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The Role of Novel Biomarkers in Predicting Acute Kidney Injury in Critically Ill Patients

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ABSTRACT:

Critically ill patients are frequently affected by the common and possibly fatal illness known as acute kidney injury (AKI). To improve patient outcomes and lower healthcare costs, early detection and prediction of AKI are crucial. The existing gold standards for detecting AKI, such as serum creatinine and urine output, frequently fall short in terms of sensitivity and specificity, which causes interventions to be postponed and patient care to be less than ideal. The expanding landscape of new biomarkers for predicting AKI in critically ill patients is examined in this review paper.

Promising biomarkers with improved accuracy and early detection capabilities have been discovered thanks to recent advances in molecular and biochemical research. Healthcare professionals may be better able to spot patients at risk of AKI by assessing these unique indicators, enabling quick intervention and customized treatment regimens.

The present state of biomarker research in AKI prediction is thoroughly discussed in this review paper, along with significant advancements, difficulties, and possible therapeutic applications. We want to clarify the clinical significance and potential uses of emerging biomarkers for detecting AKI in critically unwell patients as soon as possible.

INTRODUCTION

Acute Kidney Injury (AKI), formerly referred to as acute renal failure, is a serious and frequently fatal medical illness marked by a quick and frequently reversible loss in kidney function. Critically sick patients frequently experience this serious consequence, especially those who are hospitalised to the intensive care unit (ICU). AKI has a significant effect on patient outcomes, increasing morbidity, death, and healthcare expenditures when it occurs. For these results to be improved, AKI must be promptly and accurately detected. Two key markers, serum creatinine and urine output, have traditionally been used to diagnose AKI. Although important, these indicators have some limits. Changes in renal function have a delayed effect on serum creatinine, a waste product of muscle metabolism released by the kidneys. Because of this, it is unable to offer early identification of kidney disease, and by the time creatinine levels rise, serious harm may already have been done. Additionally, alterations in the levels of creatinine due to age, muscle mass, and hydration condition may produce misleading positives or negatives [1-5].

Urine output, another measure used to diagnose AKI, presents some difficulties. Its reliability depends on the accuracy of the urine collection, and it might not effectively capture the first stages of kidney damage. Further confounding the interpretation of urine output as a measure of kidney function in the ICU setting is the possibility that patients will be given diuretics.

Due to the shortcomings of these conventional markers, intensive research has been conducted to find novel biomarkers that can provide a more precise and timely prediction of AKI in critically ill patients. A possible

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method for enhancing AKI prediction is the use of novel biomarkers, which are frequently biochemical or molecular in nature. There are many benefits to using these new biomarkers. Due to their high sensitivity and specificity, they are able to detect minor changes in kidney function, frequently before conventional measures like creatinine do. Early kidney injury detection is crucial because it creates a window of opportunity for therapies that could lessen the severity of kidney damage and enhance patient outcomes. Additionally, because these biomarkers are unaffected by variables like age, muscle mass, or hydration level, they are more accurate across a range of patient populations [1-5].

Numerous novel biomarkers have surfaced as promising candidates in recent years for the prediction of AKI in critically ill patients. These markers are frequently linked to a variety of physiological processes, including oxidative stress, cell damage, and inflammation. Despite being hopeful, the area of novel AKI biomarkers is dynamic and constantly changing. As a result, it is crucial to give an in-depth analysis of the current research state as well as the difficulties and potential outcomes in this field [1-5].

The objective of this review paper is to enlighten readers on the rapidly developing field of new biomarkers for predicting AKI in critically ill patients. It will give a thorough overview of the current research, highlighting significant advancements and difficulties that researchers are now facing. The potential clinical uses of these novel indicators in the early detection of AKI and the ensuing individualised treatment plans will also be covered.

NEW BIOMARKERS FOR AKI PROGNOSIS

Clinical research in critical care medicine is currently focused on discovering new biomarkers for the prediction of Acute Kidney Injury (AKI). Several interesting biomarkers have been discovered in the attempt to increase early diagnosis, increase accuracy, and eventually improve patient outcomes. The most significant new biomarkers being studied right now will be included in this section.

KIM-1:

Kidney Injury Molecule-1 (KIM-1) is one of the most thoroughly investigated new biomarkers for AKI prediction. Type 1 transmembrane glycoprotein KIM-1 is only weakly expressed in healthy kidneys, but it is dramatically increased in response to renal damage. Numerous investigations have shown that KIM-1 can predict AKI in a variety of clinical scenarios [1].

Due to its sensitivity and specificity for renal damage, KIM-1 is useful as a biomarker. It has the ability to identify harm at an early stage, frequently before traditional markers like serum creatinine exhibit any anomalies. For prompt intervention and better patient outcomes, this early detection capability is essential [2]. While KIM-1 shows great potential, there are still issues that need to be resolved, such as standardising testing techniques and establishing clinically significant thresholds [3].

NGAL:

Another new biomarker that has received a lot of attention is neutrophil gelatinase-associated lipocalin (NGAL). In reaction to kidney injury, neutrophils and injured renal tubular cells release NGAL, a protein. It is a useful marker for detecting early AKI because of its expression's quick rise after injury [4].

AKI can be predicted in a variety of clinical settings, including post-cardiac surgery and sepsis-related AKI, and this is where NGAL excels [5]. Concerns exist regarding NGAL's specificity for renal injury, as it can be raised in non-renal diseases such inflammation. Its interpretation in a therapeutic setting must therefore be carefully considered [6].

cyclostatin C

Low molecular weight protein known as cystatin C is produced continuously by nucleated cells and is readily filtered by the glomerulus. The potential of cystatin C to provide a more precise estimate of glomerular filtration rate (GFR) and, consequently, an early indicator of AKI, has made it a recognised new biomarker [7].

Cystatin C has a number of benefits, including the fact that it is not dependent on age or muscle mass, two variables that can alter blood creatinine values. It responds to changes in GFR more quickly and can more accurately identify people at risk for AKI [8]. Cystatin C has drawbacks since it can be impacted by non-renal variables such thyroid function and corticosteroid use [9].

CHALLENGES IN CLINICAL IMPLEMENTATION

Even while emerging biomarkers have great potential for AKI prediction, their clinical application is not without

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difficulties. In this section, we'll talk about some of the challenges that need to be overcome before these biomarkers can be used in clinical settings.

Standardization and Assay Variability:

The absence of standardised assays is one of the main obstacles to the use of new biomarkers for AKI prediction. Different reference ranges and measurement units might be produced by various test techniques and platforms, making it more difficult to understand and compare these results across research. The first steps towards a trustworthy clinical application are standardising clinical significance levels and laboratory techniques [10].

The cost and availability:

Both the price of biomarker assays and their accessibility in clinical settings are serious issues. These tests may only be used in select patient populations because not all hospitals or healthcare systems have access to them. For advanced AKI prediction tools to be accessible to all people, financial and physical constraints must be removed [11].

Scientific Validation:

A biomarker needs to go through rigorous validation across a range of patient demographics and clinical situations before it can be used in clinical practise. To persuade doctors of the biomarker's utility, solid proof must be provided for its accuracy, sensitivity, and specificity [12]. To assess the added utility of biomarkers in AKI prediction, they should also be examined in conjunction with more conventional markers such serum creatinine [10-12].

Analysis and Integration:

Another problem is how to interpret new biomarker data in the context of clinical decision-making. To obtain useful diagnostic and prognostic information, it is necessary to carefully analyse the combination of numerous biomarkers and the integration of them into already-established clinical pathways [10-12].

In order to successfully integrate novel biomarkers into clinical practise, improve the early detection of AKI, and ultimately improve patient treatment and outcomes, it is imperative to address these obstacles. The next parts will go in-depth on the prospective technological developments and multidisciplinary strategies to address these difficulties in this field of study.

Future Research Directions

Numerous intriguing new research possibilities are opening up as the field of novel biomarkers for the prediction of acute kidney injury (AKI) continues to develop. We will look at some of the potential future developments and directions in this part that could improve the ability to forecast AKI in critically ill patients.

Multi-Omics Methodologies:

Biomarker discovery is undergoing a revolution thanks to new tools in genomes, transcriptomics, proteomics, and metabolomics. A thorough knowledge of the molecular mechanisms underlying AKI is made possible by integrating data from many omics domains. These methods may help identify new biomarkers and improve on already known ones, enabling a more accurate prediction of AKI [1,5,11,12].

Machine learning and artificial intelligence:

The use of machine learning and artificial intelligence (AI) in healthcare is a rapidly growing topic. These tools are capable of analysing huge datasets, finding intricate patterns, and creating prediction models. AI can assist in the integration of multiple clinical and biomarker data in the setting of AKI prediction to enhance early detection and risk stratification [10].

Biomarker panels, which combine several biomarkers, have the potential to improve AKI prognosis. In order to increase sensitivity and specificity and produce more precise diagnoses, a panel of biomarkers that focus on several facets of kidney impairment may be used. The best way to combine these markers is still being investigated, as well as the most productive combinations [1,7].

Personalised Medicine

Healthcare is placing more and more emphasis on the idea of personalised medicine. Results can be improved by adjusting treatment plans for individual patients in light of their specific characteristics. AKI prediction research is evolving in this direction, taking into account not only biomarker profiles but also patient-specific elements such genetics, comorbidities, and medication [1,5,6,8].

Point-of-Care Testing:

There is considerable research being done on the creation of point-of-care testing tools for AKI biomarkers. These transportable, quick diagnostic instruments could make prompt decisions easier at the patient's bedside. In

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numerous clinical settings, point-of-care testing has the potential to greatly enhance AKI prognosis and patient treatment [1,9].

These upcoming research directions mark a fascinating new area for AKI prediction. They have the power to completely alter how AKI is identified, treated, and managed in seriously ill patients. Clinicians, researchers, engineers, and data scientists will all need to work together in a multidisciplinary manner to integrate these improvements.

A MULTIDISCIPLINARY APPROACH

A multidisciplinary team effort is necessary for the effective creation and application of new biomarkers for AKI prediction. We will discuss the value of a multidisciplinary approach in this part, as well as how several disciplines might advance AKI prediction.

Clinical Cooperation

The connection between research and patient treatment is crucially facilitated by clinicians. Their opinions and practical knowledge are vital for identifying clinical requirements, establishing biomarker cutoffs, and guaranteeing the applicability of AKI prediction systems in varied healthcare settings. The successful application of novel biomarkers depends heavily on close clinician-researcher collaboration [2,10].

Bioinformatics and Data Analysis:

Experts in bioinformatics and data analysts play a key role in managing the enormous amount of data produced by omics technologies and biomarker research. They can uncover the promise of new biomarkers for AKI prediction thanks to their skills in data interpretation, pattern identification, and predictive modelling. They are essential for standardising data analysis techniques and assuring reproducibility [2,13].

Science and technology

By creating cutting-edge diagnostic tools, such as point-of-care testing equipment, engineers and technologists make a contribution. Their knowledge is essential for converting research results into useable applications that may be made at the patient's bedside. Additionally, engineers can enhance the effectiveness and affordability of biomarker assays [2,12].

Control of Regulations:

Examining and approving medical diagnostics and treatments is the responsibility of regulatory authorities, such as the Food and Drug Administration (FDA) in the US. Before novel biomarkers are widely used in clinical settings, cooperation with regulatory organisations is essential to ensuring that they meet safety and efficacy requirements. A crucial step in moving biomarkers from the bench to the bedside is regulatory approval [2,3].

Advocacy for patients and morality

The direction of AKI prediction research is heavily influenced by patients and their supporters. It is crucial to make sure that the rights, opinions, and privacy of patients are respected. Multidisciplinary talks also need to carefully address ethical issues such informed permission, data sharing, and the responsible use of biomarkers [11,12].

Researchers can more easily navigate the complexity of AKI prediction and hasten the discovery and application of novel biomarkers by encouraging collaboration among these many disciplines. In order to improve patient care in high-stakes situations, multidisciplinary teams offer a complete approach that tackles clinical, technological, regulatory, and ethical issues.

CONCLUSION

In conclusion, the development of novel biomarkers for the early detection of acute kidney injury (AKI) in critically sick patients marks a major achievement in the field of critical care medicine. When compared to conventional markers, several biomarkers, like KIM-1, NGAL, and cystatin C, hold out the possibility of early detection and increased accuracy. The therapeutic application of these biomarkers, meanwhile, poses difficulties with standardisation, expense, and clinical validation.

Exciting opportunities for improving AKI prediction exist in the fields of multi-omics methods, artificial intelligence, and personalised therapy. For the discipline to advance and to guarantee that innovative biomarkers have a real influence on patient treatment, a multidisciplinary strategy involving physicians, researchers, engineers, data analysts, regulatory agencies, and patient advocates is crucial.

Collaboration between these fields will be essential to maximising the potential of emerging biomarkers as the area of AKI prediction develops, ultimately improving patient outcomes in the critical care situation.

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REFERENCE

1. Han WK, Waikar SS, Johnson A, et al. Urinary biomarkers in the early diagnosis of acute kidney injury. Kidney Int. 2008;73(7):863-869.
2. Ichimura T, Bonventre JV, Bailly V, et al. Kidney Injury Molecule-1 (KIM-1), a putative epithelial cell adhesion molecule containing a novel immunoglobulin domain, is up-regulated in renal cells after injury. J Biol Chem. 1998;273(7):4135-4142.
3. Parikh CR, Devarajan P, Zappitelli M, et al. Postoperative biomarkers predict acute kidney injury and poor outcomes after pediatric cardiac surgery. J Am Soc Nephrol. 2011;22(9):1737-1747.
4. Mishra J, Dent C, Tarabishi R, et al. Neutrophil gelatinase-associated lipocalin (NGAL) as a biomarker for acute renal injury after cardiac surgery. Lancet. 2005;365(9466):1231-1238.
5. Haase M, Bellomo R, Devarajan P, Schlattmann P, Haase-Fielitz A. Accuracy of neutrophil gelatinase-associated lipocalin (NGAL) in diagnosis and prognosis in acute kidney injury: a systematic review and meta-analysis. Am J Kidney Dis. 2009;54(6):1012-1024.
6. Singer E, Elger A, Elitok S, et al. Urinary neutrophil gelatinase-associated lipocalin distinguishes pre-renal from intrinsic renal failure and predicts outcomes. Kidney Int. 2011;80(4):405-414.
7. Dharnidharka VR, Kwon C, Stevens G. Serum cystatin C is superior to serum creatinine as a marker of kidney function: a meta-analysis. Am J Kidney Dis. 2002;40(2):221-226.
8. Laterza OF, Price CP, Scott MG. Cystatin C: an improved estimator of glomerular filtration rate? Clin Chem. 2002;48(5):699-707.
9. Murty MS, Sharma UK, Pandey VB, Kankare SB. Serum cystatin C as a marker of renal function in detection of early acute kidney injury. Indian J Nephrol. 2013;23(3):180-183. doi:10.4103/0971-4065.111840
10. Bayless RL, Moore AR, Hassel DM, Byer BJ, Landolt GA, Nout-Lomas YS. Equine urinary N-acetyl-β-D-glucosaminidase assay validation and correlation with other markers of kidney injury. J Vet Diagn Invest. 2019;31(5):688-695. doi:10.1177/1040638719867124
11. Tsuji S. et al. Sex differences in the excretion levels of traditional and novel urinary biomarkers of nephrotoxicity in rats. J Toxicol Sci 2017;42:615–627.
12. Zhang X. et al. Combined detection of urinary micro albumin, α1-microglobulin and N-acetyl-β-D-glucosaminidase in the early diagnosis of diabetic nephropathy. Pak J Med Sci 2017;33:1324–1327.