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Podocyturia an emerging biomarker for kidney injury

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Abstract

Podocyte injury is an established hallmark of kidney disease progression. Podocyte loss is a widely proven hypothesis to explain, in part, glomerular damage. Regardless of the underlying kidney disease, the pathophysiologic processes frequently involve the glomerulus. A growing body of evidence considered that podocytes detachment (podocytopathy) and their presence in the urine (podocyturia) are the hallmark of glomerular disease progression. As such, developing new tools to monitor disease progression non-invasively is of major clinical importance. Detection of podocytes in the urine as a biomarker of disease progression would be a major achievement toward the development of such tools. This review summarizes current knowledge about podocyturia.

Introduction

Podocytes- cells within the glomerular structure

The kidney glomerulus is the anatomical site where filtration defects are particularly localized. It harbors multiple cell types including glomerular podocytes, mesangial cells, and fenestrated endothelial cells. Glomerular podocytes and capillary endothelial cells are separated by a thick glomerular basement membrane (GBM) which altogether form the glomerular filtration barrier (GFB) [1]. Podocytes are highly differentiated epithelial cells that counteract the elastic distention of the glomerular capillary and contribute to the size-selective nature of the GFB [2]. While glomerular capillary endothelial cells cover the inner surface of the GBM, podocytes cover the outer surface located in Bowman's space. Glomerular capillaries are covered by several podocytes that are interconnected together through their interdigitating foot processes along the capillary surface. In addition to the location, the unique architecture of the podocytes render them targets in many renal diseases. The major processes extend from the cell body and branch out as foot processes. The basal membrane of each foot process adheres to the GBM and establishes an interdigitating pattern with a foot process from a neighboring cell. At the interface of two opposing foot processes, a number of proteins are found, including nephrin, CD2-associated protein (CD2AP), transient receptor potential 6 (TRPC6) ion channel, podocin, P-cadherin, β-catenin, ZO-1, and NEPH1. Together, these proteins form the slit diaphragm a modified adherence junction that establishes the molecular sieve of the GFB.

Podocytes and glomerular injury

The maintenance of the slit diaphragm complex is critical to the sieving qualities of the glomerular filter. Indeed, many glomerular diseases exhibit reduced expression of these proteins. Alterations in podocyte function may underlie characteristic changes to podocytes that include

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foot process effacement, cell hypertrophy, apoptosis and detachment from the GBM [3, 4]. Foot processes retraction and effacement of the podocyte are the most characteristic alterations resulting in a diffuse cytoplasmic covering sheet al.ong affected areas on the GBM. The slit diaphragm ceases to exist when foot processes are effaced [3, 4]. The most established progression of kidney diseases at the cellular and molecular levels exists in DN. Therefore, DN is used as model example to evaluate the glomerular changes secondary to molecular alterations in podocyte cells. Accumulating evidence suggest that damage to, or within the podocytes and/or endothelial cells plays a key role in the initiation of DN [5–11]. The etiology of sclerotic glomeruli may be inflammatory, dysregulative and degenerative pathways - each involving dysfunctional podocytes and endothelium [12]. The inflammatory mode of sclerosis yields podocyte proliferation followed by adhesion to the parietal basement membrane to initiate sclerosis formation [13]. The 'dysregulative' model requires damage-inducing processes that promote podocyte dedifferentiation and proliferation. The so-called 'degenerative' mechanism sees a progressive loss (via apoptosis) or detachment of podocytes from the GBM. The remaining podocytes compensate for the loss of filtration capacity by hypertrophying and migrating into exposed areas of GBM. However, once a threshold of podocyte loss is crossed, parietal epithelial cells from Bowman's capsule form a bridge to the naked GBM and an adhesion tuft ensues as extracellular matrix accumulates. In recent years, patients with diabetic nephropathy (DN) benefit from multitude of treatment options. Accordingly, newer treatments like sodium-glucose cotransporter-2 inhibitors (SGLT2i), non-steroidal mineralocorticoid receptor antagonists (nsMRA), and glucagon-like peptide-1 receptor agonists (GLP-1RA) have shown remarkable proteinuria lowering properties and and delayed the progression of glomerular damage in combination with conventional measures like dietary changes, stringent glycemic control, and renin-angiotensin-aldosterone system (RAAS) blockade. For instance, by encouraging glucose excretion and perhaps lowering podocyte damage through glucose-independent pathways, SGLT2i has demonstrated notable advantages in lowering pathologic albuminuria levels and improving renal outcomes in DN patients [14, 15]. By inhibiting mineralocorticoid receptors and lowering inflammation and fibrosis, nsMRA, such as finerenone, was shown to lower proteinuria and maintain renal function [16]. GLP-1RAs have demonstrated possible kidney protective properties, such as lowering albuminuria, in addition to their role in glucose regulation [17]. Although research on their impact on podocyturia in particular is still ongoing, preliminary data indicated that they might have protective effects on podocyte survival and function [17].

Additionally, there are currently a number of therapeutic options for primary glomerular disorders linked to podocyturia, including minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS), and IgA nephropathy, that are either available or currently under investigation in clinical trials. Therapies including immunosuppressants, corticosteroids, and the complement inhibitor eculizumab have demonstrated potential in slowing the course of IgA nephropathy [18]. New treatments for FSGS that target the immune system or podocyte function, like sparsentan, a tyrosine kinase inhibitor, and rituximab, an anti-CD20 monoclonal antibody, have shown notable benefits in reducing proteinuria and maintaining kidney function [19, 20]. These include new small compounds, immunomodulatory treatments, and targeted biologics, all of which have potential for controlling podocyte damage and halting the development of glomerulosclerosis. While lower levels of attrition (~20%) result in persistent albuminuria without scarring, evidence from genetically generated glomerulosclerosis rodent models indicated that podocyte loss surpassing a threshold of 40% causes irreversible disease development and progression [21]. The latter emphasizes the importance of early intervention to maintain podocyte integrity and prevent permanent damage. Thus, optimized treatment plans will require an understanding of the mechanisms by which newly developed drugs affect podocytes and the entire glomerular apparatus. Accordingly, podocyturia can be an attracting biomarker nor only to detect early reversible glomerular damage, but also can be used to monitor the efficiency of a selected clinical pharmacologic intervention.

Podocytopathy

Although the physiological function of podocytes in the kidney is well established, its importance has become more prominent in the etiology of kidney diseases. Several diseases that cause kidney injury, in fact, occur at the level of the podocyte and are defined as *podocytopathies* [22]. Early kidney disease progression can irreversibly alter the molecular composition of the podocyte slit diaphragm. Previous studies illustrated that various mechanisms can lead to podocyte impairment including loss of the slit diaphragm integrity, alterations in podocyte charge at the level of the GBM, podocyte loss and detachment, as well as apoptosis [23, 24]. Interestingly, podocyte loss and foot processes effacement are hallmark of several kidney diseases including membranous nephropathy (MN), focal and segmental glomerulosclerosis (FSGS), HIV-associated nephropathy (HIVAN), minimal change disease (MCD), diabetic nephropathy (DN), crescentic glomerulonephritis, and thrombotic microangiopathies [3, 11]. Because podocytes are major contributors to the formation and maintenance of a functional

glomerular filtration barrier, it is not surprising that all forms of proteinuria and nephrotic syndromes are associated with podocyte injury [25]. Of note, the number of existing podocytes remains unchanged postnatally [26]. In addition, cell culture data suggested that differentiated podocytes have no proliferative activity [22]. Glomerular diseases might cause inevitable podocyte exhaustion by vacuolization and subsequent detachment from the underlying GBM. As podocytes detach secondary to injury, they are subsequently shed into the urine [27]. Thus, the presence of podocytes or podocyte markers in urine is termed *podocyturia*.

Podocyturia

Podocyturia or presence of podocytes in urine is currently considered a promising tool to follow glomerular damage secondary to chronic illnesses. It is evidenced by the identification of viable podocytes by immunostaining or detection of mRNA of podocyte markers in urine such as, but not limited to, podocin and nephrin. Growing body of evidence suggested that loss of podocytes into the urine is the hallmark of an early phase of glomerular disease progression where values of kidney function and albuminuria are still within the normal range [28, 29]. Regardless of the involved chronic illness, early kidney damage progressing toward established chronic kidney disease (CKD) will eventually cause podocyte injury and/or loss prior to clinically detect signs of kidney damage including microalbuminuria. Unfortunately, no human data are yet available to demonstrate the accuracy of using urinary podocyte markers as a tool to monitor disease progression. Several animal models emphasized the importance of podocytes in glomerular function and demonstrated that the loss of podocytes precede glomerular damage [30]. Accordingly, albuminuria was evident after 30–40% of podocytes were lost [31]. This early stage of podocytes loss preceded the presence of microalbuminuria and remains associated with normal kidney function. Wickman et al. showed that urinary podocyte mRNA was significantly increased prior to remission of kidney diseases in different cohorts of adult and pediatric kidney patients [32]. It is noteworthy to mention that podocyte markers can still be found at baseline levels in normal individuals with no known previous chronic illnesses [32]. Such observation does not necessitate further investigation, as it can be explained by the normal aging process. It is highly likely that podocyturia can reflect disease progression and remission but the threshold of podocyte loss after which glomerular damage is irreversible is still controversial.

Limitations of podocyturia as a biomarker

The full clinical usefulness of podocyturia remains a challenge because present evidence demonstrates various obstacles that decrease its actual value due to increased results variability. Medical detection methods that identify podocytes in urine samples combined with clinical population characteristics and collection timing procedures are among the factors observed in data inconsistencies. While different evaluation outcomes for podocyturia with high sensitivity and specificity were documented in early glomerular damage, much less agreement demonstrated in non-diabetic kidney diseases [28, 29].

Urinary podocyte mRNA levels are significantly increased before kidney disease remission but with various expression patterns between patient groups [32]. Early detection of type 2 diabetic nephropathy suggested that urinary podocyte mRNAs preceded microalbuminuria but the clinical threshold for podocyte damage-induced glomerular vulnerability remains uncertain [33]. Thus, standard detection and measurement methods for podocytes to minimize test errors and strengthen the clinical value of podocyturia biomarkers are not fully validated.

The detection of podocytes faces further challenges in urine analysis because of their limited numbers and co-existing urinary particles that may generate either false-positive or false-negative results based on the selected detection approach [27, 34].

Both physiological elements like diurnal variation, hydration status and medical conditions including hypertension and cardiovascular disease influence podocyturia measurement, which affect its effectiveness as a biomarker [33, 35].

Also, some podocytes markers are expression in other type of cells. Of note, podocalyxin is expressed in endothelial cells, platelets and other cell types that may results in inaccurate experimental data readings [30, 36]. Pool of podocyte-specific markers e.g., nephrin and podocin should be used for better detection accuracy of podocyturia because they reduce data bias and enhance the diagnostic precision [23, 37]. Theses markers show reduced expression levels during early stages of the disease making their application challenging [22].

Detection of podocytes and podocyte-specific mRNA and proteins in urine

Podocyte loss is an important factor in glomerular disease development. The recent rationale justifies that abnormal presence of podocytes in urine as a potential marker of disease activity and resultant prognosis [32, 34]. Many techniques have been employed to detect the presence of podocytes in urine. Detection of podocyte-related proteins and mRNA as well as cytology and urinary podocyte cultures are the mainstay of podocyturia-related studies. Podocyturia is a promising future clinical test and may be superior to existing diagnostic

techniques. Of note, the implications and limitations of podocyturia were previously discussed in many kidney related illnesses [38]. Conventional methods, including assessing serum creatinine and albuminuria, frequently identify kidney impairment at a later stage, when irreversible damage already occurred. On the other hand, podocyturia offers the possibility to detect glomerular damage earlier at "pre-microalbuminuric phase of the disease, where disease-modifying treatments can still be possible. Thus, early therapeutic interventions may show significant positive clinical outcomes and either stop or prevent kidney function deterioration. Furthermore, podocyturia provides a dynamic and simple urine monitoring test that is useful in assessing treatment outcomes and directing individualized care plans and most importantly ensure patient's compliance due to its non-invasive aspect. This highlights its potential as a better alternative/addition to existing techniques, especially in high-risk groups such as kidney transplant, diabetic nephropathy, IgA nephropathy, and preeclamptic patients.

The most utilized markers of urinary podocytes in research are CD2-Associated Protein (CD2AP), podocalyxin (PDX), nephrin (NPHS1), podocin (NPHS2), synaptopodin (SYNPO), glomerular epithelial protein-1 (GLEPP-1), and Wilms' tumor-1 (WT-1). Whereas nephrin, CD2AP, synaptopodin and podocin were used in both mRNA and protein-based detection techniques, podocalyxin, GLEPP-1 and WT-1 are mainly used in protein-based detection of podocyturia. Semiquantitative RT-PCR is the most common technique used in the recognition of podocyte related mRNA in urine [27, 34]. On the other hand, ELISA and western blotting [26], and immunofluorescence [39, 40] have been frequently employed in the detection of podocyte-related proteins in urine. For assessing podocyte ultrastructure, electron microscopy has long been the gold standard because it offers unmatched insights into its complex architecture, including cytoplasmic vacuolization, slit diaphragm changes, and foot process effacement [26]. This method provides useful diagnostic and prognostic information for a number of glomerular illnesses, including diabetic nephropathy, focal segmental glomerulosclerosis, and preeclampsia, by enabling the detailed observation of subcellular alterations in podocytes. Super-resolution microscopy, atomic force microscopy, and podocyte-specific molecular imaging are examples of more recent developments that provided supplementary or alternative methods with improved accuracy and wider applicability. These new instruments have the potential to advance our knowledge on podocyte pathophysiology and enable the early identification of glomerular damage. A more thorough assessment of podocyte shape and function can be obtained by combining the above-mentioned various approaches, in order to advance nephrology research and related clinical applications.

Markers

Podocalyxin (PDX) is a glycoprotein that is by far the most commonly used protein marker for podocyte detection in urine [30]. However, its significance in research was countered by the fact that PDX expression is not podocyte specific. According to Vogelmann et al., only 30–40% of cells staining positive for PDX, also stained positive for other podocyte specific markers. Conversely, positively stained cells for other podocyte-specific markers showed positive staining for PDX (2). PDX was also detected in endothelial cells, platelets, megakaryocytes, hemangioblasts, and parietal epithelial cells (PECs) [3, 8, 11, 31, 34, 41, 42]. Therefore, the use of PDX as a marker for podocyturia remains debatable because the amount of PDX shed in the urine cannot be podocyte-exclusive [36].

Nephrin and podocin are protein components of the slit diaphragm and are highly specific for podocytes when used in conjunction [23]. However, they are less used for detecting podocyturia since their expression seems to be significantly downregulated in early disease states [22].

Another podocyte specific protein is synaptopodin, an actin cytoskeleton-associated protein, which orchestrates actin organization and cell motility within the podocyte [43, 44]. Similar to nephrin and podocin, synaptopodin expression is reduced in biopsies of patients with renal diseases [45], thus, synaptopodin is recognized as a marker of podocytes loss.

GLEPP1 is a membrane-bound protein-tyrosine phosphatase that regulates the structure and function of the foot processes [43]. Alternatively, WT-1 is a zinc finger protein distinctive for adult podocytes and responsible of transcription regulation of both PDX [37] and nephrin [46]. Both GLEPP1 and WT1 were used as markers to identify urinary podocytes, but they are usually not applied as single markers. Their clinical use may be comparable to synaptopodin, owing to the fact that these markers are strongly reduced in various disease states [47–50].

CD80, another name for B7-1, is a costimulatory molecule that has historically been linked to immunological activation via T-cell regulation [51]. However, previous studies showed that CB80 overexpression is highly relevant in the pathophysiology of a number of renal disorders [52–54]. When podocytes are stressed or injured, as in minimal change disease (MCD), lupus nephritis, and diabetic nephropathy, CD80 expression is be upregulated. Proteinuria and foot process effacement secondary to aberrant CD80 overexpression can also compromise the actin cytoskeleton [37]. Furthermore, CD80 might contribute to the development of the illness by mediating

immunological activation and inflammation in the glomerular milieu. In MCD and other proteinuric disorders, targeting CD80 has demonstrated therapeutic promise, highlighting its potential as a renal biomarker and therapeutic target [55]. Given its complex function, CD80 is a crucial mediator between systemic immune dysregulation and podocyte failure in glomerular disorders.

Podocyturia and diabetic kidney disease

Diabetic kidney disease (DKD) is considered as one of the major causes of kidney failure [56, 57]. The incidence of DKD is increasing worldwide due to the increasing prevalence of type 2 diabetes, largely driven by increased incidence of obesity [58]. In addition, obesity and associated clusters of risk factors for the metabolic syndrome including insulin resistance, dyslipidemia and hypertension can contribute to the progression of DKD. These metabolic derangements likely interact and increase the severity of kidney injury. Because kidney failure is a major public health concern, and diabetic glomerulopathies comprise a significant proportion of these patients, it is essential to understand its molecular basis in order to develop effective treatments and preventative strategies. The early clinical hallmarks of diabetic nephropathy include an increase in glomerular filtration rate (GFR) with associated elevations in intraglomerular capillary pressure (P_{GC}), increased albumin excretion in urine and glomerular hypertrophy [59, 60]. Renal biopsy often shows nodular glomerulosclerosis, diffuse intercapillary glomerulosclerosis, mesangial expansion and extracellular matrix deposition [61]. Interestingly, obese individuals and diabetic patients show similar early changes in kidney function including hyperfiltration and increased albumin excretion in urine [62]. Moreover, the glomeruli of both groups are characterized by glomerulomegaly, mesangial expansion and podocytopenia (loss of podocytes) leading to focal glomerulosclerosis [62]. Finally, adipose tissue in both patient groups is marked by macrophage infiltration and acts as a reservoir for various types of pro-inflammatory mediators [63].

Loss of podocytes in diabetic nephropathy is a pivotal factor in the advancement of kidney disease; this is primarily because podocytes are key player in maintaining normal glomerular filtration barrier that becomes compromised as diabetes progresses [56, 64]. Furthermore, podocyturia has garnered considerable attention as an early indicator of diabetic nephropathy, which reflects glomerular injury and podocyte dysfunction. Accordingly, it was shown that podocyturia precede microalbuminuria in patients with progressed type 2 diabetic nephropathy [33]. Also, several studies have indicated that podocyturia can be detected in individuals with type 2 diabetes mellitus even before microalbuminuric stage manifests [65]. Vlad et al. (2–17) HMG-CoA reductase inhibitors reduced urinary podocytes excretion as well as tubular damage in type 2 diabetes mellitus patients [66]. Urinary podocytes, podocyte-associated chemicals, and indicators of proximal tubule dysfunction were all markedly decreased by atorvastatin and rosuvastatin [66]. However, further research is needed to determine the best dosage and length of treatment to validate the results and optimize therapeutic effectiveness. Thus, podocyturia holds the promise of functioning as an early diagnostic instrument for diabetic nephropathy and a biomarker for disease progression.

Podocyturia and preeclampsia

Preeclampsia is a debilitating and life-threatening disease characterized by microvascular damage that can cause kidney damage and progression to end stage kidney failure. Various molecular techniques used to detect podocyturia (quantitative PCR [67, 68], Mass spectrometry [69–71] or immunohistochemistry [72]), documented an association between podocyturia and preeclampsia manifestation [73–76]. Preeclamptic women manifest acute and transient podocytes loss in the urine accompanied by proteinuria [77]. Others found significant association between nephrinuria, proteinuria and podocyturia [75]. In addition, podocyturia preceded proteinuria and was found as an early sign of preeclampsia [74, 78]. At the molecular level, preeclamptic podocytes were characterized by loss of slit diaphragm proteins, alteration of podocyte's phenotype, as well as a decrease in GLEPP1 and nephrin expression levels [79–81].

Podocyturia and Fabry disease

Fabry disease is a rare and hereditary condition that affects roughly 1:8,454 to 1:117,000 men and 1 in 100,000–160,000 women [82]. The synthesis of the enzyme alpha-galactosidase A is influenced by this illness [83]. It aids in the breakdown of globotriaosylceramide (GL3), a fatty molecule. GL3, when accumulating the in the body, can injure cells in many different organs including the kidneys causing Fabry nephropathy [83]. Interestingly, Podocyturia occurred early in Fabry nephropathy [84]. Furthermore, patients with Fabry nephropathy have lower podocalyxin to synaptopodin ratios that is used a measurement of the quantity of glycocalyx on the podocytes. Glycocalyx acts as a protective coating made of sugar molecule involved in blood filtration. Therefore, damage to the glycolalyx in Fabry nephropathy could result in impaired kidney function. The latter was highlighted by a cross-sectional study conducted by Trimarchi, H., et al., (2016) which found that urinary CD80 levels which is a protein expressed on the surface of podocytes, are significantly increased in Fabry disease patients compared to the control group [85]. The results of these studies imply that podocyturia

might be an important diagnostic tool. Additionally, podocyturia levels and estimated glomerular filtration rate (eGFR) were found to be inversely associated [86]. eGFR declines as renal disease becomes more advanced. This negative and significant association between podocyturia and eGFR in Fabry nephropathy indicates that podocyturia could serve as an early diagnostic method. Enzyme replacement therapy (ERT) substituting for the missing alpha-galactosidase A enzyme, has been studied for its efficacy in Fabry disease [87]. Accordingly, ERT was effective in reducing Fabry disease's symptoms. Furthermore, Trimarchi, H., et al., (2016) examined whether Fabry patients receiving placebo or ERT developped podocyturia [85]. Thus, podocyturia was more prevalent in untreated patients compared to the treated patients' group. Additionally, untreated patients with podocyturia showed worse kidney function outcomes. These findings suggested that ERT could serve as an effective treatment for Fabry disease and that podocyturia can be an effective follow-up biomarker.

Podocyturia and IgA nephropathy

The detection of podocyturia in IgA Nephropathy (IgAN) patients indicated glomerular damage and correlated with the level of disease severity and progression [88]. Podocyturia was demonstrated to be associated with increased proteinuria, a key clinical feature of IgAN, but importantly can serve as a non-invasive biomarker for early diagnosis [89]. Moreover, the level of podocyturia has been linked to the degree of histological damage observed in renal biopsies, suggesting its potential use in monitoring disease activity and response to treatment [90]. Early identification of podocyturia can facilitate timely therapeutic interventions, potentially slowing the progression of IgAN and preserving renal function [40]. The growing body of evidence underscores the need for incorporating podocyturia assessment in the routine evaluation of IgAN patients to enhance clinical outcomes and guide therapeutic strategies. Since effective treatments frequently lessen podocyte loss, measuring urine podocytes may also aid in evaluating therapy response [40]. Podocyturia may improve the therapeutic management of IgAN by offering non-invasive insights on glomerular health, opening the door to more individualized treatment strategies.

Podocyturia and kidney transplantation

Podocyturia serves as an important biomarker in kidney transplantation, thus, providing insights into graft health and function. Following transplantation, podocyturia can indicate early glomerular injury and predict subsequent graft dysfunction [91, 92]. Elevated levels of urinary podocytes have been linked to acute rejection episodes and chronic allograft nephropathy, reflecting ongoing damage to the glomerular filtration barrier [91]. This early detection is crucial for timely intervention and improving long-term outcomes for transplant recipients. Furthermore, monitoring podocyturia can aid in identifying evidence for persistent glomerular damage and podocytes injury throughout the kidney allograft lifespan [93]. By providing a non-invasive and sensitive method for assessing graft health, podocyturia offers a valuable tool for clinicians to individualize immunosuppressive therapy and other treatments in kidney transplant patients [94]. Integrating podocyturia evaluation into routine post-transplant care could also significantly enhance the management and prognosis of kidney transplant recipients, helping to preserve graft function and prolong graft survival.

Podocyturia and cardiovascular diseases

Podocyturia may also be a risk factor for cardiovascular disease. According to research by Eid et al. (2022), patients with podocyturia have a higher chance of developing heart diseases and stroke compared to patients without the condition, and that the risk further increases as podocyturia becomes more severe [34]. Although the precise method by which podocyturia causes these health issues is still unclear. Panek-Laszczyska et al. (2018) hypothesized that podocytes generate a protein called podoplanin that can harm the blood vessel lining [95]. Such damage can cause inflammation and plaque buildup, which raise the risk of heart disease, stroke, and other illnesses. The results of these studies indicated that podocyturia is indeed a valuable marker for identifying patients who are at risk for cardiovascular diseases.

Conclusion

In conclusion, podocyturia is increasingly considered as an early sign of kidney injury secondary to a wide range of acute and chronic illnesses. In addition, it is widely acknowledged that if validated, podocyturia will be as an important non-invasive clinical biomarker to monitor the progression of kidney function in both kidney recovery and injury states.

Author contributions

Conception: Wissam H. Faour and Sola Aoun Bahous; Literature, analysis and paper writing: all authors; all authors read and agreed on the final version of the paper WHF is a previous fellow of the KRESCENT (Kidney Research Scientist Core Education and National Training) Program and SAB is a consultant nephrologist both working at the Lebanese American University Gilbert & Rose-Marie Chagoury School of Medicine.

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Data Availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Conflict of interest
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