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ACUTE KIDNEY INJURY: PATHOPHYSIOLOGY, BIOMARKERS, AND MANAGEMENT (NARRATIVE REVIEW WITH SYSTEMATIC SEARCH ELEMENTS)

Michał Wabiszczewicz[1] ✉, ***Albert Lompart[2]***, ***Albert Kosarewicz[3]***, ***Łukasz Woźniak[4]***, ***Patrycja Krysiak[5]***

[1]Medunit Primary Care Clinic, Gdańsk, Poland
[2]Saint Wojciech Hospital, Gdańsk, Poland
[3]University Clinical Centre of Gdańsk Medical University, Gdańsk, Poland
[4]West Pomeranian Center for the Treatment of Severe Burns and Plastic Surgery, Gryfice, Poland
[5]Medical University of Łódź, Łódź, Poland

✉ ***michalwabi@gmail.com***

ABSTRACT

Background: Acute kidney injury (AKI) is a common complication with high morbidity and mortality, especially in intensive care. Early recognition remains difficult as current standards rely on delayed indicators such as serum creatinine and urine output.

Aims: This review summarises recent evidence on AKI, focusing on pathophysiology, classification systems, biomarkers, management strategies, and future research priorities.

Materials and Methods: A structured narrative review of the English-language literature (2015-2025) was conducted in PubMed/MEDLINE with supplementary searches in Google Scholar. Eligible studies included randomized trials, systematic reviews, meta-analyses, original research, and narrative or consensus reviews. Priority was given to large multicentre studies, systematic reviews, and biomarker evaluations. No formal risk-of-bias assessment or meta-analysis was undertaken.

Results: Hospital incidence is about 5-7.5% overall and 30-60% in intensive care. Mechanistic studies implicate ischemic, toxic, inflammatory, and maladaptive repair processes, including regulated cell death pathways such as ferroptosis. KDIGO criteria remain the standard but rely on delayed functional markers. Novel biomarkers (e.g. NGAL, KIM-1, TIMP-2/IGFBP7, IL-18, CCL14) improve early detection and risk stratification. Management centres on balanced fluid strategies, individualised timing of renal replacement therapy, and evaluation of targeted interventions.

Conclusions: Early recognition before functional decline is essential. Integrating validated biomarkers with precision fluid management and tailored renal replacement therapy may improve outcomes. Implementation requires cost-effective assays and context-specific care, particularly in low-resource settings. Future multicentre studies should refine biomarker-guided protocols and evaluate emerging pharmacologic and regenerative therapies.

Keywords: acute kidney injury, biomarkers, pathophysiology, classification, treatment, KDIGO, Acute Disease Quality Initiative, renal replacement therapy,

1. INTRODUCTION

Acute kidney injury AKI is a heterogeneous and rapidly evolving syndrome that leads to rapid loss of kidney function and remains a major global health problem with high morbidity and mortality across care settings [1]. Each year the condition affects millions. Studies show that hospital incidence is increasing, with AKI reported in approximately 5 to 7.5 percent of all admissions and in 30 to 60 percent of patients who require intensive monitoring and support in the intensive care unit ICU [2].

The relevance of AKI is underscored by its growing burden in both general and critical care [2], its strong association with excess mortality and progression to chronic kidney disease [3]. A focused synthesis of pathophysiological mechanisms, emerging biomarkers for early detection, and evolving treatment strategies is therefore clinically pertinent and aligns with the scope of this journal [2].

The clinical impact of acute kidney injury extends beyond the kidneys, because dysregulated pathophysiology can affect multiple organs and influence long term outcomes after hospital discharge. Studies show that even brief or mild episodes of acute kidney injury are associated with a higher risk of subsequent chronic kidney disease and may accelerate progression to end stage kidney failure [3].

Research in molecular biology has clarified mechanisms underlying acute kidney injury, including ischemia and hypoperfusion, direct cellular injury, inflammation, oxidative stress and maladaptive repair [4]. Studies have identified regulated cell death pathways such as ferroptosis and necroptosis, which represent potential therapeutic targets for prevention or mitigation of injury [5].

The current diagnostic approach according to KDIGO relies on serum creatinine and urine output, yet these measures often fail to detect injury early and can postpone initiation of therapy. Although serum creatinine is widely available, standardized and rapidly measured, it is a delayed indicator and may increase only after substantial nephron loss [6].

Recent studies have reported several promising biomarkers that may enable earlier detection and risk stratification compared with standard measures, including tubule specific proteins such as neutrophil gelatinase associated lipocalin (NGAL) and kidney injury molecule 1 (KIM-1), cellular stress markers such as tissue inhibitor of metalloproteinases 2 (TIMP-2) and insulin like growth factor binding protein-7 (IGFBP7), and inflammatory mediators such as interleukin 18 (IL-18) and C-C motif chemokine ligand-14 (CCL14) [7-9].

Management of acute kidney injury has evolved beyond supportive care. Current practice emphasizes more precise fluid management, clearer criteria for initiation of renal replacement therapy, and evaluation of targeted agents that modulate injury pathways [10].

This review synthesizes current knowledge of AKI pathophysiology, with particular focus on regulated cell death and maladaptive repair; evaluates emerging biomarkers relative to traditional measures for early detection and prognostication; and appraises fluid management, renal replacement therapy, and targeted interventions with respect to outcomes and safety. A further aim is to consider implementation challenges in resource-limited settings and to identify research priorities. The novelty of this work lies in integrating mechanistic insights with biomarker translation and therapeutic evidence, thereby providing clinicians, investigators, and policymakers with up-to-date findings to refine care pathways and guide future studies.

2. METHODS

This study is a structured narrative review aiming to synthesize the most relevant and recent clinical evidence on acute kidney injury from January 1, 2015 and August 1, 2025. A systematic search was performed in PubMed/MEDLINE and Google Scholar (for supplementary references), using predefined terms including “acute kidney injury” OR “acute renal failure” OR “AKI” OR “KDIGO” OR “ NGAL” or “KIM-1” OR “TIMP-2” OR “IGFBP7” OR ” renal replacement therapy” OR “dialysis”.

Eligible studies were full-text, peer-reviewed publications in English involving adult patients (≥19 years), including randomized controlled trials, meta-analyses, original research, systematic reviews, and narrative or consensus reviews. Abstracts, case reports, preprints without peer review, and studies with insufficient methodological detail were excluded. The initial search identified 4340 records; after removing duplicates and screening, 78 full texts were assessed and 38 studies were included in the final synthesis: 8 original research articles, 10 systematic reviews/meta-analyses, 16 narrative or consensus reviews, and 4 randomized controlled trials or trial protocols. No formal risk-of-bias assessment or quantitative meta-analysis was undertaken, as the aim was to provide a clinically oriented qualitative synthesis.

3. RESULTS

3.1 EPIDEMIOLOGY AND CLINICAL IMPACT

Current epidemiological research indicates that acute kidney injury (AKI) has become one of the most common and serious complications seen in hospitalised patients around the world. Recent multicenter studies demonstrated that AKI arises in roughly 5 to 7.5 percent of general admissions, but the incidence increases substantially in intensive care, reaching 30 to 60 percent among critically ill patients [2].

AKI cases global burden does not fall evenly, showing large geographical and economic gaps. In low- and middle-income countries the disease affects up to 13.3 million people each year, a rate far higher than in wealthier nations [11].

Recent multicenter cohort studies have quantified the mortality implications of AKI. Even small increases in serum creatinine within the KDIGO definition (≥0.3-0.5 mg/dL) are associated with higher in-hospital mortality and adverse kidney events. Mortality rises stepwise with the AKI stage, reaching the highest rates in stage 3 across heterogeneous ICU cohorts [2]. Beyond the index admission, the duration of AKI independently predicts long-term risks of chronic kidney disease (CKD) and cardiovascular events [12].

Additionally, the adverse impact extends beyond hospital discharge. Jensen et al. (2024) [12], demonstrated that survivors face higher rates of chronic kidney disease, repeat hospital visits and increased mortality, straining both patients and the healthcare system for years afterward.

3.2 PATHOPHYSIOLOGICAL MECHANISMS

The pathophysiology of AKI extends beyond a simple reduction in glomerular filtration rate, involving a complex interplay of multiple mechanisms, for its pathophysiology draws on a complex interplay of mechanisms. Recent work demonstrated that failure builds through altered blood flow, direct cell harm, a complex cascade of immune signaling molecules, rising oxidative stress and repair attempts that go awry [1].

Prerenal acute kidney injury (AKI) accounts for roughly 60 to 70 percent of all cases and occurs when blood flow to the kidneys drops because of low fluid volume, reduced cardiac output, or changes in blood flow within the organ [11]. Recent studies stress the importance of the kidney's own autoregulation, a process that keeps glomerular filtration fairly steady across wide swings in blood pressure by fine-tuning the diameters of afferent and efferent arterioles.

At the molecular level, prerenal AKI arises when the body activates the renin-angiotensin-aldosterone system, activates the sympathetic nervous system and releases vasopressin; each step is meant to hold on to fluid and keep blood flowing to crucial organs. These responses become harmful, however, if they persist, creating long-lasting vasoconstriction, lowering filtration and setting the stage for intrinsic damage unless the original problem is quickly fixed.

Intrinsic AKI occurs when kidney parenchyma is directly injured, as seen in acute tubular necrosis (ATN), acute interstitial nephritis, or glomerulonephritis. ATN is the most frequent form and usually follows ischaemic episodes or exposure to toxic agents that exceed the cells ability to adapt. New insights into ATNs disease course have highlighted several molecular routes to tubular-cell death, including classical apoptosis and necrosis as well as newer types like ferroptosis and necroptosis [5].

Ferroptosis, which hinges on iron-fuelled lipid damage that weakens cell membranes, is considered a promising target for protecting the kidneys during injury. Ferroptosis, a form of regulated cell death, occurs when glutathione peroxidase 4 (GPX4) loses function, lipids pile up as peroxides and the mitochondria dysfunction ensues, killing tubular epithelial cells. Insights into this pathway now encourage therapies based on removing excess iron, adding antioxidants and fine-tuning how the cell manages fats.

Acute kidney injury (AKI) also sparks inflammation through a tangled network of resident renal cells, invading immune cells and signaling molecules carried in the blood. Tubular cells under stress release damage-associated patterns (DAMPs) that engage Toll-like receptors and inflammasomes; this loop sustains inflammation and worsens injury [13].

Oxidative stress further contributes to AKI damage because faltering mitochondria and dwindling scavengers leave cells unable to cope. Key enzymes such as superoxide dismutase, catalase and glutathione peroxidase are overwhelmed during severe insult, causing reactive oxygen species to build up and harm surrounding tissue. Emerging work identifies mitochondrial targets, focusing on boosting biogenesis and ramping up antioxidant enzymes as potential rescue strategies [14]

Repair after AKI is itself intricate, as dying cells restart the cycle, epithelial-to-mesenchymal transition occurs

and the remaining tissue is reshaped. Successful kidney repair involves a well-timed burst of surviving tubule cells, the rebuilding of tight epithelial seals and the gradual fading of inflammation. When this reparative process becomes dysregulated, recovery stalls and persistent leukocyte infiltration, fibroblast activation, collagen deposition and capillary rarefaction drive progression to chronic kidney disease [3].

3.3 CURRENT CLASSIFICATION SYSTEMS AND THEIR EVOLUTION

Ever-more sophisticated ideas about acute kidney injury (AKI) and its real-world effects have pushed classification systems farther forward. The 2012 guidelines from Kidney Disease: Improving Global Outcomes (KDIGO) now stand as the gold standard, flagging AKI when serum creatinine jumps by 26.5 µmol/L (0.3 mg/dL) within 48 hours, rises 1.5 times baseline in seven days, or urine output drops below 0.5 mL/kg/hour for 24 hours [15].

KDIGO then sorts AKI into three stages, grading severity by how far creatinine climbs and how serious oliguria becomes.

Stage 1 acute kidney injury (AKI) is diagnosed when serum creatinine rises to 1.5-1.9 times its baseline, or when it reaches 26.5 µmol/L or higher, or when urine output drops below 0.5 mL/kg/h for six to twelve hours.

Stage 2 AKI is identified when creatinine climbs to 2.0-2.9 times baseline, or when urine output remains below 0.5 mL/kg/h for twelve hours or longer.

Stage 3 AKI occurs when creatinine increases to 3.0 times baseline or beyond, or reaches 353.6 µmol/L (four milligrams per deciliter) or greater, or when renal replacement therapy begins, or when urine output falls below 0.3 mL/kg/h for twenty-four hours or more, or when the patient is anuric for twelve hours or longer.

Despite its broad use, the KDIGO grading system has notable weaknesses that complicate both bedside decision-making and research findings. Because the system centers on serum creatinine, important changes in kidney function may go unnoticed for a day or two, as creatinine does not rise until roughly twenty-four to forty-eight hours after substantial nephron damage [6].

Baseline creatinine values estimated using the Modification of Diet in Renal Disease (MDRD) formula can misclassify the severity of acute kidney injury (AKI), particularly in older adults, individuals with low muscle mass and those with pre-existing chronic kidney disease [16]. The recognition of acute kidney disease (AKD) as a distinct clinical phase has prompted experts to reconsider how AKI cases are categorized.

Recent studies support more refined classification tools that blend biomarker readings, root cause analysis and traits unique to each patient. Efforts to group cases by molecular fingerprints and circulating proteins could yield personalized classification schemes that mirror the body’s true disease picture and forecast how well a given therapy will work [17].

The KDIGO 2012 criteria remain the current gold standard for defining and staging acute kidney injury. Table 1 summarizes the KDIGO staging system, including thresholds for changes in serum creatinine and urine output.

Table 1. KDIGO classification criteria for acute kidney injury.

Stage	Creatinine criteria	Urine output criteria
Stage 1	↑ creatinine to 1.5-1.9 × baseline or ≥0.3 mg/dL increase	<0.5 ml/kg/h for 6-12h
Stage 2	↑ creatinine to 2.0-2.9 × baseline	<0.5 ml/kg/h for ≥12h
Stage 3	↑ creatinine to 3.0 × baseline or ≥4.0 mg/dL, or initiation of renal replacement therapy	<0.3 ml/kg/h for ≥24h or anuria for ≥12h

3.4 CONTEMPORARY TREATMENT APPROACHES AND EVIDENCE BASE

For now, the care of AKI is mainly supportive: clinicians aim to address precipitating causes, mitigate further injury, optimize fluid and electrolyte management and start dialysis or other replacement methods when the situation calls for it.

Because no specific drugs exist to treat acute kidney injury (AKI), preventing the condition and delivering solid supportive care are the best ways to help patients.

Fluid management sits at the heart of care for AKI; clinicians should ensure adequate fluid to perfuse tissues while steering clear of the swelling and organ strain that fluid overload can cause. Large recent randomized controlled trials have begun to clarify which fluids to use and how to deliver them safely. The SMART trial demonstrated that balanced crystalloids reduce major adverse kidney events when compared with normal saline in critically ill patients, with a number needed to treat of 794 patients to avert one case of long-lasting renal impairment, new dialysis, or death [18].

Blood pressure care in AKI must be tailored to each person, taking into account the cause of injury, existing illnesses and the current hemodynamic picture. Whereas guidelines for the general population often urge lower targets, patients with AKI usually need mean arterial pressures of 65 to 75 mmHg to keep blood flowing through the kidneys [2].

Several recent investigations have focused on the most appropriate blood-pressure targets in distinct settings of acute kidney injury (AKI); in cardiac-surgery patients, maintaining a mean arterial pressure of at least 75 mmHg during the perioperative period appears to lower AKI rates [19]. Pharmacologic support for circulation in these patients has grown more nuanced, as newer evidence indicates that different vasopressors may vary in their effects on renal tissues.

In most cases of distributive shock norepinephrine still serves as the first-line agent, yet studies in specific cohorts point to possible protective roles for vasopressin analogues and angiotensin II. Thus, the selection of a vasopressor must weigh classic hemodynamic goals alongside its likely consequences for renal perfusion.

The timing of initiation of renal replacement therapy (RRT) is a hot topic but some large randomized studies have recently provided important evidence. As an example, the STARRT-AKI trial, inclusive of 3,019 patients with severe AKI being critically ill, did not find a significant variation in 90-day mortality between a fast-paced strategy and the slower standard level [20].

Subsequently, the RRT modality, such as single-session hemodialysis, continuous therapies, should fit with patient profiles, hemodynamic stability and available resources. However, in the clinical practice, intermittent hemodialysis can serve as a viable option since it can remove solutes and fluid relatively fast in people with stable blood pressure, but continuous renal replacement therapy (CRRT) is more likely to be the essential solution since the blood pressure of some patients is very fragile. Mixed modes, such as sustained low-efficiency dialysis (SLED) that reportedly attempts to combine moderate fluid clearance with reasonable solute clearance in the special circumstances, have also started to be tested by clinicians.

It is essential, but often overlooked, that drug doses should be adjusted in acute kidney injury (AKI), as impaired renal clearance may lead to drug accumulation and increased toxicity. Healthcare teams are encouraged to individualize and adjust drug dosing according to current kidney function and, when applicable, renal replacement therapy settings [21].

3.5 BIOMARKER DEVELOPMENTS AND CLINICAL TRANSLATION

In the last decade, studies of AKI biomarkers have exploded, with a number of new compounds significantly outperforming the older tests, such as serum creatinine. These signals are separated by the investigators into functional, damage and stress types, which all illuminate various stages of kidney damage and repair.

Among them, tubular injury markers receive the most attention, with neutrophil gelatinase-associated lipocalin (NGAL) being the most extensively studied candidate for clinical implementation. NGAL is a 25-kDa protein that is usually present in tissues at barely detectable levels, yet its production rises markedly following damage to renal tubules and it appears in both urine and blood within hours. Recent meta-analyses showed that NGAL outperforms serum creatinine, with pooled sensitivity of 0.76 and specificity of 0.82 for predicting AKI [22]. The diagnostic performance is often reported as the area under the receiver operating characteristic curve (AUC), where 1.0 indicates perfect discrimination and 0.5 indicates no diagnostic value. For NGAL, AUC values are typically in the 0.75-0.82 range, indicating good but not perfect accuracy [23].

Kidney injury molecule-1 (KIM-1) is another tubule-specific marker that can be measured in urine after proximal tubular cell injury, and recent systematic reviews confirm its value with reported AUC values in the range of 0.74-0.80 [24]. It is particularly helpful for differentiating acute tubular necrosis from other AKI types and recent reports have documented its excellent performance in settings such as drug-induced nephrotoxicity and ischaemic damage [25].

Liver-type fatty acid-binding protein (L-FABP) has been investigated as an early marker of tubular injury, particularly in situations where changes in serum creatinine may be delayed. A meta-analysis by Chiang et al. (2022), including 27 studies, reported a pooled sensitivity of approximately 0.74 and specificity of 0.78, with an area under the ROC curve (AUC) of about 0.82, indicating reliable performance across diverse clinical settings, including intensive care, surgery, and contrast-induced AKI [26].

Finally, cell-cycle arrest biomarkers-tissue inhibitor of metalloproteinases-2 (TIMP-2) and insulin-like growth factor-binding protein-7 (IGFBP7) - belong to a new class of stress indicators that signal cellular injury long before glomerular or tubular function begins to drop. The combined biomarkers TIMP-2/IGFBP7 marketed as NephroCheck®, have received FDA clearance for forecasting AKI risk in critically ill patients [27]. When the score exceeds 0.3 (ng/mL)²/1000, individuals are at high risk of developing moderate-to-severe AKI within 12 hours, providing an opportunity for early intervention [9]. Multicentre validation studies have reported areas under the ROC curve (AUC) of approximately 0.82-0.84, confirming good predictive performance [1, 28]. Importantly, interventional trials such as PrevAKI demonstrated that applying KDIGO care bundles in patients identified as high risk by TIMP-2/IGFBP7 reduced the incidence of moderate-to-severe AKI by 16.6% compared with routine management [29, 30].

Other inflammatory markers deepen understanding of the immune shifts that happen as AKI sets in and as patients recover. Interleukin-18 (IL-18) reliably signals impending injury across many settings (AUC ~0.70 in meta-analyses), while C-C motif chemokine ligand-14 (CCL14) appears especially useful for identifying patients with persistent severe AKI who may require dialysis earlier, with AUC values around 0.85 [7, 31].

Table 2 summarizes the key biomarkers for acute kidney injury, including their type, time to detection, main advantages, diagnostic performance (AUC) and limitations.

Table 2. Key biomarkers for acute kidney injury - types, detection time, advantages, diagnostic performance (AUC) and limitations.

Biomarker	Type	Time to detection	Advantages	Diagnostic performance (AUC)	Limitations
NGAL	Tubular injury	2-4h	High sensitivity, early detection	AUC 0.75-0.82	Cost, test availability
KIM-1	Proximal tubular injury	Hours	Differentiates ATN	AUC 0.74-0.80	Changes in CKD
L-FABP	Injury, oxidative stress	Hours	Useful in CKD	AUC 0.82	Lower specificity
TIMP-2/ IGFBP7	Cellular stress	<24h	Predicts AKI risk (NephroCheck®)	AUC 0.82-0.84	Cost, availability
IL-18	Inflammation	Hours	Inflammatory marker	AUC ~0.70	Limited specificity
CCL14	Inflammation	Hours	Predicts persistent severe AKI	AUC ~0.85	Limited use

Abbreviations: NGAL - neutrophil gelatinase-associated lipocalin; KIM-1 - kidney injury molecule-1; L-FABP - liver-type fatty acid-binding protein; TIMP-2 - tissue inhibitor of metalloproteinases-2; IGFBP7 - insulin-like growth factor-binding protein-7; IL-18 - interleukin-18; CCL14 - C-C motif chemokine ligand-14; AUC - area under the receiver operating characteristic curve, a measure of overall diagnostic accuracy.

Recent investigations suggest that hemodynamic-guided fluid therapy reduces complications and may improve outcomes in selected adult cohorts [32].

Nevertheless, there are still important barriers that do not allow these tests to become regular care in hospitals. There is the necessity of reproducible assays, universal thresholds, affordable costs and uninterrupted connections to handoffs and shift notes. It is thus that expert panels request validation across different wards and clinics prior to adhering to any one marker as normal practice [11].

3.6 EMERGING THERAPEUTIC STRATEGIES AND FUTURE DIRECTIONS

The current therapeutic approach to AKI is also changing tremendously, as new approaches like specific direction to a certain pathophysiological mechanism other than mere supportive treatment are currently being developed. These emerging methods include pharmacological treatment methods, regenerative medicine solutions and precision medicine solutions based on biomarker data and genetics.

Modeling Pharmacological interventions targeting inflammatory pathways have taken flight in preclinical studies and in small-scale clinical trials. Other possible interventions that are under investigation are anti-inflammatory agents, such as corticosteroids, complement inhibitors and bespoke immunomodulatory therapies as they may have the potential to decrease injury severity and help with recovery [33].

Antioxidant therapies represent another promising therapeutic avenue, with strategies aimed at enhancing endogenous antioxidant systems and reducing oxidative stress. N-acetylcysteine, whilst showing mixed results in contrast-induced nephropathy prevention [34], continues to be investigated in other AKI contexts [35].

Regenerative medicine approaches, including stem cell therapies and tissue engineering strategies, offer potential for promoting kidney repair and recovery following injury [36]. Mesenchymal stem cells demonstrated protective effects through paracrine mechanisms, immunomodulation and promotion of endogenous repair processes [37]. Recent clinical trials of adipose-derived stem cells in patients with AKI showed safety and preliminary efficacy signals, supporting continued investigation [38].

Artificial intelligence and machine learning technologies are revolutionising AKI prediction and management through real-time risk assessment and decision support systems. Recent studies demonstrated that machine learning models incorporating electronic health record data, laboratory values and biomarker profiles can predict AKI development with superior accuracy compared to traditional risk scores [4].

4. DISCUSSION

Acute kidney injury (AKI) is a frequent and severe complication in hospitalised patients, with the highest incidence reported in intensive care settings [2]. Epidemiological studies estimate that AKI occurs in 5-7.5% of general ward admissions and in 30-60% of critically ill patients [2]. Mortality remains considerable, particularly among patients requiring renal replacement therapy (RRT), which underscores the importance of timely recognition and intervention [10].

The pathophysiology of AKI is multifactorial and often involves overlapping ischemic, toxic, and inflammatory processes. The KDIGO classification has improved diagnostic consistency, but its reliance on serum creatinine and urine output limits sensitivity for early detection [6]. Novel biomarkers such as neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule-1 (KIM-1), together with stress response markers including tissue inhibitor of metalloproteinases-2 (TIMP-2) and insulin-like growth factor binding protein-7 (IGFBP7), as well as inflammatory mediators such as interleukin-18 (IL-18) and C-C motif chemokine ligand-14 (CCL14), show promise for earlier risk stratification [7,8]. Liver-type fatty acid-binding protein (L-FABP) has also shown promise as an early marker of tubular injury, particularly in patients with chronic kidney disease and in acute presentations such as poisoning, where creatinine changes may lag behind cellular damage [23]. For example, pooled analyses indicate that NGAL predicts AKI with sensitivity of ~0.76 and specificity of ~0.82 [22], while the TIMP-2/IGFBP7 combination (NephroCheck®) identifies patients at risk of moderate-to-severe AKI within 12 hours at a threshold of 0.3 $(ng/mL)^2/1000$ [9, 27]. Despite these advances, routine integration remains limited due to cost, availability of assays, and the need for broader validation across diverse clinical contexts.

Supportive therapy remains the cornerstone of AKI management. Recent evidence suggests that balanced crystalloids, compared with normal saline, modestly reduce the risk of major adverse kidney events, with an estimated number needed to treat of 794 critically ill patients to prevent one adverse outcome [18]. Hemodynamic management should be individualised, especially in patients with chronic hypertension, in order to minimise both hypoperfusion and fluid overload [10].

Renal replacement therapy remains essential for patients with severe or refractory AKI. However, current evidence supports tailoring the timing of RRT initiation to individual clinical trajectories rather than applying a uniform early initiation strategy. The STARRT-AKI trial, including more than 3,000 critically ill patients, demonstrated no significant mortality benefit at 90 days with accelerated initiation compared to a standard approach [20].

Limitations

This review has several limitations. No formal risk-of-bias assessment or meta-analysis was performed, and only 38 studies were included, which restricts the strength of causal inferences.. The search was limited to English-language publications from 2015 onward, which may have excluded relevant earlier or non-English

studies. Most of the evidence originates from high-income countries, potentially reducing applicability to low-resource settings. Publication bias is also possible. Additionally, no formal protocol registration (e.g., PROSPERO) was undertaken, which may limit reproducibility. Despite these constraints, the synthesis highlights actionable points for improving AKI recognition and management and outlines directions for future research.

5. CONCLUSIONS

Acute kidney injury remains a major global health problem, with hospital incidence of approximately 5-7.5% in general admissions and 30-60% in intensive care, and with persistently high mortality and risk of progression to chronic kidney disease [2,3]. Early recognition prior to overt functional decline is critical, given the limitations of serum creatinine and urine output as delayed indicators [6]. The cell-cycle arrest biomarkers TIMP-2/IGFBP7 can identify patients at high risk within 12 hours at a threshold of 0.3 $(ng/mL)^2/1000$, supporting earlier intervention alongside tubular injury markers such as neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), and liver-type fatty acid–binding protein (L-FABP), as well as inflammatory and prognostic mediators including interleukin-18 (IL-18) and C-C motif chemokine ligand-14 (CCL14) [7, 8, 9, 23, 27]. Balanced crystalloids reduce major adverse kidney events compared with normal saline, with an estimated number needed to treat of 794 in critically ill adults, while the timing of renal replacement therapy should be individualized, as an accelerated initiation strategy did not reduce 90-day mortality in a large randomized trial [18, 20]. Moreover, biomarker-guided bundles such as PrevAKI reduced moderate-to-severe AKI by ~16.6% in high-risk patients [29,30]. Implementation strategies must ensure cost-effective biomarker access and context-specific care models, particularly in low-resource settings. This review synthesised mechanistic insights with emphasis on regulated cell death and maladaptive repair, evaluated the comparative performance of emerging biomarkers, and assessed evidence for fluid and RRT strategies. It also highlighted practical steps and research priorities to support translation of advances into routine clinical practice.

DISCLOSURES

AUTHOR CONTRIBUTIONS :

Conceptualization: Łukasz Woźniak, Patrycja Krysiak

Methodology: Albert Kosarewicz, Patrycja Krysiak

Software: Michał Wabiszczewicz, Albert Lompart

Validation: Michał Wabiszczewicz, Łukasz Woźniak

Formal Analysis: Albert Lompart, Łukasz Woźniak

Investigation: Patrycja Krysiak, Łukasz Woźniak

Resources: Michał Wabiszczewicz, Albert Lompart, Albert Kosarewicz

Data Curation: Albert Kosarewicz, Łukasz Woźniak

Writing - Original Draft: Michał Wabiszczewicz, Patrycja Krysiak, Albert Kosarewicz, Albert Lompart

Writing - Review & Editing: Michał Wabiszczewicz, Albert Kosarewicz, Albert Lompart

Visualization: Albert Kosarewicz, Patrycja Krysiak

Supervision: Michał Wabiszczewicz

Project Administration: Michał Wabiszczewicz

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CONFLICT OF INTEREST

The authors deny any conflict of interest.

USE OF AI

In preparing this work, the authors used ChatGPT for the purpose of improving language and readability. After using this tool, the authors have reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

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