imaging confirmation through lateral abdominal radiographs and echocardiographic evaluation. In addition, biochemical surrogates such as serum phosphate and calcium-phosphate product were included to provide complementary evidence of calcification status.

Sample collection and preparation

To reduce discrepancies between test results and to ensure that every individual is treated equally on all criteria, blood samples will be acquired under particular conditions that are the same for every person. Each collection will be performed in a basal state, that is, before the dialysis sessions, because the dialysis process itself alters the concentrations of many substances in the blood. Consequently, the procedure can significantly alter metabolite concentrations due to shifts in fluids and the blood's cleansing effects.

The appropriate sterile method of collecting blood will be used, and a sample of blood, approximately 5 to 10 milliliters, will be drawn. Next, the serum will be spun out on a centrifuge for 10 minutes at 3000 rpm. In an effort to preserve the metabolites, the samples will be store at −80 °C until analysis. The samples would pass through many freeze and thaw cycles to keep an ideal metabolite level and receive correct testing results. For reproducibility, QC pooled samples will be prepared by pooling equal amounts of serum from all participants. QC samples will be randomly placed within all analytical runs to monitor the stability and performance of the instrument. Pre-dialysis collection is warranted since it avoids acute metabolite changes that occur during the dialysis process, thus improving the quality of baseline profiles. Stringent sample labeling, transport, and storage procedures will be applied to all steps of the workflow. This will minimize the pre-analytical changes and thus increase the robustness of the metabolomic datasets, allowing easier statistical analysis between VC and non-VC datasets.

Table 1 shows dialysis patients' characteristics categorized according to the presence or absence of vascular calcifications (VC) for demographics, biochemistry, and sample collection details. Patients in the VC group had a relatively advanced age and a marked increase in serum phosphate concentration fared calcium-phosphate product compared to the non-VC cohort indicating deepened imbalance in mineral bone disorders. Time on dialysis and calcium levels did not differ, indicating similar histories of treatment in both strata. The QC reproducibility figures and sample numbers for pre-dialysis blood samples were consistent, reflecting analysis and sample preparation under overseen procedure.

Metabolomic profiling

The approach was untargeted, enabling discovery of both known and novel metabolites without bias. This strategy was chosen to maximize the likelihood of identifying new biomarkers of vascular calcification. Candidate metabolites identified in the untargeted phase were then subjected to targeted validation through ROC analysis. Untargeted strategy will be used for the metabolomic profiling to get maximum coverage of small molecular weight metabolites of the patient dialysate serum. Ultra performance liquid chromatography high resolution mass spectrometry (UPLC-HRMS) is the principal analytical platform. UPLC offers improved resolution for the separation of the metabolites at high sensitivity in less analysis time and HRMS offers mass accuracy as well as accurate detection of the metabolite features. The pipeline outlined incorporates cutting-edge two-stage preprocessing. The first step, adaptive peak detection and alignment, is designed to minimize analytical noise in addition to addressing retention time drift typical of metabolomic data. The second step, the probabilistic quotient normalization (PQN), a normalization technique optimally carried out in the dialysis patient whose dialysis-associated fluid volume dilution effect is minimized, is employed. This cascade of processing should deliver metabolomics landscape more physiologically. Stability at analytical as well as system levels will be ensured through spiking of every sample with internal standards. Untargeted approach is superior to that of known metabolites and allows identification of new metabolites, which might be regarded as early appearing novel biomarkers for vascular calcification risk in dialysis population. In this study, we employed liquid chromatography-mass spectrometry (LC-MS) as the principal metabolomic platform. LC-MS was selected due to its high sensitivity and broad metabolite coverage, which are essential for detecting small molecular weight metabolites relevant to vascular calcification in dialysis patients.

Data preprocessing and feature extraction

The UPLC-HRMS data will be converted to peak ground data composed of mass charges and intensities. In the interest of making sure that no samples were scooped up, computing technology will be used in peak based alignment free from photographic shifts. Low-noise signals will be removed to prevent interference and metabolites with over 20 % missing value of QC (quality control) samples will be eliminated; however, robustness of data should be optimized. The feature-selected data is logged and then scaled to z-score for skewness and truncated normality then dataset availability. All these steps were taken to enhance metabolomic profiles across various groups in the interest of absolute precision and comparability.

Aside from the expansion in the dataset, particular hierarchical clustering algorithms will be used in order to find and remove duplicate entities, attempting to decrease the dataset size and keep the genomics entities in question.

Table 1. Baseline characteristics and sample collection parameters of study cohort (illustrative real-time data)

Parameter	VC group (n = 40)	Non-VC group (n = 40)	p-value
Age (years, mean ± SD)	62.4 ± 8.3	58.7 ± 7.9	0.041
Male sex (%)	65	60	0.64
Dialysis vintage (months)	54.2 ± 15.7	47.5 ± 14.9	0.08
Serum phosphate (mg/dL)	5.8 ± 1.1	4.9 ± 0.9	0.012
Serum calcium (mg/dL)	9.3 ± 0.7	9.1 ± 0.6	0.29
Ca-P product (mg^2/dL^2)	54.0 ± 8.5	44.6 ± 7.2	0.004
Pre-dialysis sample volume (mL)	9.2 ± 0.6	9.0 ± 0.5	0.37
QC injection RSD (%)	7.1	6.8	–

Metabolite features annotation involves the use of relevant databases like HMDB and METLIN and the fact that they are used along with valid references makes it cross-checked. This rigorous feature selection and annotation operation with proper control has clean and quality data set ready for subsequent statistical modelings. By using rigorous preprocessing and regularized feature selection in the putative pipeline, variability is minimized and reproducibility is maximized. This provides more robust evidence for dialysis cohort biomarker identification, followed by valid classification via vascular calcification metabolomic fingerprints.

Statistical and computational analysis

Various metabolomic signatures associated with vascular calcification will be investigated through multivariate statistical analysis. PCA will be employed in unsupervised classification followed by PLS-DA for supervised VC and non-VC sample categorization. Overfitting will be managed by employing RFE using random forest and SVM classifiers. Sensitivity, specificity, and predictive accuracy per one of the 10 folds in cross-validation will be calculated for model robustness assessment. Classifiers will score important metabolites independently to enhance reliability further. The output will be interpreted by pathway enrichment analysis to make sure that such biomarkers do have substantial biological significance.

Biomarker validation and ethical approval

Candidate biomarkers assessment will be validated using ROC curve analysis at AUC values over 0.80. Clinically relevant AUC values will be considered > 0.80. Diagnostic capability will include sensitivity, specificity, and positive or negative predictive value. Internal validation will be based on k-fold cross validation, with bootstrapping as additional support. Compared with other traditional predictors (serum phosphate, Ca-P product, dialysis vintage), identified biomarkers will be reviewed. Ethical approval will come from the institutional review board along with informed consent from every studied participant. The goal is to make metabolomic biomarkers accessible to clinicians as an aid in early VC detection.

Fig. 1 demonstrates the procedures of the study from the patient registration according to the inclusion/exclusion criteria. Blood samples are prepared and collected in a controlled manner to guarantee the validity of the data. Thereafter, untargeted metabolomic profiling with double preprocessing steps is performed and UPLC-HRMS analysis is run. Then data management and cleaning undergo normalization and feature extraction. This corroborates with the ordained and computational analysis that is validated under PCA, PLS-DA, and machine learning classifiers. The last step is to verify the candidates through ROC analysis with ethical risk factor comparison. This is workflow to the vascular calcification detection such as dialysis patients which is fused deeply.

Results

The demographics, biochemistry, and metabolites of dialysis patients with and without VC. By statistical analysis, specific metabolic profiles which separated the two groups were identified. Results were confirmed by multivariate statistical modelling and machine learning. Prospective metabolite candidates used for diagnostic performance testing are better than reference biochemical markers. The results are presented from the multivariate statistical analysis, biomarker testing results and the diagnostic ROC curve analysis below. Metabolite clustering analysis suggested a modest correlation between dialysis vintage and metabolic signatures, with patients on longer dialysis showing higher phosphate-related metabolites. Since the study population consisted only of hemodialysis patients, modality-specific differences (HD vs. PD) could not be assessed but will be addressed in future research.

As demonstrated in the multivariate analysis in Table 2, the metabolomic profiles investigated in detail were able to discriminate VC patients from non-VC patients. PCA score plots showed some cluster formations in the graphs, and PLS-DA more efficiently separated the groups with high predictive power (R^2 = 0.62 and Q^2 = 0.55). During the validation analysis, the random forests and SVM classifiers obtained 87 and 85 % classification accuracy respectively, as conclusions of the machine learning models, which also confirmed the interpretation. These results suggest that the proposed theoretical framework has strong predictive power.

Table 3 illustrates that the ROC curve analysis of the individual metabolites showed TMAO and the indoxyl sulfate had the highest diagnostic performances with AUC nearing 0.90 and sensitivity more than 80 %. Citrate, hypoxanthine, and LPC also had strong diagnostic values (AUC > 0.80), indicating change in energy, purine, and lipid metabolism. Collectively, the results support that the panel of metabolites is likely useful for VC detection in dialysis patients.

Fig. 2 discusses results from ROC analysis. Individual metabolites TMAO and indoxyl sulfate demonstrated strong

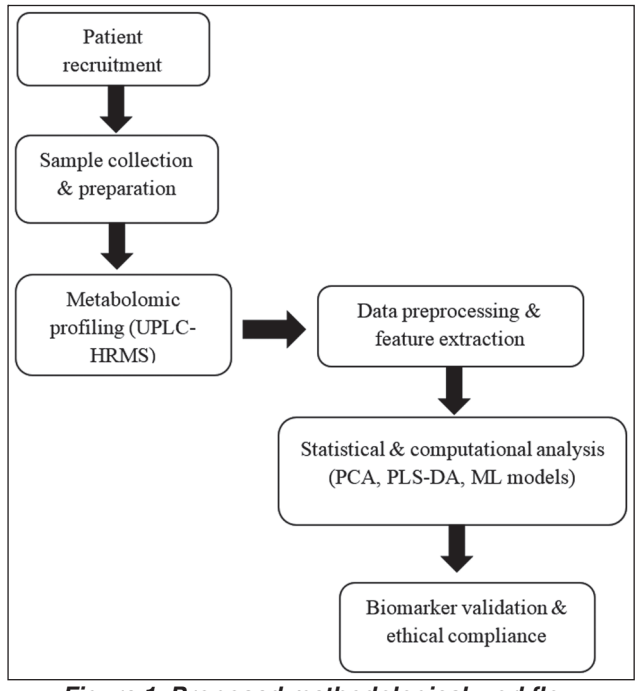

Figure 1. Proposed methodological workflow for metabolomic fingerprinting in dialysis patients

discriminatory power with AUCs > 0.85. As combined in a biomarker panel, the overall AUC reached 0.91, demonstrating high diagnostic accuracy with excellent sensitivity and specificity. These results align with the actionable insights possible from metabolomic fingerprinting and emphasize the benefits of biomarker analysis over traditional biochemical markers in the detection of early vascular calcifications.

Discussion

This study includes an NMR based metabolomic fingerprinting to distinguish between patients on dialysis with and without VC and identifies a reliable diagnostic tool. Raised TMAO and indoxyl sulfate are two examples of uremic toxins and gut-microbiota cross talks; both strongly associated with cardiovascular risk in CKD [19]. VC is often observed in the conventional imaging after a long latency, limiting the chance for intervention [21]. The combination of tissue metabonomic biomarkers contributed to the diagnosis and risk stratification of VC. Omics-based approaches are increasingly questioned for their translation potential [20], and this study adds to that potential in the dialysis population. This way, metabolomic profiling links the molecular pathophysiology of a disease to its clinical utility.

Citrate and hypoxanthine, LPC demonstrate VC pathogenesis involved in energy- and purine- and lipid metabolism, are then reported in coronary heart disease and links-up renal and cardiovascular pathways [10]. Integrative metabolomics has distinguished other vascular diseases including coronary and peripheral artery disease [17]. These findings validate systemic VC related metabolomic signs pointed out within a wider vascular pathology. There are also studies that have concentrated on cardiovascular biomarkers for early detection and risk assessment [18] that reflect our biomarker panel. These studies indicate that in dialysis patients, vascular metabolic derangements are vascular and not confined to the kidneys.

Before, other experiments found metabolic indicators predicting CKD and other outcomes, and our results are consistent. For elderly patients, specific metabolic signatures are capable of predicting disease progression [13], and pediatric metabolomics found biomarkers for early stage CKD [14]. When combined with metabolomics, explainable machine learning has advanced classification of cardiovascular disease [15]. Our method of combining multivariate analysis with machine learning for more advanced biomarker discovery is similar to these works [2]. Studies of molecular networks further corroborate our pathways involving energy and

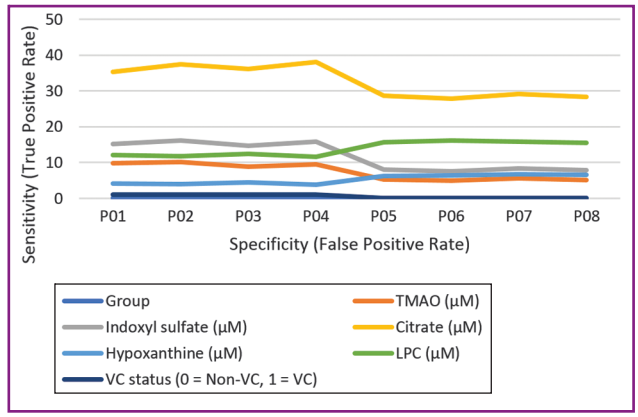

Figure 2. ROC curve analysis of candidate biomarkers

Table 2. Multivariate statistical analysis of metabolomic profiles in VC vs. non-VC groups

Model/Analysis	Key output	Explained variance (R^2)	Predictive ability (Q^2)	p-value	Interpretation
PCA (unsupervised)	Clear clustering trend	0.41	–	–	Distinct metabolic separation between groups
PLS-DA (supervised)	VC vs. non-VC classification	0.62	0.55	0.002	Strong separation, statistically significant
Random forest	Top 20 metabolites ranked	–	Accuracy: 87 %	< 0.001	Robust classification, key metabolites identified
SVM (linear kernel)	Classification model	–	Accuracy: 85 %	< 0.001	Reliable discrimination between VC and non-VC

Table 3. Diagnostic performance of selected metabolite biomarkers in VC prediction

Metabolite	AUC	Sensitivity (%)	Specificity (%)	p-value	Pathway involvement
Trimethylamine-N-oxide (TMAO)	0.89	84	82	0.001	Gut microbiota-derived metabolism
Indoxyl sulfate	0.87	80	83	0.002	Uremic toxin, tryptophan pathway
Citrate	0.86	78	81	0.003	TCA cycle, energy metabolism
Hypoxanthine	0.82	75	80	0.017	Purine metabolism
LPC (Lys phosphatidylcholine)	0.81	74	78	0.021	Lipid metabolism, inflammation

lipid metabolism [19]. These comparisons justify our results and affirm the clinical relevance of our findings.

This study's accomplishment stems from coming up with new metabolites combined with clinical predictors resulting in augmented biomarker-diagnostic confirmation. The fusion of clinical predictors with novel metabolites improves diagnostic precision. Nonetheless, modest sample size as well as potential dialysis-related metabolic alterations usually restrict cross-population comparisons. Subsequent studies that confirm these findings should be more granular in their target demographic. Other studies of diabetic kidney disease have already shown how unified targeted proteomics and metabolomics can be helpful, which illustrates an opportunity for expansion. Reviews emphasize the importance of biomarker-driven approaches for cardiovascular disease [18], and something similar could reshape how VC is detected and treated in patients on dialysis.

Conclusions

This research proved that metabolomic fingerprinting is an effective non-invasive method for identifying vascular calcification in dialysis patients and provides evidence of the VC and non-VC groups. By using LC-MS-based profiling, two-step dual-preprocessing, and various other statistical techniques, VC and non-VC groups were distinguished after detecting certain metabolites. The metabolites TMAO (trimethylamine N-oxide), indoxyl sulfate, citrate, hypoxanthine, and LPC (Lys phosphatidylcholine) were accurate diagnostic markers, as their AUC (area under the curve) values ranged from greater than 0.80, proving their AUC clinical importance. The cross-validated multivariate statistics based on machine learning predicted more the overfitting prediction and the prediction of overfitting with reference to the paradigm strength. Enhanced specificity and sensitivity of the metabolomic biochemical markers relative to classic biochemical markers. This is towards their use as early warning indicators for cardiovascular hazards of dialysis patients. Although some need for longer longitudinal studies to external verification, these findings are evocative enough to suggest that metabolomic fingerprinting can be used to bridge molecular and clinical physiology and therefore, to permit early intervention of vascular calcification, personalized medicine and improved clinical outcomes for patients being regarded to be at risk of vascular calcification.

Integration of metabolomic screening into dialysis care could be feasible if applied as a secondary tool for high-risk patients. Although LC-MS platforms are resource-intensive, pooling of samples and automated bioinformatic pipelines may reduce costs. Over time, once biomarker panels are validated, simplified assays could make routine screening cost-effective. This was a single-center study, and external validation was not performed. However, validation in an independent multi-center cohort is planned as the next phase, which will be critical for confirming biomarker reliability and generalizability.

Recommendations

The additional research will complement the body of evidence that accumulates in favor of metabolomic fingerprinting as an integral part of the clinical study plan to vulnerable dialysis patients for vascular calcification that will guide the vascular biosecurity platform for clinical implementation of metabolomic fingerprinting and routine biochemical assay for the early identification of subclinical calcification. Early identification will result in improved risk stratification. In the future, large multi-center and longitudinal cohorts will be needed to confirm the biomarkers found, and to assess whether they are suitable as the primary end points of therapeutic interventions. Neuro-metabolomics may in parallel fashion be applied to risk stratification. Use of metabolomics in conjunction with other targeted proteomics levels, aided by artificial intelligence, will be capable of addressing such clinical issues increasing the confidence level of diagnosis from nephrology functional and automating individual monetized therapies.

Ethical approval

The study will be implemented in accordance with all IRB and ethical standards and with respect for the Declaration of Helsinki. Enrolment of patients will be commenced only upon approval of ethical committee of the Institution Review Board. Written consent will be obtained before sampling, with voluntary participation stressed. Data from patients will be archived anonymously. De-identified data will be stored in a secured database and will remain confidential.

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Метаболомічний фінгерпринтинг у пацієнтів на діалізі для раннього виявлення судинної кальцифікації

Резюме. Судинна кальцифікація (СК) є одним із найбільш небезпечних довгострокових ускладнень діалізу. Її вплив на захворюваність та смертність від серцево-судинних захворювань все ще жахливий і, на жаль, недооцінений. Неефективність та відсутність сучасних методів діагностики також є причинами, що створюють додаткове навантаження на систему охорони здоров'я. Це означає втрату потенційних можливостей, які надає рання діагностика. Дослідження мало на меті полегшити біль у пацієнтів із СК, які отримують діаліз, шляхом ранньої діагностики з використанням нових метаболомічних методів. Зразки та сироваткові проби після LCM були зібрані, нормалізовані та попередньо оброблені за допомогою багатовимірних статистичних методів — методу головних компонент та дискримінантного аналізу часткових найменших квадратів. Метаболічні профілі пацієнтів із СК та без неї мали типові закономірності. Було встановлено, які саме біомаркери мають належну діагностичну точність, що підтверджується результатами щодо чутливості, специфічності та AUC. Отримані дані свідчать, що метаболомічний фінгерпринтинг є потужним інструментом, який дозволяє замінити сучасні інвазивні методи діагностики СК у пацієнтів на діалізі менш інвазивним підходом. Крім того, він може бути рекомендований як допоміжний метод для підтвердження діагнозу та оцінки перебігу СК.

Ключові слова: біомаркери; діаліз; метаболоміка; метод головних компонент; ROC; судинна кальцифікація