Definition, Management, and Outcomes of Acute Kidney Injury: An International Survey of Nephrologists

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Keywords

Acute kidney injury · Dialysis · Nephrologists · Renal replacement therapy · Survey

Abstract

Background: Acute kidney injury (AKI) is a complex disease burdened by uncertainties of definition, management strategies, and prognosis. This study explores the relationship between demographic characteristics of nephrologists and their perceptions about the definition, management, and follow-up of AKI. **Methods:** We developed a Web-based survey, the International Survey on Acute Kidney Injury (ISAKI), consisting of 29 items in 4 categories: (1) demographic and practice characteristics, (2) definition of AKI, (3) management of renal replacement therapy (RRT) in AKI, and (4) sequelae of AKI. A multivariable stepwise logistic regression model was used to examine relationships between the dependent variables and the demographic characteristics of the respondents. **Results:** Responses from 743 nephrologists from 90 countries were analyzed. The majority (60%) of respondents reported using RIFLE and/or AKIN criteria regularly to define AKI, although US nephrologists were less likely to do so (OR: 0.58; 95% CI: 0.42–0.85). The most common

initial RRT modality was intermittent hemodialysis (63.5%), followed by continuous RRT (23.8%). Faculty affiliation was associated with a higher likelihood of using a dialysis schedule of ≥ 4 times a week (OR: 1.75; 95% CI: 1.20–2.55). The respondents believed that a single episode of AKI increases the likelihood of development of chronic kidney disease (CKD) (55%), subsequent AKI (36%), and rapid progression of pre-existing CKD (87%). US nephrologists were less likely to recommend follow-up after resolution of AKI (OR: 0.15; 95% CI: 0.07–0.33). **Conclusions:** Our findings highlight the need for a widely accepted consensus definition of AKI, a uniform approach to management, and improved follow-up after resolution of AKI episodes.

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Introduction

Acute kidney injury (AKI) is a complex disorder with a wide variation in definitions [1, 2]. Serum creatinine and urine output are frequently used parameters in defining renal function; however, a consensus on when these parameters represent AKI has been difficult to reach [3, 4]. In 2004, the Acute Dialysis Quality Initiative (ADQI)

working party published the RIFLE criteria, which differentiate 3 levels of AKI severity (risk, injury, and failure) and 2 outcome stages (loss and end-stage renal disease [ESRD]) [5, 6]. In 2005, Chertow et al. [7] demonstrated that an even smaller change in serum creatinine ≥ 0.3 mg/dL during hospital admission was independently associated with a 4-times increased likelihood of in-hospital death. Furthermore, acute coronary syndrome-associated AKI is associated with a >3 -fold increase in early mortality and a >2 -fold increase in long-term mortality [8]. In 2007, a modified version of the RIFLE criteria was published by the AKIN (Acute Kidney Injury Network), known as the AKIN criteria, in which the categories of risk, injury, and failure were replaced by stage 1, 2, and 3, respectively, and the outcome categories loss and ESRD were eliminated. An absolute increase in serum creatinine level of ≥ 0.3 mg/dL has been added to the minimum requirements for stage 1, with the recognition that small changes in renal function may portend adverse outcomes [9, 10].

The current consensus definitions, based on serum creatinine and urine output, are perceived as inadequate and suboptimal [11, 12]. In a retrospective review of the quality of documentation and clinical management of all patients with AKI from a cohort of 1,577 patients admitted to a university hospital during a 1-month period, AKI was unrecognized in 23.5% of the patients. The authors concluded that clinicians need to be more watchful in their recognition of AKI [13]. The acknowledgment of different levels of renal dysfunction has the potential to guide therapeutic strategies and prognostication [14, 15]. The usefulness of a standardized definition system in everyday clinical practice is not well known. A systematic review found the definition of AKI not to be uniform among 21 studies [16]. A recent paper highlights the need for a standardization of the AKI definition [17]. In another systematic review of 76 clinical and 75 preclinical studies of AKI, a total of 57.8% of the clinical studies defined AKI using the standard criteria, while the majority of the preclinical studies defined AKI according to the increase in serum creatinine and blood urea nitrogen. The authors conclude that differences between studies in regard to the definition of AKI may affect the translation of preclinical findings into the clinical setting [18]. Heterogeneity in the criteria for defining AKI has been shown to lead to variations in the inclusion of patients in clinical studies of AKI [6].

In addition to the variability in the definition of AKI, many aspects of the management of renal replacement therapy (RRT) in AKI remained debated. A large, multi-

center, prospective trial comparing an intensive RRT regimen with a less intensive RRT regimen found no significant difference in mortality, improvement of renal function, or reduction in the rate of nonrenal failure between the two regimens [19]. An optimal dose of RRT has yet to be defined, although a “minimum” dose of RRT (≥ 35 mL/h/kg for continuous RRT [CRRT] or ≥ 1.2 Kt/V for daily intermittent hemodialysis [IHD]) has been proposed. Nevertheless, the clinical approach to AKI management still shows uncertainty and a lack of standardization among many clinicians worldwide.

The long-term outcomes after an AKI episode, including risk of development of chronic kidney disease (CKD) and progression of preexisting CKD to ESRD and death, have been examined in multiple studies [20–31]. The perceptions of the nephrology community worldwide regarding long-term sequelae and outcomes after an AKI episode are not well known. Approaches to AKI are also different between developed and developing countries [32]. Detection of AKI in developing countries is complicated by limited laboratory resources, availability of previous serum creatinine values, and financial constraints, leading to inability to measure serial creatinine [33, 34]. Not only is there a lack of resources for detecting AKI, but there is also lack of information regarding the epidemiology of AKI in developing countries [35]. Depending on availability and experience, the timing and modality of treatment of AKI varies significantly between various parts of the world [36–41].

The objective of this study was to explore the relationship between the demographic characteristics of nephrologists and their perceptions regarding the definition, management, and sequelae of AKI.

Materials and Methods

We developed a Web-based survey, the International Survey on Acute Kidney Injury (ISAKI), to explore the opinions of nephrologists worldwide regarding the definition, management, and outcomes of AKI. The research protocol and the survey instrument were approved by the Pennsylvania State University College of Medicine Institutional Review Board. Survey items were generated based on evaluation of the literature and discussions among the investigators. A preliminary version of the questionnaire was pilot tested by sending the survey via e-mail to a multinational group of 18 nephrologists and 6 nephrology fellows from 3 training programs in the USA. Based on comments received from this group regarding its clarity, format, and content, the survey instrument was modified.

The final questionnaire consisted of 29 items in the following 4 categories: (1) demographic and practice characteristics ($n = 11$), including duration of nephrology experience, academic affiliation,

practice settings, time spent in clinical activity, and estimated number of new patients with AKI seen per month; (2) definition of AKI ($n = 5$), including criteria used to define AKI and most appropriate threshold for rise in serum creatinine and decline in urine output in defining AKI (the Likert scale was utilized to rate frequency of use of the RIFLE/AKIN criteria to define AKI and usefulness in clinical practice); (3) management of RRT in AKI ($n = 10$), including type of modality available (IHD, CRRT, sustained low-efficiency dialysis [SLED], and acute peritoneal dialysis), most commonly used modality for initial therapy, preemptive use of RRT, and IHD schedule/frequency per week (5 questions focused on CRRT, including type of solutions, anticoagulation, and order set used to prescribe CRRT; importance of patient weight when prescribing the CRRT effluent flow rate; and comparison with IHD); and (4) outcomes of AKI ($n = 3$), i.e., opinion about long-term outcomes after an episode of AKI, recommendation for nephrology follow-up after an AKI episode, and duration of dialysis dependence after AKI for considering ESRD.

Sources of e-mail addresses included lists provided by some national and regional societies of nephrology and a list compiled by searching PubMed for e-mail addresses of corresponding authors affiliated with divisions/departments of nephrology. For the latter, our search consisted of combining the following terms “(section OR department OR division) AND (nephrology)” AND Internet domain suffix listings using Internet country codes and domains such as “.edu,” “.com,” “.net,” “.ac,” and “.gov” with the OR operator. We merged all the lists prepared with the mentioned strategies, eliminated duplicate entries, and created a database of 7,566 unique e-mail addresses. We sent the survey link using Survey Monkey via e-mail to the identified nephrologists, worldwide. The invitation e-mail, with the subject heading “Research Survey on Acute Kidney Injury,” contained an explanation of the research, reassuring the potential participants of the confidentiality and anonymity of their responses. Two follow up e-mails (2 weeks and 4 weeks after the initial invitation) were sent to the recipients of the original e-mails, requesting completion of the survey if not already completed. No financial incentive was offered.

The aggregate data were summarized using descriptive statistics. Two-way tables and χ^2 testing were performed for categorical variables. A multivariable stepwise logistic regression model was used to examine the relation of the dependent variables with the demographic characteristics of respondents such as age, years of practice, country of practice, academic affiliation, rural/urban location of practice, and response to important questions. All statistical analyses were performed using SAS software version 9.2 (SAS Institute, Cary, NC, USA), and $p < 0.05$ was considered statistically significant.

Results

A total of 2,335 of the 7,566 e-mails were returned as being undeliverable. Of the 5,231 recipients of the delivered e-mails, 1,085 (20.6%) attempted the survey and 342 respondents did not complete the survey. The responses from a total of 743 nephrologists were analyzed. The demographic characteristics of the participants are presented in Table 1.

Table 1. Characteristics of the respondents

Characteristic	<i>n</i>	%
Age		
<50 years	419	58
≥50 years	305	42
Gender		
Male	548	75
Female	176	25
Nephrology practice		
In training	22	3
>10 years	462	64
<10 years	229	33
Country of practice		
USA	199	28
Other countries	525	72
Practice location		
Urban/suburban	682	94
Rural	37	6
Academic/faculty affiliation		
Yes	511	71
No	207	29
Clinical activity		
<30%	54	7
30–60%	244	34
>60%	425	59
Predominant type of practice		
Inpatient	587	81
Outpatient	136	19
New patients with AKI seen per month		
<10	319	44
10–20	269	37
>20	136	19
AKI, acute kidney injury.		

The majority of the participants were <50 years of age (58%), male (75%), with >10 years of practice experience in nephrology (64%), affiliated with a teaching hospital (71%), and working in urban/suburban settings (94%). There were responses from 90 countries, with the largest proportion (28%) from the USA.

Definition of AKI

The majority (60%) of the respondents indicated using the RIFLE and/or AKIN criteria regularly to define AKI (Table 2). Only 14% of the respondents use an absolute increase in serum creatinine of 0.3 mg/dL to define AKI. Overall, 69% of the respondents use a threshold of less than doubling from baseline creatinine to diagnose AKI, and 55% of the respondents believe that the increase in serum creatinine should be sustained for ≥24 h before diagnosing AKI.

Table 2. Criteria used for the definition of acute kidney injury by respondents

Criterion	Respondents using the criterion, %
RIFLE and/or AKIN criteria	60
Absolute increase of ≥ 0.3 mg/dL from baseline	14
Less than doubling of serum creatinine from baseline	69
≥ 24 h sustained rise in serum creatinine	55

Table 3. Availability and use of modality of renal replacement for acute kidney injury

	Modality available to respondents, %	Modality used by respondents, %
Intermittent hemodialysis	95	63.5
Continuous renal replacement therapy	69	23.8
Peritoneal dialysis	46	5
Sustained low-efficiency dialysis	38	7.7

In the multivariable logistic regression analysis, US nephrologists were less likely to use the RIFLE and/or AKIN criteria to define AKI (OR: 0.58; 95% CI: 0.42–0.85); they were also less likely to consider the RIFLE and AKIN criteria useful in clinical practice (OR: 0.24; 95% CI: 0.14–0.38). US nephrologists were more likely to consider the threshold of an absolute increase in serum creatinine of ≥ 0.3 mg/dL in defining AKI (OR: 1.84; 95% CI: 1.17–2.90).

Management of RRT in AKI

IHD was available to 95% of the respondents and CRRT was available to 69% of the respondents (Table 3). Only 46% of the respondents had acute peritoneal dialysis available at their facility, and 38% of the respondents reported an availability of SLED. The most common RRT modality used as initial therapy for AKI was IHD (by 63.5% of the respondents), followed by CRRT (by 23.8%), SLED (by 7.7%), and acute peritoneal dialysis (by 5%). Typical IHD treatment schedules were 3 times a week (35%), 4 times a week (28%), and >4 times a week (30%). Among those respondents who had CRRT available at their center, 34% used it as the initial treatment. The majority (73%) of the nephrologists were somewhat likely or extremely likely to agree with the following statement: “In the absence of a clear indication for initiation of RRT such as severe volume overload, hyperkalemia, metabolic acidosis, or overt uremic manifestations, how likely would you consider starting RRT preemptively in response to progressive azotemia or oliguria?”

Among those respondents who use CRRT at their center, 54% use either preprinted order sets or computerized order entry systems, 68% use premixed, commercially available solutions, 65% use unfractionated heparin as an anticoagulant, and 18% use citrate as an anticoagulant. The majority (95%) of the respondents reported a patient’s weight to be considered important when prescribing the CRRT effluent flow rate.

In comparison with IHD, CRRT was considered to be better tolerated (72% of the respondents), preferred for patients with hemodynamic instability (93%), preferred for patients with AKI and multisystem organ failure (73%), likely to lead to improved optimization of the volume (70%), likely to provide a better electrolyte and acid-base balance (51%), associated with an increased risk of bleeding (38%), likely to provide better clearance (41%), likely to lead to improved overall outcomes (25%), and more cost effective (18%).

In the multivariable logistic regression analysis, a faculty affiliation to a medical school/college/university was associated with a higher likelihood of using a dialysis treatment schedule of ≥ 4 times a week (OR: 1.75; 95% CI: 1.20–2.55).

Outcome of AKI

The respondents believe that a single episode of AKI increases the likelihood of development of CKD (51%), subsequent AKI (36%), and rapid progression of preexisting CKD (87%) (Table 4). In order to determine whether a person has developed ESRD following an episode of AKI, ≥ 12 weeks of dialysis dependence was considered

Table 4. Perceived outcomes of acute kidney injury

Outcome	Respondents agreeing with stated outcome, %
Acute kidney injury leads to chronic kidney disease	51
An episode of acute kidney injury predisposes to subsequent episodes of acute kidney injury	36
Acute kidney injury predisposes to more rapid progression of chronic kidney disease	87

necessary by 58% of the respondents. The majority (75%) of the respondents recommended nephrological follow-up after resolution of an episode of AKI. In the multivariable logistic regression analysis, compared with non-US nephrologists, US nephrologists were less likely to recommend follow-up after resolution of AKI (OR: 0.15; 95% CI: 0.07–0.33).

Discussion

In this international survey, we used a Web-based questionnaire to explore the relationship between demographic characteristics of nephrologists and their perception of the definition, management, and sequelae of AKI. We found that US nephrologists were less likely to use the RIFLE and/or AKIN criteria to define AKI and less likely to consider these criteria useful in clinical practice, but they were more likely to consider the threshold of an absolute increase of serum creatinine of ≥ 0.3 mg/dL in defining AKI. We found that a faculty affiliation to a medical school/college/university was associated with a higher likelihood of using a dialysis treatment schedule of ≥ 4 times per week. We also found that US nephrologists were less likely to recommend follow-up after resolution of an AKI episode. Some of our findings were similar to those of a study on nephrologists in a meeting in Italy, in which 55% of the respondents used the RIFLE criteria [42]. Both studies show a trend toward an increasing awareness of RRT dosing. In our study, the majority of the respondents reported a patient's weight to be considered important when prescribing the CRRT effluent flow rate, which reflects the recommendations of the 17th ADQI International Consensus from 2016 [43]. This is in contrast to another survey in the USA which suggested that monitoring of the delivered dosage of hemodialysis was only infrequently assessed [44]. It is possible that the results of recent trials might have improved the knowledge of the respondents.

The major limitation of our study is respondent bias. Considering that response rates to Web-based surveys of health-care providers range from 11 to 52% [45–50], the response rate of 21% in this study appears reasonable. The nature of the survey, which was Internet based, excluded those without Internet access. This is likely to have led to sampling a less representative group of nephrologists. The observations (Table 1) that 71% of the respondents practiced in an academic setting and 94% practiced in urban/suburban areas highlight this limitation. Our search for e-mail addresses of nephrologists through their publications is likely to have led to a biased sampling of academic nephrologists. Another limitation of our study is that it does not address the impact of other potential factors, such as the quality of medical school education and the extent of continuing medical education on nephrologists' perceptions. Our study is also limited by the variability in income levels between the countries of the respondents and the available therapeutic options in the different regions of the world, which might have an impact on their management decisions.

A strong feature of this study is that it includes a large number of respondents from all over the world ($n = 1,085$ from 90 countries) with diverse practice patterns. The sample includes transplant and general nephrologists, academic and private nephrologists, and nephrologists practicing in rural and urban settings. The diversity in practice patterns and demographics allowed for a detailed analysis of the interaction of multiple factors with the dependent variables.

Conclusions

The proposed criteria for AKI definition are used by the majority of nephrologists worldwide; the variation in the definition of AKI in clinical practice is related to the nephrologists' geographical location. Teaching hospital-

affiliated nephrologists are more likely to use intensive dialysis schedules, and US-based nephrologists are less likely to recommend follow-up after resolution of AKI. Our findings highlight the need for a widely accepted consensus definition of AKI, a uniform approach to management, and improved follow-up after resolution of AKI episodes.

Statement of Ethics

The research protocol and the survey instrument were approved by the Pennsylvania State University College of Medicine Institutional Review Board.

Conflict of Interest Statement

The authors declare no conflicts of interest.

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