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Article

Clinical Biochemical Diagnosis of Acute Kidney Injury Using Neutrophil Gelatinase-Associated Lipocalin (NGAL): A Narrative Review

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Abstract: Acute kidney injury (AKI) is a severe clinical disorder when the renal function starts to deteriorate rapidly, resulting in the accumulating of metabolic wastes and electrolyte and fluid imbalance. The early diagnosis of AKI has continued to pose a significant issue in clinical practice due to the fact that the traditional biomarkers, including serum creatinine and the blood urea nitrogen, tend to increase when the kidney is already damaged to a great extent. Over the recent years, neutrophil gelatinase associated lipocalin (NGAL) has been developed as a promising early biomarker to detect and monitor AKI. This narrative review will summarize the existing evidence on the clinical biochemical usefulness of NGAL in diagnosing and prognosing acute kidney injury. NGAL is a minor glycoprotein that is released by damaged tubular epithelial cells of the kidney and activated neutrophils in reaction to renal stress, ischemia or toxin damage. Because of its quick excretion into the plasma and urine within several hours of renal insult, it is a very sensitive marker of kidney damage early onset. It has been demonstrated by a considerable amount of experimental and clinical evidence that NGAL levels increase much sooner than classical renal biomarkers and allow an earlier diagnosis, risk selection, and timely therapeutic intervention. Furthermore, NGAL has presented potential usefulness in a number of clinical practices such as sepsis-related AKI, allopatric surgery-related renal injury, contrast-related nephropathy, and critical illness. These immunoassays or biosensor-based technologies of measuring NGAL have further increased its utility in clinical laboratories of routine. In view of these encouraging results, there are still certain limitations such as cutoff variability, effects of systemic inflammation as well as absence of universal standardization of tests. Altogether, NGAL is a potent biochemical indicator that would greatly enhance the early clinical diagnosis and treatment of AKI in combination with other traditional renal functional tests and clinical examination.

Keywords: Acute Kidney Injury, NGAL, Biomarkers, Renal Dysfunction, Early Diagnosis

1. Introduction

Acute renal failure (AKI) is a frequent complication among hospitalized patients, which is related to high morbidity and mortality [1]. The susceptibility of AKI development is increased in intensive care units where 10-40 per cent of the patients develop this condition, and in cardiac surgery patients, prevalence rates are 33-73 per cent and in patients with multiple organ failure 50-70 per cent. Proper and timely detection of the severity of AKI is an important element in the prognosis and treatment of patients. Serum creatinine level is the most commonly used marker to determine impairment of the kidneys [2,3]. The level of serum creatinine rises about 24-48 hours following the injury onset and therefore cannot be used during the first few initial days. Neutrophil gelatinase-associated lipocalin (NGAL) is an effective biomarker in the initial diagnosis of AKI. Its levels are very high as early as 1 hour after renal insult and they will keep being high up to 72 hours in the recovery period [4].

Acute kidney injury (AKI) has been a serious clinical dilemma, and sensitive biochemical markers are required to identify renal dysfunction before conventional markers, and neutrophil gelatinase-associated lipocalin (NGAL) is a promising biomarker in the diagnostic workflow that may guide better performance across a wide range of clinical environments, demonstrating possible results in comparison to traditional markers and exploring its use as an element of a diagnostic algorithm to prove the presence of NGAL to complement the conventional AKI biomarkers. The incorporation of NGAL in diagnostic algorithms could enhance a prompt detection of kidney injury and the guided early intervention and monitoring approaches to prevent the advancement to severe AKI and the morbidity associated with it [5,6]. The inclusion of NGAL into diagnostic algorithms has the potential to enhance the quality of timely detection of kidney damage and the implementation of early intervention and follow-up procedures to limit the disease to progress further to severe AKI and its related morbidity. We assess the justification behind the use of NGAL as a small, biomarker of tubular injury, and discuss its diagnostic value in a wide range of clinical scenarios, such as in critical illness, nephrotoxic state, and postoperative care in the present study. We also put into consideration standardized assay platforms, specimen- consideration, and implication of including NGAL into multivariate risk tools and AKI care pathways [7].

2. Background on Acute Kidney Injury

Acute kidney injury (AKI) is the condition that is marked by the sudden decline in the filtration ability of the kidney leading to the accumulation of nitrogenous wastes like urea and creatinine. The parameters to categorize AKI has changed to being merely dependent on serum creatinine as a single parameter to incorporating other clinical information on urine output and increasing levels of serum creatinine. The diagnosis should involve time, as AKI has a high morbidity and death rate. The existing diagnostic modalities do not allow prediction of AKI correctly and timely. Neutrophil gelatinase-associated lipocalin (NGAL) is the one of the most popular non-invasive biomarkers of AKI that involves the possibility of prognosticating the facility early [8,9].

The spectrum of etiologies and pathophysiological pathways that disrupt the normal renal perfusion, renal tubular functioning, and glomerular filtration is the characteristics of AKI, which requires timely biomarkers like NGAL to enhance early detection and risk stratification. NGAL has emerged as a sensitive early biomarker of tubular injury, rising prior to conventional markers such as creatinine, and reflecting neutrophil gelatinase-associated lipocalin release from injured tubular epithelial cells and neutrophils [10,11]. NGAL is also upregulated in proximal tubular cells and neutrophils in response to ischemic or nephrotoxic injury, making it an early indicator of AKI before rises in serum creatinine. This chapter reviews the biological basis of NGAL production, its kinetics after renal insult, and the implications for clinical diagnosis and risk stratification in acute kidney injury [12]. This chapter reviews the biological basis of NGAL production, its kinetics after renal insult, and the implications for clinical diagnosis and risk stratification in acute kidney injury. NGAL is rapidly upregulated in tubular epithelial cells and neutrophils following ischemic or nephrotoxic injury, leading to elevated levels in blood and urine within hours [13,14].

3. NGAL: Biochemistry and Pathophysiology

NGAL is a member of the lipocalin superfamily, which is a class of small secreted proteins that transport hydrophobic molecules in biological fluids 2. Lipocalins are characterized by a β-barrel structure with an internal binding pocket. The human NGAL gene (LCN2) is located on chromosome 9q34.11 and encodes a 178-amino-acid polypeptide. Following proprotein cleavage, the 25–amino-acid signal peptide is removed, and the active 153-amino-acid form enters blood and urine after cellular release [15,16]. NGAL is synthesized by neutrophils and is also secreted by several epithelial tissues, especially the renal tubules, in response to injurious stimuli; it thus plays a role in innate immunity and extracellular iron transport 15. In the kidney, NGAL is produced in proximal tubular cells after ischemic, toxic or infective injuries. Its transit into blood is a powerful and early AKI signal. NGAL is detectable in human blood and urine before formal serum creatinine rises. Therefore, its predictive immediate injury potential is greater than standard creatinine estimates, which are also affected by non-KIDNEY parameters. Because of these and other advantages, NGAL concentration measurements have emerged as a leading hallmark diagnostic method for AKI [17,18].

4. NGAL as a Biomarker for Acute Kidney Injury

Acute kidney injury (AKI) affects a significant proportion of hospitalized patients and is associated with increased morbidity and mortality. Neutrophil gelatinase-associated lipocalin (NGAL) was introduced as a risk marker for the early detection of AKI. The association between AKI and NGAL levels was found in several experimental toxicological studies. Most of the literature on NGAL as a novel early biomarker refers to the urinary form of the protein (uNGAL), although other studies assessed the plasma form (pNGAL) [20,21]. In adults, plasma NGAL appears to be preferable due to the shorter half-life (approximately 3 hours) and the often-sustained elevation of uNGAL after the initiation of kidney injury, which prevents its use as an early marker. Different protocols for the measurement of pNGAL exist and some agree well with the widely used uNGAL assays, suggesting that single measurement of either form within a few hours of an acute event would allow a timely diagnosis of AKI [22].

The organ-protective role of NGAL during the acute inflammatory response and its early release in a variety of acute stress conditions, including AKI, highlight its potential as a noninvasive early risk marker in critically ill patients [23]. Such detection remains nevertheless limited as NGAL can participate in non-injury-related processes and different sources determine the biological relevance of variations in its concentration 1. A significant increase of pNGAL suggests an organ injury or an acute stressed state but is not sufficient for AKI diagnosis. Its applicability to kidney injury would be made clear by the integration of clinical data and the use of programmed algorithms [24].

NGAL has proven to be a powerful, early biomarker of acute kidney injury, which is related to tubular damage and response to inflammation, and rapidly increases in plasma and urine during the first hours of injury and is associated with severity and prognosis, and therefore supports early onset of nephroprotective interventions and closer monitoring of patients. results also predict long-term outcomes, allowing risk stratification and determining therapeutic interventions in the management of AKI [23]. In that regard, NGAL can be used as an early warning of tubular injury and inflammation to enable clinicians to recognize patients at the risk of transition to multiorgan dysfunction and exhibit better timelines to nephrology care. (continued): and renal recovery, NGAL measurement can be used to guide decision-making around early nephroprotective strategies and timely nephrology consultation, ultimately improving patient outcomes in acute kidney injury. Serial NGAL evaluations could also be used to aid in tracking the response to therapy and subclinical worsening, prior to increases in serum creatinine being detected [23,24]

5. Analytical Methods for NGAL Measurement

NGAL (neutrophil gelatinase-associated lipocalin) is a small-secreted protein involved in several biological processes, including the transport of small molecules and modulating inflammation. It is considered a promising new biomarker for acute kidney injury, providing an alternative to

conventional biomarkers such as serum creatinine and urinary output, which reflect a state of kidney injury rather than a specific early injury signal [25]. Monitoring NGAL is relevant in various clinical settings, including renal transplantation, cardiac surgery, and critical care, to predict the onset of AKI 25. Such measurements can identify patients at increased risk for AKI and warrant closer monitoring or intervention to delay or prevent progression to more severe AKI [26].

NGAL is elevated in serum from patients with acute kidney injury due to a broad array of insults, including ischemia, toxicity, sepsis, obstruction, or other acute processes not directly affecting the kidneys. It is also expressed in various extrarenal tissues, including the nasal epithelium and the intestine 26. The NGAL protein tends to be enzymatically degraded after release, so levels fall rapidly if an insult has resolved and the protein can no longer be produced. As AKI is an insult that compromises, or at least temporarily halts, the ability of the kidneys to produce a variety of substances, the elevation of NGAL during acute injury distinguishes it from other clinical scenarios where renal function eventually recovers [27,28].

The clinical practice of analytical evaluation of NGAL demands a strong assay validation to determine specificity, sensitivity, and reliability across various populations of patients including established protocols of sample management, comparison to defined reference standards and strict quality control procedures to warrant credible interpretation of data with regards to acute kidney injury. Also, to assure good performance of the NGAL measurement in AKI assessment, the assay performance was to be tested in terms of analytical sensitivity (limit of detection and limit of quantification), linearity in the clinically relevant range, precision (inter- and intra-assay variability), and possible presence of matrix effects in serum, plasma, or urine samples. Such measures as the creation of cross-matrix equivalence, the evaluation of the potential interference of common biologic constituents, and standardized calibration procedures should be implemented to allow comparable interpretation of NGAL products in AKI diagnosis and prognosis across various patient groups. evidence-based thresholds, quality controls, and standardized reporting are needed in clinical practice, to assure that the analytical products of NGAL can be uniformly applied across laboratories. This and the demand need intense assay validation such as calibration curve integrity, limit of detection, linearity, interference studies and strong quality control measures. Standardized reporting should encompass assay methodology, specimen type, pre-analytical handling, reference ranges, and population-specific cutoffs to facilitate comparability and meta-analytic synthesis for AKI diagnosis and prognostication. effects on diagnostic performance across diverse populations. Standardized reporting should also specify the assay platform (e.g., ELISA, chemiluminescent immunoassay), lot-to-lot verification, calibration procedures, and any sample matrix considerations (plasma vs. serum) to support cross-study comparability and robust meta-analyses in AKI characterization. serum) to support cross-study comparability and robust meta-analyses in AKI characterization. Comprehensive analytical methods for NGAL measurement should include standardized pre-analytical handling, validated assay platforms (e.g., immunoassays with NGAL-specific antibodies), and rigorous quality control procedures to ensure reproducibility across laboratories and populations [28].

6. NGAL in Different Clinical Settings

Neutrophil gelatinase-associated lipocalin (NGAL) is a promising noninvasive biomarker for the diagnosis and prognosis of acute kidney injury (AKI) in different clinical settings. With rapidly changing AKI diagnostic criteria, the clinical need for NGAL testing has surged. NGAL is significantly elevated in patients with AKI induced by various aetiologies. For example, in the critically ill, NGAL is a valid diagnostic option in infections where sepsis is the most common cause of AKI. Its suitability is related to the frequent association of these conditions with acute tubular injury [29]. A population study involving patients undergoing percutaneous coronary intervention (PCI) for acute coronary syndrome indicated that NGAL was a promising multifactorial AKI biomarker applicable in settings where creatinine increase was multifactorial. In cirrhosis, NGAL is an early biomarker in AKI caused by sepsis where other methods had limited predictive capability. Because NGAL remains elevated in some patients after sepsis resolution, it may also reflect other acute events [29].

In septic children, raised NGAL levels occur with or without AKI. Early determination in these patients enables risk assessment during a critical stage of the disease. NGAL measurement has emerged as a versatile biomarker in diverse clinical contexts beyond traditional AKI assessment, including nephrotoxic injury, sepsis, cardiac surgery, and critical illness, where its rapid rise in plasma and urine can facilitate early risk stratification, timely intervention, and improved patient management. NGAL measurement has emerged as a versatile biomarker in diverse clinical contexts beyond traditional AKI assessment, including nephrotoxic injury, sepsis, cardiac surgery, and critical illness, where its rapid rise in plasma and urine can facilitate early risk stratification, timely intervention, and improved patient management. In both environments, NGAL has the potential to supplement traditional renal function testing by detecting subclinical tubular injury, directing nephroprotective efforts, and tracking therapeutic response to prevent the development of overt AKI [30]. in the acute care setting, NGAL has the potential to be helpful as an early biomarker of tubular injury, allowing risk stratification and timely nephroprotective intervention. NGAL measurements can also be used with traditional markers of acute kidney injury (creatinine and urine output) to detect injury early and to guide escalating care, including prompt mitigation of nephrotoxic exposure, fluid balance, and consideration of renal replacement therapy when indicated before data interpretation can occur [31]. before the data interpretation can be performed, NGAL changes over time can be used to distinguish between intrinsic and prerenal AKI and to promptly mitigate nephrotoxic exposure, fluid balance, and renal replacement therapy when indicated. About the NGAL measurements, in this section, the results are discussed in various clinical contexts in order to demonstrate their diagnostic and prognostic value. Here, the NGAL measurements have been discussed in various clinical contexts to demonstrate their diagnostic and prognostic value. In particular, NGAL is analyzed in the context of acute kidney injury (AKI) and helps to identify tubular damages, predict risks, and track renal recovery, and in the general critical illness scenarios to learn about its functions as a biomarker of tubular damages and inflammation [32].

7. Interpretation of NGAL Levels and Diagnostic

NGAL measurements offer a rapid, specific biomarker-based approach to interpreting renal tubular injury, enabling risk stratification and differentiation between prerenal and intrinsic AKI while guiding timely therapeutic decisions [33]. NGAL measurements offer a rapid, specific biomarker-based approach to interpreting renal tubular injury, enabling risk stratification and differentiation between prerenal and intrinsic AKI while guiding timely therapeutic decisions. In clinical practice, NGAL levels rise early after tubular damage, often preceding creatinine elevation, which enhances early diagnostic accuracy and supports prompt intervention to mitigate progression and improve patient outcomes. and this enables clinicians to distinguish NGAL elevations due to acute kidney injury from other causes. In this context, NGAL levels are interpreted alongside clinical signs, imaging, and complementary biomarkers to refine staging and guide timely therapeutic decisions [34]. The interpretation of the NGAL results should be done in the clinical context that takes into account the baseline renal function, comorbidities, and concurrent biomarkers to differentiate AKI and chronic kidney disease or other sources of tubular injury. The interpretation of the thresholds should be made in regard to defined cutoffs and calibration assay. NGAL levels in AKI begin to increase several hours post injury and may also be associated with the extent of tubular injury; relative changes will be dampened by lower NGAL baseline values in subjects with stable CKD or chronic tubular stress [35,36]. Thus, to be interpreted NGAL and classic biomarkers (creatinine, urine output) and imaging observations, including the time after injury. When the NGAL levels are mild or discordant to clinical presentation, other etiologies (ischemia, nephrotoxins, inflammatory conditions) and the retesting of the levels to determine the trend are to be taken into consideration. The inclusion into a diagnostic algorithm should be based on the priorities of dynamic changes over single-point values and be related to the context of the patient and comorbid conditions. Moreover, the NGAL levels have the ability to signify the presence of tubular damage and inflammation, and the use of NGAL in combination with other biomarkers, e.g. uNGAL/Cr or plasma NGAL, can enhance the diagnostic value of the AKI development and progression in the clinical course [37,38].

8. Comparative Effectiveness: NGAL versus Traditional Biomarkers

NGAL is an improved biomarker over conventional ones especially in the case of early or physiologic AKI. In a systematic review and meta-analysis, the comparative accuracy of different biomarkers including those with NGAL to predict hospital-acquired AKI was tested in 2022. Tests containing NGAL had been linked to the highest predictive values in the medical patients and with urinary NGAL, the number required to test to predict AKI was less than other known biomarkers [39]. Urine samples may also be challenging to collect at an early period in patients undergoing major surgery and serum creatinine is a gold standard in AKI diagnosis. Plasma NGAL makes possible a successful screening during the transition phase. The longitudinal behaviour of biomarkers is an effective tool in critically ill patients because it can be tested at the initial admission and at successively a longer time interval. At successively longer time points, 2 sets of biomarkers containing NGAL have a fixed predictive power [40].

NGAL has become a strong complement to traditional markers of renal injury, offering earlier identification and better sensitivity in a wide range of clinical settings, and underlining the shortcomings of this protein in terms of specificity and non-renal effect on its concentrations. NGAL has become a potent addition to traditional markers of renal injury and demonstrates earlier expression and greater sensitivity in a wide range of clinical settings, and points out shortcomings in specificity and the effects of non-renal influences on its concentrations. With regard to comparative studies, NGAL tends to show an early rise in contrast to creatinine, cystatin C and the established urine output measures, making it possible to stratify the risk in a timely way [41].

Nevertheless, variability of assay systems and pretreatment conditions may also be a factor in absolute values, and the NGAL increase could be observed in non-renal inflammatory conditions, infection, or overall comorbidity. Thus, a pragmatic approach is to use NGAL together with proven biomarkers to improve the diagnostic accuracy, and section 8 will involve translating findings into a comparative framework, where NGAL will be balanced against conventional biomarkers, to define its incremental value to early AKI detection, prognosis, and therapeutic decision making. and in order to quantify NGAL added value over traditional biomarkers, such as serum creatinine and urine output, we would compare sensitivity, specificity, and predictive values of early AKI detection In this regard, NGAL shows better early diagnosis in high-risk patients of AKI, which allows earlier stratification of risks and may also serve as a predictor of proactive management [41,42].

Initial research shows that NGAL provides incremental value above other conventional biomarkers like creatinine, BUN, and urine output. NGAL can enhance sensitivity in the detection of AKI on a first-line basis, within the first few hours after the renal insult, and in conjunction with conventional biomarkers, including serum creatinine, urine output, and cystatin C, can be used to improve risk stratification and facilitates timely intervention and optimization of the nephroprotective response. NGAL can be used to identify tubular injury earlier than creatinine increase and is associated with severity of AKI, and guide escalation of monitoring, hydration optimization, and nephrotoxic avoidance [42,43]. NGAL can be used to refine prognostic models, distinguish prerenal and intrinsic AKI, and improve the ability to assess eligibility to renal replacement therapies when combined with traditional markers, thereby improving eligibility of patients to undergo renal replacement therapies, timely escalation or de-escalation of care, and predicting AKI progression. Within this comparative context, NGAL illustrates the earlier identification of tubular injury that allows clinicians to institute nephroprotective measures earlier, personalize fluid management, and modify medications that can aggravate kidney performance, and unnecessary escalation in low-risk patients. Within this framework of comparison, NGAL exhibits different temporal profiles than conventional biomarkers including creatinine, cystatin C and measures of urine output levels; NGAL increments may precede observable creatinine variants, thus allowing AKI to be diagnosed earlier and appropriate therapeutic changes to be made. When NGAL is used together with traditional biomarkers, it may improve the classification of risks, especially in cases when a patient has the high baseline risk or has co-morbid factors like sepsis or exposure to nephrotoxins. The section puts forward possible benefits of precision medicine, but it also mentions such weaknesses as assay standardization, biological variance and cost. Finally, the

NGAL-based approaches may optimize the discharge planning, triage on the basis of biomarkers, and resource distribution and lead to better long- and short-term renal and cardiovascular outcomes [43,44].

9. Limitations and Confounding Factors

Acute kidney injury (AKI) is a heterogeneous disease, and it leads to dysfunction of filtration and excretion of nitrogen waste. The AKI has high mortality and morbidity meaning that it should be diagnosed at an early age. Based on this, the plasma neutrophil gelatinase-associated lipocalin (NGAL) has been suggested as a potential AKI-biomarker [44].

Clinical utility of NGAL as an early biomarker of AKI is determined by reliability and accuracy of analytical methods of measurements and clinical scenarios. Volume and perfusion assessment indices may be useful in stratifying AKI risk during invasive procedures in which a contrast media or nephrotoxic drug is used [45].

In intensive care conditions, AKI is quite common but still an 80% mortality rate and high readmission rate of patients are recorded despite the low-care intensive treatment and ongoing observation of vital signs. Transflection of NGAL, hemoglobin and pretransfusion model-based estimated blood volume, and blood loss is a paradigm schema in normohydrated normotensive AKI-prone patients undergoing high-risk surgery [44,45].

10. Future Directions in NGAL-Based Diagnosis

NGAL-based diagnostics have potential to predict acute kidney injury at an earlier stage and make decisions, and future research centered on harmonization of assay protocols, establishing clinically significant thresholds, and translating biomarkers signals into clinical actions may be valuable in prospective, multicenter trials [46].

Provisions of NGAL-based diagnostics can provide an opportunity to detect nephron injury earlier and make timely therapeutic decisions based on the consistency of assay protocols, identification of clinically meaningful thresholds, and confirmation of utility in different patient populations in prospective, multicenter studies. In the long run, the combination with supplementary biomarkers and imaging information may provide more refined risk stratification, inform nephroprotective interventions, and valuable individual management approaches of patients at risk of AKI. In the long run, the combination with supplementary biomarkers and imaging information may provide more refined risk stratification, inform nephroprotective interventions, and valuable individual management approaches of patients at risk of AKI. Here, NGAL has the potential to be included in multi-marker assays to augment early disease identification, supervise therapeutic reaction, and predict the time to initiate renal replacement treatment as a part of a precision medicine strategy in nephrology. Future studies need to consider standardized assay platforms, develop threshold values in various patient groups, and study NGAL dynamics relative to etiology, severity, and recovery curves to inform individualized management decisions. and allows cross-validated thresholds, harmonization across multiple centers, and dynamic monitoring of NGAL relative to other biomarkers to improve early AKI detection and risk stratification [47]. The next-generation work must entail the incorporation of NGAL with new biomarkers, machine learning to harness the timing and thresholds, and validation of NGAL-based algorithms in different populations of patients and clinical environments to improve the level of diagnostic accuracy and prognostic potential of acute kidney injury [48].

11. Conclusion

Neutrophil gelatinase-associated lipocalin (NGAL) has been widely recognized as a valuable biomarker for the early diagnosis of acute kidney injury (AKI). Numerous studies have demonstrated its utility, resulting in a surge of interest from both academic researchers and commercial companies globally 3. Sequential block, sandwich-enzyme-linked immunosorbent or lateral flow assays for serum and/or urine NGAL evaluation are highly sensitive and selective, with a number of commercial kits based on the human NGAL molecule now widely used. NGAL testing is included in clinical protocols

adopted in many intensive care units. Nevertheless, NGAL measurement remains costly and may not be routinely available in low-income settings. Research continues to pursue simpler approaches, such as the development of predictive algorithms including standard clinical data or alternative AKI-associated biomarkers. These avenues aim to favourably position NGAL into clinical and minimally resourced settings. AKI is characterized by a rapid decline in glomerular filtration rate and results in the accumulation of excessive nitrogenous wastes in the blood, is associated with deteriorating outcomes in hospitalized patients. AKI exhibits a complicated underlying mechanism in which circulatory failure may not be the primary cause. The prevention of further injuries depends on early identification of patients susceptible to kidney injury 1. In cases of AKI, both urine and serum NGAL concentrations increase substantially prior to the increase of creatinine. Neutrophil gelatinase-associated lipocalin (NGAL) offers a timely and alternative approach to prediction of AKI against a background of disrupted homeostasis.

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