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NAVIGATING CHALLENGES IN ACUTE KIDNEY INJURY DIAGNOSIS AND MANAGEMENT: RECENT INSIGHTS

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Abstract:

Introduction: Acute kidney injury (AKI) management in intensive care units (ICUs) is globally crucial, including in Pakistan. Recent developments in AKI diagnosis and management are reviewed, focusing on AKI recognition and extracorporeal therapy.

Diagnostic Criteria and Challenges: Standard diagnostic criteria based on creatinine and urinary volume variations have improved AKI definition and classification. Challenges persist in differentiating AKI causes and accurately assessing prognosis.

Limitations of Creatinine-based Diagnosis: Creatinine-based diagnosis lacks indicators for parenchymal renal damage, aetiology, prognosis, or treatment response. Scenarios of creatinine increase without structural renal damage highlight the need for a nuanced approach.

Alternative Markers for Early Detection: Exploration of alternative markers includes reduced glomerular filtration, tubular damage, upregulated proteins, and molecules responsive to pathological triggers.

Diagnostic Pathway: The diagnostic pathway for AKI involves various tests like pharmacological history, renal ultrasound, intra-abdominal pressure measurement, and urinary sediment analysis.AKI in the Context of Infection: Discussion on AKI aetiology complexity in critically ill patients, focusing on AKI in bacterial endocarditis, glomerulonephritis, and drug-induced interstitial nephritis.

Conclusion: Advancements in AKI diagnosis and biomarker research are acknowledged, while challenges remain in their integration into clinical practice.Emphasis on nephrologist involvement

for a holistic approach considering functional and pathological aspects of renal damage in critically ill patients

KEYWORDS: Nephrological skills, Extracorporeal therapy, Creatinine, Glomerular filtration rate (GFR), Diagnostic criteria, Renal excretory capacity, Tubular damage, Parenchymal damage, Renal plasma flow, Biomarkers, Fractional excretion of sodium (FeNa).

Introduction:

Acute kidney injury in critically ill patients admitted to intensive care is frequently managed in Pakistan as in other countries by intensive care units. This substantially impacts both nephrological skills and the patient's clinical management. The available literature concerns, with a few exceptions, two prevalent areas: the recognition of acute kidney injury, understood as the quantification of the reduction in renal excretory capacity, and the management of any necessary extracorporeal therapy (Wang, Niu et al. 2024).In recent years, the creation of standard diagnostic criteria has made it possible to define and classify acute kidney injury based on variations in creatinine and urinary volume, overcoming the severe limitation of the diversity of definitions, which until then had made in-depth study complicated and unproductive. of the problem, both from an epidemiological and clinical point of view (Wang, Niu et al. 2024).

As regards the initiation and management of extracorporeal purification techniques, the available studies are often carried out by doctors and researchers who work in intensive care and who, also thanks to the simplification of the methods and technological progress, manage the treatments independently, not infrequently with the approval of the nephrologist who however does not participate in the decision-making and planning phase (Wang, Zhao et al. 2024)

The diagnosis of AKI

The definition and staging of acute kidney injury are based on the Increase in creatinine and the consequent variation in glomerular filtration rate associated with the reduction in diuresis. Many studies have also highlighted how more advanced stages of acute kidney injury are associated with a worse prognosis in both the short and long term. However, it should not be forgotten that both creatinine and diuresis are indicators of the excretory capacity of the kidney but do not give information on its other functions (metabolic, endocrine, immunological) and are data that can be misinterpreted in some clinical contexts (Wang, Niu et al. 2024).

Table 1: Diagnostic Criteria for Acute Kidney Injury (AKI)

Criteria	Description
Increase in Creatinine	Increase in serum creatinine by ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours OR Increase in serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within the prior seven days OR Urine volume <0.5 mL/kg/h for 6 hours.
Urinary Volume	Reduction in urinary volume to <0.5 mL/kg/h for 6 hours
Standard Diagnostic Criteria	Definition and staging of AKI based on variations in creatinine and urinary volume, standardized to overcome limitations of diverse definitions
Parenchymal Damage vs. Renal Dysfunction	Creatinine-based diagnosis may not reflect the presence of parenchymal damage or provide information on the cause, prognosis, pathogenesis, or treatment response.
Subclinical AKI	Occurs when creatinine remains within normal limits despite renal parenchymal damage, often observed in critically ill patients, delaying diagnosis; indicative of structural damage even with minor effects on filtration function
Delay in Creatinine Increase	Creatinine increase occurs 48-72 hours after reduction in glomerular filtration rate and renal insult, delaying AKI diagnosis and treatment initiation.
Biomarkers	Over 700 clinical studies in the past five years; four categories: Markers of reduced glomerular filtration, reduced function and tubular damage, upregulated proteins, molecules produced in response to pathological trigger; no single test universally applicable or easily usable in daily clinical practice

Table 2: Diagnostic Tests for Identifying Causes of AKI

Test	Description
Pharmacological History	Identification of medications with potential nephrotoxicity, including mechanisms such as tubular epithelial damage, interstitial nephritis, glomerular disease, and obstructive crystal nephropathy
Renal Ultrasound	Identifies obstructive causes of AKI, assesses renal morphology, size, structural alterations, echogenicity of parenchyma, and vascularization
Measurement of Intra-abdominal Pressure	Assesses risk of abdominal hypertension and compartment syndrome as potential causes of AKI
Fractional Excretion of Sodium (FeNa%) and Urea	Evaluates renal sodium and urea excretion as indicators of hydration status and kidney function, distinguishing prerenal AKI from acute tubular necrosis; FeNa% and FeU% calculations provide insight into sodium and urea clearance.
Urinary Electrolytes and Urinary Osmolarity	Assess urinary chloride and potassium concentrations, providing information on renal electrolyte imbalances.
Urinary Sediment	Analyzes urinary sediment for the presence of tubular cells, granulose casts, dysmorphic red blood cells, leukocytes, bacteria, or fungi, aiding in differentiation between transient insult from hypoperfusion and acute tubular necrosis; various scoring systems proposed for quantifying severity of tubular damage.

Creatinine is a metabolite of creatine, a molecule synthesized from the amino acids glycine and arginine in the liver, pancreas and kidneys, and which serves as an energy reserve for the muscle. Creatinine production depends on the quantity generated through the diet (for example, by consuming red meat) and muscle function. The diagnosis of AKI based on creatinine is, therefore, imprecise for two reasons (Salmito, Mota et al. 2024):

- it does not define whether parenchymal renal damage is present or not;
- · in patients with renal parenchymal damage, it does not provide information on the cause, prognosis, pathogenesis, or response to treatment.

As was illustrated in an article by Moledina et al., renal damage must be considered from two different aspects: increased creatinine and structural alterations. When a diagnosis of acute kidney injury is made in a nephrological setting, it is believed that the Increase in creatinine mainly reflects the presence of parenchymal damage. However, in critically ill patients, there are clinical pictures in which these two pathological alterations of the kidney do not coexist, and only one of the two is present. In these cases, the patient with AKI may have a kidney problem that does not meet the KDIGO clinical criteria (Rout, Mishra et al. 2024).

The first possibility is observed when there is an increase in creatinine in the absence of structural renal damage; a rise of 0.3 mg/dl or 50%, as defined by the KDIGO classification, corresponds to many different AKIs, even in intensive care. A septic, hypotensive patient with a urinary sediment rich in granular casts or signs of parenchymal damage will have an unfavourable renal prognosis. Therefore, being aggressive from a therapeutic point of view will be advisable. Conversely, a patient with the same creatinine level hospitalized for severe heart failure treated with high doses of diuretics, currently being treated with ACE inhibitors or ARBs, or with recent correction of marked hypertension, will probably have an increase in retention not associated with harm parenchymal and the prognosis will be more favourable (Ng, Ip et al. 2024).

A reduction in renal plasma flow and glomerular filtration, as observed in cardiorenal and hepatorenal syndrome, or as a transient glomerular hemodynamic effect of drugs inhibiting the renin-angiotensin system, can therefore cause an increase in creatinine in the absence of documentable parenchymal damage, as happens during therapy with some medications, such as trimethoprim, which cause a reduction in the tubular secretion of creatinine without a consensual decrease in GFR (Nadim, Kellum et al. 2024).

The opposite condition is that creatinine remains within normal limits despite renal parenchymal damage; this occurs in patients with water overload, which reduces plasma creatinine concentration, or who have pathologies associated with reduced muscle mass. Low creatinine values in these cases will delay the diagnosis of AKI. Critically ill patients often fall into this category, which can be defined as subclinical AKI, in which the effects of tubular damage and reduced GFR are compensated by other, undamaged and functioning nephrons, which constitute the so-called renal

reserve; the Increase in creatinine is observed when more than 50% of the renal parenchyma is damaged (Murphy 2024).

It is a phase that is believed to anticipate actual renal damage. It has an unfavourable prognosis precisely because structural damage is present, even in cases where the apparent repercussions on the filtration function are minor. Furthermore, creatinine increases later (48-72 hours later) compared to the reduction in glomerular filtration rate and renal insult; this delay is problematic as it postpones the diagnosis of AKI and consequently also the timely start of adequate therapies (Legrand, Bagshaw et al. 2024).

For this reason, much attention is paid to identifying alternative markers that change promptly or can even predict which patients are at risk of AKI. Over the last five years, more than 700 clinical studies regarding AKI biomarkers have been published. Without going into the analysis of individual markers, which is not the subject of this brief review, it is essential to remember that biomarkers can be divided into four categories (Kobeisy, Ali et al.):

- Markers of reduced glomerular filtration: small molecules filtered by the glomerulus, not secreted or reabsorbed by the tubule, such as creatinine and cystatin C. Some studies have shown how combining the two markers better predicts short- and long-term outcomes than single markers [6].
- · Markers of reduced function and tubular damage: the loss of tubular function is well assessable with fractional excretion of sodium (FeNa%) and stress testing with furosemide [7]. FeNa%, as we will see later, correlates with the kidney's ability to reabsorb filtered sodium, which is reduced or lost when the tubule is damaged. Therefore, increased sodium urination and high FeNa% will indicate tubular damage. Microalbuminuria is also a marker of tubular damage; although mainly a marker of glomerular damage, albumin reabsorption in the proximal tubule is reduced during AKI. For this reason, in theory, it could be a promising marker of parenchymal damage. Still, in reality, its usefulness is poor as it does not allow us to distinguish which part of the nephron is damaged and whether the microalbuminuria does not rather pre-exist the acute damage (Baeseman, Gunning et al. 2024).
- Upregulated proteins: this category includes, among others, neutrophil gelatinase-associated lipocalin (NGAL), widely tested in the early diagnosis of AKI, and kidney injury molecule-1 (KIM-1), upregulated at the tubular level in response to pathological insult and modulator of the renal immune response (Wang, Niu et al. 2024).
- Molecules produced in response to the pathological trigger: the activation of inflammation and the recruitment of inflammatory cells at the renal level represent an early response to the damage. IL-18, for example, is a mediator of renal ischemic damage and originates predominantly from the proximal tubule. MCP-1 is produced by numerous cells and mediates the recruitment of monocytes into the kidney during damage [9]. IL-6 expression increases during AKI and leads to an accumulation of leukocytes in the renal parenchyma (Wang, Zhao et al. 2024).
- However, the numerous studies conducted to overcome the limitations of traditional markers of renal damage and aimed at identifying, testing and validating new markers of the AKI phenotype have not, to date, identified a test that is valid in all clinical settings and easily applicable in practice—daily clinic (Rout, Mishra et al. 2024).

The first level of the diagnostic path to identify the causes of AKI

As we have just seen, many clinical studies have focused on the timeliness of diagnosis of AKI. Understanding and recognizing the pathological mechanisms that cause worsening of renal function is a complementary and equally important aspect, both for implementing adequate therapy and for evaluating the medium and long-term prognosis, and is a crucial aspect of management by the nephrologist (Ng, Ip et al. 2024).

In the case of acute kidney injury evidence, the basic tests functional to understand the cause are renal ultrasound, blood and urinary electrolytes, urinalysis, and urinary sediment. Although traditional assessments are readily available in every hospital, it is expected that they are not always

available at the time of the first nephrological assessment. It is, therefore, a good idea to summarize them below (Nadim, Kellum et al. 2024).

Anamnesi pharmacologica

As has been well summarized by Pannu [12], acute kidney injury can be caused by ongoing medications. There are several possible mechanisms of direct nephrotoxicity:

- tubular epithelial damage: acute tubular necrosis (e.g. aminoglycosides) or damage on an osmotic basis (e.g. immunoglobulins, hypertonic solutions);
- interstitial nephritis: acute on an allergic basis (e.g. penicillins), chronic (e.g. calcineurin inhibitors), papillary necrosis (e.g. NSAIDs);
- glomerular disease: glomerulonephritis (e.g. penicillamines, ACE inhibitors), renal vasculitis (e.g. hydralazine, no longer on the market);
- obstructive crystal nephropathy (e.g. acyclovir).

When toxicity is indirect, it is mediated by the reduction of intrarenal plasma flow (e.g. ACE inhibitors, NSAIDs), especially in the presence of dehydration.

Renal ultrasound

Renal ultrasound allows you to quickly identify not only the obstructive causes of AKI but also the morphology and size of the manure, the possible presence of structural alterations (asymmetries, stones, cysts, ...), ultrasonographic pictures suggestive of pre-existing renal damage, the echogenicity of the parenchyma. It is possible to integrate the ultrasound with a colour Doppler ultrasound study. In that case, we will also have information regarding the renal parenchymal vascularization and the patency of the main arterial branches (Murphy 2024).

A complete nephrological consultation in an intensive care environment should include, to complete the classic semiotic examination, a bedside ultrasound, both renal and aimed at evaluating the patient's water status, to be integrated, if necessary, with a subsequent diagnostic-instrumental path more comprehensive (Murphy 2024).

Measurement of intra-abdominal pressure

The risk of abdominal hypertension is increased in intensive care, particularly in post-operative patients (aortic aneurysm, major surgery) with abdominal sepsis, recent abdominal trauma, or vascular problems (intestinal ischemia, intra-abdominal haemorrhage). The Increase in intra-abdominal pressure (>20 mmHg) can cause abdominal compartment syndrome, in which an increase in central venous pressure and electrolyte and acid-base balance alterations are also observed. Abdominal compartment syndrome can be a cause of AKI, particularly in patients who have recently undergone major surgery (Legrand, Bagshaw et al. 2024).

Fractional excretion of sodium (FeNa) and urea (FeU%)

Under normal conditions, renal sodium excretion equals dietary intake net of the small amount lost through faeces and sweat, equaling 40-220mEq per day. When blood volume is reduced, sodium urine is diminished due to the activation of the sympathetic system and the renin-angiotensin-aldosterone axis [14]. The urinary sodium concentration will then drop to values <15 mEq/L. When blood volume is corrected, sodium reabsorption is reduced, and sodium urine increases again (Kobeisy, Ali et al.).

Sodiuria can be used indirectly to measure hydration status and the kidney's ability to maintain it. However, the urinary sodium concentration depends on the amount of urinary free water, i.e. on the renal reabsorption of water; if water reabsorption is reduced, we may have a low sodium concentration even in the absence of hypovolemia; similarly, concentrated urine can cause an increase in urinary sodium concentration even if total sodium is low. To evaluate sodium diuretics, considering water reabsorption, FeNa% can be used, a simple but rarely used test, particularly by intensivists. FeNa is the percentage of sodium filtered by the kidney and excreted in the urine (Baeseman, Gunning et al. 2024):

(FeNa = (UAlreadyx PCr)/(PAlreadyx UCr)

Compared to urinary sodium concentration alone, FeNa provides a more accurate assessment of renal sodium clearance. It is generally used to distinguish between prerenal AKI, which can be corrected with the restoration of adequate blood volume, and AKI due to acute tubular necrosis, which cannot be corrected with hydration (which, if excessive, can lead to water overload). In the first case, the sodium will be low and the FeNa less than 1%, while in the second case, in which the kidney loses its ability to increase sodium reabsorption, the sodium will be high and the FeNa above 2%. The use of FeNa certainly has many limitations, starting with the poor reliability in cases of congestive heart failure, advanced cirrhosis, extensive burns, and conditions in which renal vasoconstriction determines the reduction of sodium clearance despite tubular function preserved. Recently, Bagshaw reported that FeNa is not helpful in septic patients because it is always low and does not help distinguish between acute and prerenal tubular necrosis (Wang, Niu et al. 2024).

The pathophysiological mechanism underlying this observation is that in sepsis, sodium reabsorption increases due to vasodilation induced by inflammation. Therefore, it may not help evaluate hypoperfusion. Even the use of high doses of diuretics (a frequent occurrence in intensive care) makes FeNa unreliable, as it is elevated even in the presence of hypovolemia. In these cases, fractional excretion of urea can be used (Wang, Zhao et al. 2024) (Salmito, Mota et al. 2024):

(FeUrea = (UUrea x PCr)/(PUrea x UCr)

In the case of hypovolemia, the reabsorption of water and urea in the proximal tubule increases; both loop diuretics and thiazides do not modify urea reabsorption as they act distal to the proximal tubule. Values lower than 35% suggest transient renal damage, and higher than 35% suggest acute tubular necrosis [18]. The reliability of FeU% is lost if the diuretics, acetazolamide or mannitol are administered, if glycosuria is present and if the patient is elderly or septic (Rout, Mishra et al. 2024).

Urinary electrolytes and urinary osmolarity

Urinary chloride is rarely used in clinical practice; similarly to sodium, urinary chloride concentration is reduced in response to hypovolemia. However, this data is affected by alterations in the acid-base balance and must be correlated with the clinical picture. The measurement of urinary potassium can be helpful when the critically ill patient has dyslexia, which is difficult to interpret. If a state of dehydration coexists, although hypovolemia stimulates aldosterone production, potassiumuria remains relatively low due to the reduction of sodium and water in the distal tubule. However, renal electrolyte imbalances are rarely associated with AKI in critically ill patients; therefore, they deserve separate treatment (Ng, Ip et al. 2024).

Urinary sediment

Another test traditionally part of the nephrologist's baggage is urinary sediment. Its use in critically ill patients is primarily underestimated for cultural and organizational reasons. The intensivist doctor generally lacks the training to analyze a urinary sediment competently. At the same time, the nephrologist often limits its use to the diagnosis and follow-up of non-critically ill patients with glomerulonephritis without extending its application to critically ill patients admitted to therapy intensive. However, its diagnostic and prognostic value may be decisive (Nadim, Kellum et al. 2024).

Indeed, carrying out the exam with an optical microscope and dedicated material requires logistical organization, which is not always available in our daily work. However, it should be reiterated that the urinary sediment, examined by a nephrologist possibly several times to follow its evolution, can provide a lot of helpful information to formulate a hypothesis on the cause of AKI in the patient we are evaluating. Among these are the presence and typification of cylinders, the presence of dysmorphic red blood cells or vice versa of a probable urological nature, and the presence of tubular cells, urate or oxalate crystals, leukocytes, bacteria or fungi (Nadim, Kellum et al. 2024).

Clinical studies which have as their object the evaluation of urinary sediment in patients with acute kidney injury, however, are generally limited to the distinction between transient insult from hypoperfusion and acute tubular necrosis or between cases of so-called "prerenal hyperazotemia" and cases of consolidated parenchymal damage. The ischemic tubule (or damaged due to tubule-toxic drugs) releases epithelial tubular cells, visible upon careful examination of the sediment, together with granulose casts. Various scores have been proposed to identify and quantify tubular damage, considering the number and type of cylinders in the urinary sediment (Murphy, 2024).

One of these, the cast scoring index (CSI), allows the sediment to be classified into 4 degrees of severity, about the presence and richness of granulose cylinders and epithelial cells; a low score will be suggestive of renal hypoperfusion and correlated with a more favourable prognosis, a higher score will vice versa be a sign of the development of tubular damage. A similar score, proposed by Bagshaw, used in critically ill patients with sepsis-related or other etiological AKI and compared with other renal damage and outcome parameters (specific biomarkers, need for dialysis, mortality) demonstrated that patients with sepsis-related AKI for the same severity of renal damage, have a worse urinary score (i.e. more numerous granulose casts and epithelial cells) and that this score does not correlate with other traditional biochemical parameters, such as FeNa% (Murphy 2024).

The available epidemiological data and daily clinical experience suggest that in critically ill patients hospitalized in intensive care, the most common causes of AKI are sepsis, acute or acute heart failure, prolonged renal hypoperfusion in cases of hemodynamic instability, and nephrotoxicity from drugs. Acute glomerular and interstitial diseases are considered relatively rare. However, a review of our case series (retrospective evaluation of 18 months, between 2017 and 2018, unpublished data) made it possible to highlight that these pictures are not at all rare: out of 163 critically ill patients with dialysis AKI, 22% had a newly detected parenchymal nephropathy (glomerular or interstitial, micro- or macroangiopathic, toxic) (Kobeisy, Ali et al.).

This epidemiological data, which is difficult to find in the mainly intensive literature, confirms that the etiological diagnosis cannot be underestimated in the global evaluation of AKI; the latter often focuses on functional assessment and neglects the pathological mechanisms mediating the damage (Baeseman, Gunning et al. 2024).

Acute kidney injury in the infected patient

It frequently happens that the critically ill patient with acute kidney injury, whom we are called upon to evaluate in consultation, presents a complex picture of comorbidities, therapies and risk factors. In this scenario, it is expected that the probability that it is AKI secondary to sepsis or nephrotoxic drugs hides a more complex pathological profile (Wang, Zhao et al. 2024).

For example, 30% of patients with bacterial endocarditis experience acute kidney injury, as highlighted in several studies over the past 20 years. The worsening of renal function can result from the infection or its treatment, pharmacological or cardiac surgery. It is more frequent in elderly patients with Staphylococcus Aureus infection, sometimes with risk factors such as valve defects, diabetes and HCV. One of the most interesting epidemiological aspects for the nephrologist is that, in the majority of cases, acute kidney injury is the first clinical manifestation of bacterial endocarditis (Wang, Niu et al. 2024).

AKI during endocarditis can have a variety of clinical manifestations: it is rarely accompanied by acute nephrotic or nephritic syndrome; more frequently, it is associated with a consumption of complement, in particular C3, about the activation of the alternative complement pathway, sometimes the blood chemistry mimics a positive ANCA vasculitis. This clinical variability reflects the variety of pathological processes involved; accurately evaluating the urinalysis and urinary sediment may help distinguish them (Wang, Niu et al. 2024).

In the case of infection-related glomerulonephritis and drug-induced interstitial nephritis (generally with penicillins, cephalosporins or quinolones) the renal alterations are very similar: hematuria, sometimes erythrocyte casts, modest proteinuria, renal failure; however, in the case of interstitial nephritis, leukocyte casts are more frequent and the onset of AKI is late (> ten days after the start of antibiotic therapy) compared to infection-related glomerulonephritis. When the cause of AKI is

glomerulonephritis related to endocarditis, the etiological agents most frequently involved are Staphylococcus Aureus (56% of cases) and Streptococcus. It should be underlined that, as illustrated by Glassock, infection-related glomerulonephritis has different characteristics than post-infectious glomerulonephritis and should not be confused with it (Baeseman, Gunning et al. 2024).
In the case of antibiotic therapy with aminoglycoside, acute renal damage secondary to direct tubular toxicity can be observed, which occurs approximately 5-7 days after treatment; in this case, the urinary sediment is different, with epithelial cells and cylinders with epithelial cells. Less frequent and sometimes with very late onset is a renal septic embolism, which can be suspected when AKI is associated with flank pain and distal signs of embolism; scintigraphy, in this case, allows you to confirm the clinical suspicion (Kobeisy, Ali et al.).

The second level diagnostic path to identify the cause of AKI

Suppose traditional tests are not conclusive in identifying the pathological mechanism underlying acute or relapsed kidney damage. In that case, it is best to continue the process with further investigations based on the clinical context in which the patient finds himself. It is not the purpose of this brief review to delve into the clinical and laboratory aspects of the less frequent causes of AKI individually; however, it may be helpful to recall them briefly as part of the correct clinical approach (Wang, Niu et al. 2024).

STEPS

The onset of sepsis can be early or late in the hospitalization setting. Even if in most patients in intensive care, sepsis is early and sometimes represents the leading cause of the patient's criticality (and is therefore already known at the time of the nephrological consultation), the late onset may be recognized more slowly. In these cases, the execution and repetition of culture tests (blood, urine, bronchoalveolar lavage, drainage) and inflammation markers can highlight a worsening infectious picture that began with a deteriorating renal function (Wang, Zhao et al. 2024).

Conclusions

Acute kidney damage in intensive care is a frequent occurrence, which, unfortunately, often does not see the nephrologist as the protagonist, neither in the diagnosis phase nor in the management of any extracorporeal treatment.
The literature of recent years has focused, in addition to the different methods of managing extracorporeal purification, on the early diagnosis of renal insult, with the study of numerous new biomarkers, sometimes promising but not yet usable in daily clinical practice, both due to costs and availability, and due to the lack of evidence of usefulness and improvement of the significant outcomes in the different clinical settings. Above all, the use of markers that anticipate the diagnosis of AKI must be a stimulus and an opportunity to enhance the involvement of the nephrologist in the diagnostic and therapeutic process. The clinical, methodological approach to acute kidney injury, if limited to the search for new diagnostic tools and delegated to non-nephrologist specialists, risks losing accuracy and unfairly marginalizing the nephrologist's role and more complex diagnostic pathways (Murphy 2024).
The few epidemiological data available do not give us an accurate picture of the frequency of the different types of renal damage in critically ill patients. Still, our experience suggests that the incidence of parenchymal nephropathies other than sepsis is high and relevant, particularly for the long-term nephrological prognosis and the related need for adequate nephrological follow-up (Legrand, Bagshaw et al. 2024).

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