Subclinical Acute Kidney Injury is an Early Stage of AKI

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Background

A recent ADQI consensus conference on utilizing biomarkers in acute kidney injury (AKI) (Murray et al Kidney Int. 2014; 85:513-21) has suggested that novel biomarkers such as NGAL, KIM-1, and IGFBP-7 can identify kidney damage prior to alterations in renal functional changes recognized by serum creatinine (sCr). Combining damage and functional markers can thus permit recognition of an early stage of AKI termed subclinical (incipient) AKI.

Objectives

a. To evaluate if damage biomarkers would allow recognition of an early stage of AKI (Subclinical AKI).

b. To assess the utility of urinary sediment score (Perazella et al Clin J Am Soc Nephrol 3:1615-19; 2008) to predict subsequent development of AKI.

c. To asses if there is a difference in mortality between clinical and subclinical AKI.

Hypothesis

In this study we tested the hypothesis that a panel of damage biomarkers could detect subclinical AKI and would predict the subsequent development of clinical (established) AKI.

Patients and Methods

- We included 50 consecutive patients admitted to our Institution medical ICU. Daily sCr, urine albumin and β2–Microglobulin levels were measured each 24 hours for 7 consecutive days. We also evaluated urine sediment and assigned a score from 1 to 3 using Perazella et al criteria as shown in table 1 (Clin J Am Soc Nephrol 3:1615-19; 2008).

- We define incipient AKI if any of the following criteria was reached in the absence of alterations in sCr: new onset of albuminuria (≥15 mg/L), urine β2-Microglobulin (≥3.2 mg/L) or a urinary sediment score ≥2.

- Clinical AKI was defined by KDIGO sCr criteria.

- We analyzed the predictive value of each of these biomarkers for the subsequent development of clinical AKI as well to predict survival.

Table 1. Scoring system based on number of granular casts and RTEC seen per high-power field for differentiating ATN from prerenal AKI[a]

Score	Description
1	RTE cells 0 and granular casts 0
2	RTE cells 0 and granular casts 1 to 5 or RTE cells 1 to 5 and granular casts 0
3	RTE cells 1 to 5 and granular casts 1 to 5 or RTE cells 0 and granular casts 6 to 10 or RTE cells 6 to 20 and granular casts 0

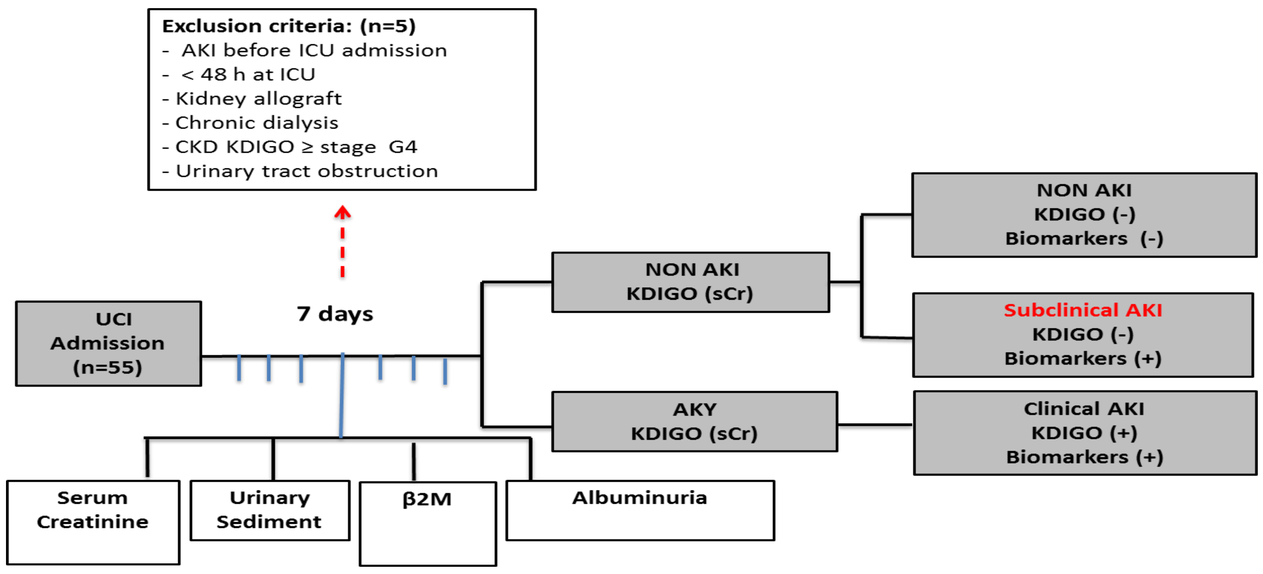
[a]ATN, acute tubular necrosis; AKI, acute kidney injury; RTEC, renal tubular epithelial cells.

Results

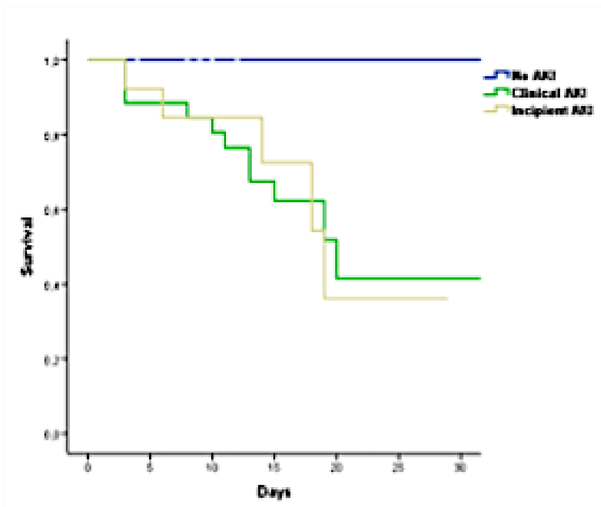
Table 2. Baseline characteristics of patients at ICU admission.

Characteristic s	NON AKI (n=11)	Subclinical AKI (n=13)	AKI KDIGO (sCr criteria((n=26)	P value
Age (years) Mean ± SD	49.36 ± 16.32	62.08 ± 20.48	70.69 ± 8.84	0.001
Female Gender(%)	8 (73)	13 (50)	5 (38)	0.24
Physiological variables				
Mean arterial blood pressure (mmHg) Mean ± SD	79.45 ± 11.18	95.54 ± 19.84	77.81 ± 16.52	0.008
Urinary volume (mL/hour) Mean ± SD	98.09 ± 58.61	115 ± 54.79	89.73 ± 39.99	0.317
Weight (Kg) Mean ± SD	62.73 ± 3.44	73.08 ± 9.02	75 ± 11.66	0.004

Of the 50 patients, 11 (22%) did not develop AKI while 39 (78%) developed incipient AKI that progressed to clinical AKI in 26 (67%) while 13 (33%) did not have a rise in sCr as shown in figure 1.



The rise in urine albumin and β2-Microglobulin levels at 24 and 48 hours predicted the development of clinical AKI (Albumin AUC 0.753 (95% CI 0.612-0.894), p = 0.02; β2-Microglobulin AUC 0.770 (95% CI 0.624-0.916), p=0.010) at 24 h and Albumin AUC 0.707 (95% CI 0.555-0.859), p=0.012; β2-Microglobulina AUC 0.703 (95% IC 0.545-0.861), p=0.14). A urinary sediment score ≥ 2 at 24 and 48 h equally predicted the development of established AKI; AUC 0.818 (95% IC 0.638-0.998), p=0.001 and AUC 0.773 (95% IC 0.580-0.965), p=0.006, respectively.



*Log Rank p=0.857

Figure 2. Twenty-eight day mortality did not differ between patients with subclinical AKI (green line) who didn't developed clinical AKI and patients with sub-clinical AKI who developed clinical AKI (blue line).

Conclusions

Our data shows a high incidence of incipient AKI that progressed to clinical AKI. These findings support the ADQI recommendations to consider subclinical AKI based on positive damage biomarkers alone as an early phase of AKI to further refine the diagnostic and staging criteria for AKI. Identification of incipient AKI would potentially allow earlier intervention with preventive and treatment strategies to reverse kidney injury and improve recovery.

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