REVIEW ARTICLE

Renal Disease and Transplantation Forum
2022, vol. 15, no. 2, 75–79

ISSN 2720–2771
e-ISSN: 2720-4189
DOI: 10.5603/RDTF.2022.0009

VIA MEDICA

Helena Żórawska[1], Alena Zhymaila[2], Jolanta Małyszko[2]

[1]Medical University of Bialystok
[2]Department of Nephrology, Dialysis and Internal Medicine, Medical University of Warsaw

Definitions and classification of acute kidney injury, acute kidney disease, and chronic kidney disease

ABSTRACT

Chronic kidney disease (CKD) is becoming more and more common. Recently, it has become a problem for public health institutions worldwide. On the other hand, with the development of medicine, acute kidney injury (AKI) is increasingly more commonly diagnosed. There is always a question of defining the disease. The definition of AKI proposed by Kidney Disease Improving Global Outcome (KDIGO) has no clinical context and is generally not helpful in daily practice. Therefore, the old pathophysiological classification of prerenal, renal, and postrenal kidney injury is still used. Recently, acute kidney disease (AKD) has been defined as abnormalities in the structure or function of the kidneys that have a significant impact on health and life, last for less than 3 months, and do not meet the definition criteria for either AKI or CKD. This can also be referred to as nonspecific kidney impairment. This article discusses the definition and classification of AKI, AKD, and CKD.

Renal Disease and Transplantation Forum 2022, vol. 15, no. 2, 75–79

Key words: acute kidney injury, acute kidney disease, chronic kidney disease

INTRODUCTION

Recently, kidney diseases have affected more and more individuals making them a public health issue [1]. Although they are well known and have been classified, their diagnosis and treatment have become a common problem. The problem is the multitude of definitions of renal syndromes: acute kidney injury (AKI) and chronic kidney disease (CKD), and a lack of guidelines for diagnosing abnormalities in the structure and/or function of the kidneys that do not meet the diagnostic criteria for AKI and CKD [2, 3]. To solve this problem, all kidney abnormalities have been combined into one new term and defined as acute kidney disease (AKD) [4].

Short-term illnesses of sudden or recent onset and reversible cause are referred to as "acute" conditions, while "chronic" conditions are long-term and persistent, thus AKI is a subcategory of AKD, which is in line with the 2012 AKI guidelines [4].

DEFINISIONS

Since 2005, more than 30 definitions of AKI have been developed because over the last quarter of the century, there have been significant changes in its epidemiology and constantly increasing therapeutic possibilities.

The most general definition of AKI is an impairment of glomerular function for up to 7 days, reflected by changes in the serum creatinine level and urine volume.

The greatest uncertainty is associated with failure to include two extreme forms of AKI in the definition, i.e. structural or functional tubular damage, previously called prerenal azotemia, which was omitted when defining AKI in the Kidney Disease Improving Global Outcome (KDIGO) classification.

Currently, AKI is diagnosed when there is an increase in serum creatinine by > 0.3 mg/dL within 48 hours. However, it is the most controversial part because creatinine is not a perfect biomarker, and its increase does not necessarily

Address for correspondence:
Jolanta Małyszko,
Katedra i Klinika Nefrologii,
Dializoterapii i Chorób Wewnętrznych,
Warszawski Uniwersytet Medyczny,
Banacha 1a, 02–097 Warszawa,
phone. 48 22 599 2660,
fax: 48 22 599 2616,
e-mail: jmalyszko@wum.edu.pl

imply kidney injury [4]. There are many causes of a transient increase in serum creatinine secondary to hemodynamic changes rather than kidney damage, e.g. in patients with hepatorenal or hepatocardiac syndrome. However, the opposite may occur when the tubules are damaged, but it is insufficient to alter serum creatinine levels. Therefore, the diagnosis of AKI may be improved by including structural biomarkers that directly indicate tubular damage.

However, in critically ill patients, the severity of AKI may be underestimated because of the dilution of serum creatinine concentration caused by fluid retention, reduced production and muscle loss; hence, the decision to initiate appropriate therapy may be delayed, which may result in a poorer prognosis, delayed renal replacement therapy or transfer to the intensive care unit and, therefore, increased mortality. In severe AKI, the most common therapy is initiation of renal replacement therapy; however, the absence of e.g. biochemical indications may worsen the patient's condition by exacerbating hemodynamic instability due to hypotension or bleeding secondary to septicemia or anticoagulation therapy. It is also impossible to predict the exact changes in pharmacokinetics of various therapeutic agents, antibiotics in particular, which greatly increases the risk of inadequate dosage, both overestimating and underestimating the correct dose.

Unfortunately, despite extensive research, no reliable structural biomarkers of AKI have been found so far, and for this reason, the KDIGO guidelines emphasize the importance of clinical trials with serum creatinine serving as the main parameter.

The second currently used criterion in the definition of AKI is the rate of diuresis, which is assumed less than 35 mL per hour. However, this method is also questionable. Despite it being inexpensive and easy to carry out, the results can be significantly altered by diuretics and fluid therapy, which may increase the false-positive rate; also, the suggested threshold remains controversial. It should be noted that, after major surgery, patients may develop oliguria in response to perioperative stress. Additionally, even when the patient is catheterized, hourly diuresis is not monitored in every health center.

In addition, the interpretation of the global data on the epidemiology of AKI remains a significant problem. This is not only due to the incomplete definition or different definitions or assessment criteria used worldwide, but also due to differences in available financial resources of each country, which directly translates into the number of diagnosed cases, treatment methods, and sometimes mortality as well [5].

The need for a clear definition of AKI is also emphasized by cardiologists because it occurs commonly in patients with acute heart failure. In cardiology, AKI is replaced by the term worsening renal function (WRF), which links biochemical changes to the clinical condition. Cardiologists distinguish two types of WRF, namely the actual and alleged WRF [4].

It should be noted that the definition of AKI proposed by KDIGO has no clinical context and is not helpful in everyday clinical practice. Therefore, most specialists, at the time of a sudden deterioration of kidney function, still use the old pathophysiological classification of AKI, even though it greatly simplifies this complex clinical phenomenon. It divides the causes of AKI into 3 groups: prerenal, postrenal, and renal, the last one being associated with ischemia, nephrotoxicity, or ongoing inflammation. Although the pathogenesis of AKI is complex, it is the most widely used framework and is still recommended for students and doctors in training. In addition, current recommendations for management of AKI focus on the initial phase, even if renal function has not been restored.

However, it should be mentioned that the definition proposed by KDIGO has clearly raised physicians' awareness of AKI, and hence the recognition of AKI at its early stages has significantly increased so that appropriate nephroprotective measures have been introduced.

Chronic kidney disease is characterized by a reduced glomerular filtration rate for more than 3 months, accompanied by severe albuminuria [3]. Thus, it can be said that the classification is based mainly on the cause of the disease and the severity of the structural abnormality, so that appropriate therapy can be instigated, and generally the more advanced the disease, the worse the prognosis.

Depending on the stage of AKI or CKD, there are different approaches and recommendations regardless of the underlying cause. It should be noted that the more advanced the stage of the disease, the worse the prognosis, and the staging systems are important in defining the final stage of a clinical examination.

All the above-listed problems led to the creation of a new term, and thus a new clinical entity known as AKD was formed. It includes

all patients with abnormalities in the structure or function of the kidneys, which significantly affect their health and life, last for less than 3 months, and do not meet the definition criteria for either AKI or CKD [2, 3]. It is also known as non-specific renal impairment.

However, defining a new clinical entity, as well as developing guidelines for its diagnosis and management approaches adapted to each stage require the time and cooperation of many research centers. It is necessary to collect as many reports on adult and pediatric patients as possible, establish a baseline appropriate for all categories and all changes in the studied parameters, and develop an appropriate approach to their assessment.

Guidelines on the diagnosis of AKD consider its underlying causes, but it should be noted that AKD may have many similar causes as both AKI and CKD including parenchymal disease, systemic scleroderma, or glomerulonephritis [4]. It is, therefore, necessary to take into account various circumstances.

All terms — AKD, AKI, and CKD — refer to abnormalities in function or structure of the kidney and are interrelated by their diagnostic criteria, complications, and test findings. However, it has been established that AKD can occur without prior history of kidney disease and underlying CKD. It is also known that AKD is not directly related to AKI. So far, a system has been proposed that distinguishes between AKD without AKI from AKD with AKI, further breaking down whether AKI onset preceded or followed an episode of AKD.

In the research conducted so far, including the study by James et al. [6], it has been shown that patients with CKD who have experienced an episode of ACD have the highest risk of complications i.e. renal failure, while CKD combined with AKI increases the patient's risk of death the most. This has also been confirmed by other studies published so far, which were carried out on patients with cardiovascular diseases [7–18].

In addition, it is known that AKI can persist for up to 3 months. The transition from the management typical for AKI to that appropriate for CKD should start within 90 days from the onset of AKD. After this time, most patients will begin to meet the criteria for CKD and will, therefore, be described as CKD with a history of AKD. On the other hand, those who fail to meet CKD criteria after a period of AKD will be described as AKD patients at an increased risk of CKD. In one person, AKI episodes may occur many times, and after their resolution, abnormalities that meet the AKD criteria may be present [19]. However, the current AKD severity assessment systems are based on different principles that cannot be combined to create a unified approach.

Considering the glomerular filtration rate (GFR) and albuminuria in the diagnosis of CKD, it was suggested that those markers also be used for AKD staging, however, there are not enough observations yet to standardize this position and accurately determine the relationship between albuminuria or the GFR level and severity of AKD.

The unification of diagnosis, staging, and management of kidney diseases is extremely important for determining the prevalence of AKI, CKD, and AKD. It has been shown that the use of four different approaches to the classification of AKI gave as much as a 15% discrepancy in the results.

It should also be noted that patients with AKI without AKD most often visit the primary care physician and, therefore, symptoms such as hemoptysis, hypercalcemia, and rash should be consulted with the specialist.

To determine the cause of AKD, it may be useful to run a urinalysis, review medications taken by the patient, especially in terms of reducing GFR, and in selected cases, a kidney biopsy should be considered, bearing in mind that it is a high-risk procedure [20–24]. The following Table 1 summarizes the guidelines for diagnosis of renal syndromes according to Lameire et al. [4].

Given all the controversies and doubts, in August 2020, KDIGO organized a conference aimed at standardizing and extending the existing definitions of renal syndromes and improving the guidelines on treatment strategies and clinical care. The key areas of research that were identified were the standardization of procedures and methods of management in CKD and AKI and their impact on public health. The work of specialists from around the world resulted in a discussion of key concepts related to the new definition of AKD, management strategies, and analysis of research priorities [4].

It was proposed to introduce a new term for all abnormalities of the kidney function and/or structure that affect one's health, collectively known as "kidney diseases and disorders" (KD). This new category includes AKD and CKD, which can be distinguished by their duration.

Table 1. Guidelines on diagnosing renal syndromes (based on KDIGO [4]

	AKI	AKD	CKD
Duration	For 7 days	≤ 3 months	> 3 months
Functional criteria	Increase in SCr by > 50% over 7 days OR increase in SCr by > 0.3 mg/dL (26.5 μmol/L) over 2 days OR oliguria ≥ 4 hours	AKI OR GFR < 60 mL/min/1.73m^2 OR increase in GFR by > 35% relative to the baseline value OR increase in SCr by > 50% relative to the baseline value	GFR < 60 mL/min/1.73m^2
	OR	OR	OR
Structural criteria	Not defined	Markers of kidney damage (the most common being albuminuria, hematuria, or pyuria)	Markers of kidney damage (the most common being albuminuria)

AKD — acute kidney disease; AKI — acute kidney injury; CKD — chronic kidney disease; GFR — glomerular filtration rate; SCr — serum creatinine

Without constant supervision of the diagnosed patients by the specialist, we will not be able to develop systems for staging and classifying the disease or to provide a specific cause of the disease.

Given the current gap in research on AKI, AKD, and CKD, there is a need for further, more precise studies making use of large clinical and administrative datasets, which will facilitate clinical decision-making and patient care.

References

1. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. 2002; 39(Suppl 1): S1–S266.
2. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney Int Suppl. 2012; 2: 1–138.
3. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl. 2013; 3(1): 1–150.
4. Lameire N, Levin A, Kellum JA, et al. Harmonizing acute and chronic kidney disease definition and classification: report of a Kidney Disease: Improving Global Outcomes (KDIGO) Consensus Conference. Kidney Int. 2021; 100(3): 516–526, doi: 10.1016/j.kint.2021.06.028, indexed in Pubmed: 34252450.
5. Macedo E, Hemmila U, Sharma SK, et al. Recognition and management of community-acquired acute kidney injury in low-resource settings in the ISN 0by25 trial: A multi-country feasibility study. PLoS Med. 2021; 18(1): e1003408, doi: 10.1371/journal.pmed.1003408, indexed in Pubmed: 33444372.
6. James MT, Levey AS, Tonelli M, et al. Incidence and prognosis of acute kidney diseases and disorders using an integrated approach to laboratory measurements in a universal health care system. JAMA Netw Open. 2019; 2(4): e191795, doi: 10.1001/jamanetworkopen.2019.1795, indexed in Pubmed: 30951162.
7. See EJ, Polkinghorne KR, Toussaint ND, et al. Epidemiology and outcomes of acute kidney diseases: a comparative analysis. Am J Nephrol. 2021; 52(4): 342–350, doi: 10.1159/000515231, indexed in Pubmed: 33906191.
8. Xiao YQ, Cheng W, Wu Xi, et al. Novel risk models to predict acute kidney disease and its outcomes in a Chinese hospitalized population with acute kidney injury. Sci Rep. 2020; 10(1): 15636, doi: 10.1038/s41598-020-72651-x, indexed in Pubmed: 32973230.
9. Nagata K, Horino T, Hatakeyama Y, et al. Effects of transient acute kidney injury, persistent acute kidney injury and acute kidney disease on the long-term renal prognosis after an initial acute kidney injury event. Nephrology (Carlton). 2021; 26(4): 312–318, doi: 10.1111/nep.13831, indexed in Pubmed: 33207040.
10. Hsu CK, Wu IW, Chen YT, et al. Acute kidney disease stage predicts outcome of patients on extracorporeal membrane oxygenation support. PLoS One. 2020; 15(4): e0231505, doi: 10.1371/journal.pone.0231505, indexed in Pubmed: 32268348.
11. Mizuguchi KA, Huang CC, Shempp I, et al. Predicting kidney disease progression in patients with acute kidney injury after cardiac surgery. J Thorac Cardiovasc Surg. 2018; 155(6): 2455–2463.e5, doi: 10.1016/j.jtcvs.2018.01.093, indexed in Pubmed: 29548590.
12. Cho JS, Shim JK, Lee S, et al. Chronic progression of cardiac surgery associated acute kidney injury: Intermediary role of acute kidney disease. J Thorac Cardiovasc Surg. 2021; 161(2): 681–688.e3, doi: 10.1016/j.jtcvs.2019.10.101, indexed in Pubmed: 31959433.
13. Matsuura R, Iwagami M, Moriya H, et al. The clinical course of acute kidney disease after cardiac surgery: a retrospective observational study. Sci Rep. 2020; 10(1): 6490, doi: 10.1038/s41598-020-62981-1, indexed in Pubmed: 32300140.
14. Chen YT, Jenq CC, Hsu CK, et al. Acute kidney disease and acute kidney injury biomarkers in coronary care unit patients. BMC Nephrol. 2020; 21(1): 207, doi:

10.1186/s12882-020-01872-z, indexed in Pubmed: 32487168.
15. Kofman N, Margolis G, Gal-Oz A, et al. Long-term renal outcomes and mortality following renal injury among myocardial infarction patients treated by primary percutaneous intervention. Coron Artery Dis. 2019; 30(2): 87–92, doi: 10.1097/MCA.0000000000000678, indexed in Pubmed: 30422833.
16. Long TE, Helgadottir S, Helgason D, et al. Postoperative acute kidney injury: focus on renal recovery definitions, kidney disease progression and survival. Am J Nephrol. 2019; 49(3): 175–185, doi: 10.1159/000496611, indexed in Pubmed: 30699414.
17. Tonon M, Rosi S, Gambino CG, et al. Natural history of acute kidney disease in patients with cirrhosis. J Hepatol. 2021; 74(3): 578–583, doi: 10.1016/j.jhep.2020.08.037, indexed in Pubmed: 32918956.
18. Mima A, Tansho K, Nagahara D, et al. Incidence of acute kidney disease after receiving hematopoietic stem cell transplantation: a single-center retrospective study. PeerJ. 2019; 7: e6467, doi: 10.7717/peerj.6467, indexed in Pubmed: 30842899.
19. Kellum JA, Sileanu FE, Bihorac A, et al. Recovery after acute kidney injury. Am J Respir Crit Care Med. 2017; 195(6): 784–791, doi: 10.1164/rccm.201604-0799OC, indexed in Pubmed: 27635668.
20. Fenoglio R, Sciascia S, Baldovino S, et al. Acute kidney injury associated with glomerular diseases. Curr Opin Crit Care. 2019; 25(6): 573–579, doi: 10.1097/MCC.0000000000000675, indexed in Pubmed: 31689245.
21. Kolhe NV, Reilly T, Leung J, et al. A simple care bundle for use in acute kidney injury: a propensity score-matched cohort study. Nephrol Dial Transplant. 2016; 31(11): 1846–1854, doi: 10.1093/ndt/gfw087, indexed in Pubmed: 27190331.
22. Chen S, Tang Z, Xiang H, et al. Etiology and outcome of crescentic glomerulonephritis from a single center in China: a 10-year review. Am J Kidney Dis. 2016; 67(3): 376–383, doi: 10.1053/j.ajkd.2015.07.034, indexed in Pubmed: 26388283.
23. Chu R, Li C, Wang S, et al. Assessment of KDIGO definitions in patients with histopathologic evidence of acute renal disease. Clin J Am Soc Nephrol. 2014; 9(7): 1175–1182, doi: 10.2215/CJN.06150613, indexed in Pubmed: 24789552.
24. Moledina DG, Luciano RL, Kukova L, et al. Kidney biopsy-related complications in hospitalized patients with acute kidney disease. Clin J Am Soc Nephrol. 2018; 13(11): 1633–1640, doi: 10.2215/CJN.04910418, indexed in Pubmed: 30348813.