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Emerging Concepts in AKI and RRT

Urinary Microscopy to Identify Subclinical AKI

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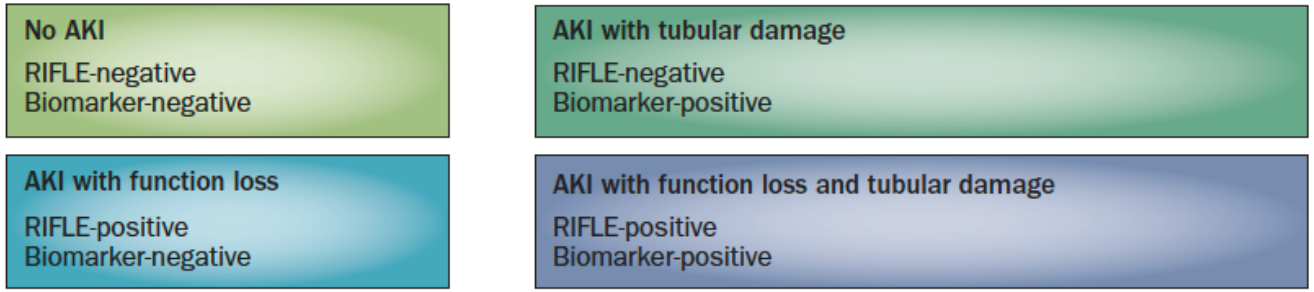
VIEWPOINT

Subclinical AKI is still AKI

Claudio Ronco*[1], John A Kellum[2] and Michael Haase[3]

CRITICAL CARE

- Tubular damage without glomerular function loss was demonstrated to be associated with worse renal and overall outcomes.
- The term ***'subclinical' AKI*** has been introduced, challenging the traditional view that a kidney problem is clinically relevant, only when a loss of filtration function becomes apparent.
- AKI diagnosis could then include functional criteria and damage criteria.
- This may have an impact on the epidemiology, prevention, and management of AKI.



Ronco *et al. Critical Care* 2012, **16**:313
http://ccforum.com/content/16/3/313

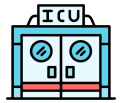
Subclinical acute kidney injury: a novel biomarker-defined syndrome

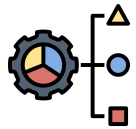
Sean M Bagshaw

Table 1. Summary of outcomes stratified by aggregate subgroups of NGAL and sCr[11]

	NGAL(–)/sCr(–)	NGAL(+)/sCr(–)	NGAL(–)/sCr(+)	NGAL(+)/sCr(+)
No. (%)	1296 (55.8%)	445 (19.2%)	107 (4.6%)	474 (20.4%)
Median peak NGAL, ng/mL (IQR)	59 (20–97)	213 (117–1124)	69 (21–118)	354 (208–1888)
RRT, no. (%)	2 (0.015%)	11 (2.5%)	8 (7.5%)	38 (8.0%)
Composite,* no. (%)	63 (4.9)	69 (15.5)	10 (9.3)	84 (17.7)
Median ICU stay, days (IQR)	4.2 (2.2–6.4)	7.1 (5.4–10.3)	6.5 (3.0–11.7)	9.0 (8.0–14.0)
Median hospital stay, days (IQR)	8.8 (7.7–19.0)	17 (8.4–24.2)	17.8 (5.1–26.4)	21.9 (15.8–29.9)

ICU = intensive care unit. IQR = interquartile range. NGAL = neutrophil gelatinase-associated lipocalin. RRT = renal replacement therapy. sCr = serum creatinine. * Composite = RRT or death.





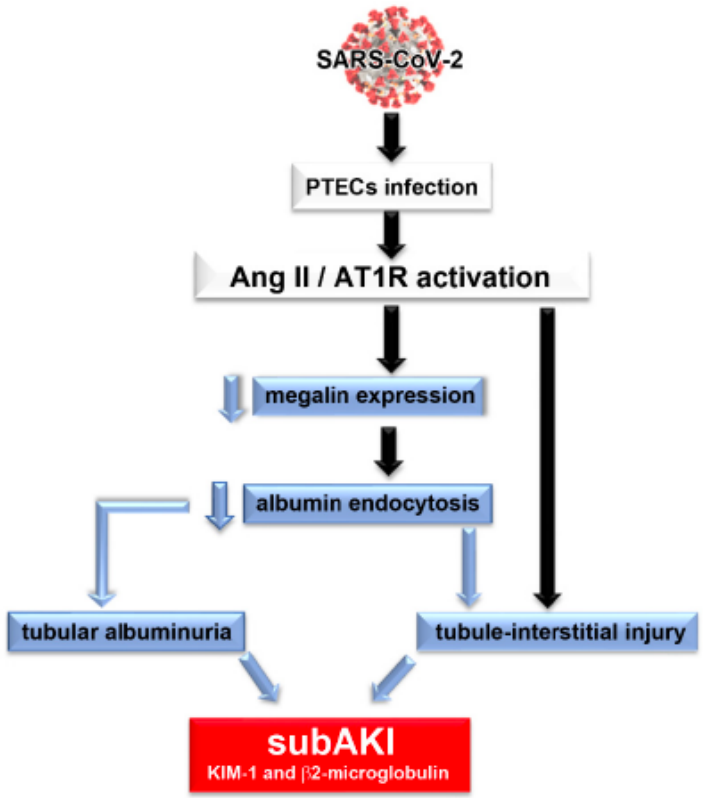
International Journal of
Molecular Sciences

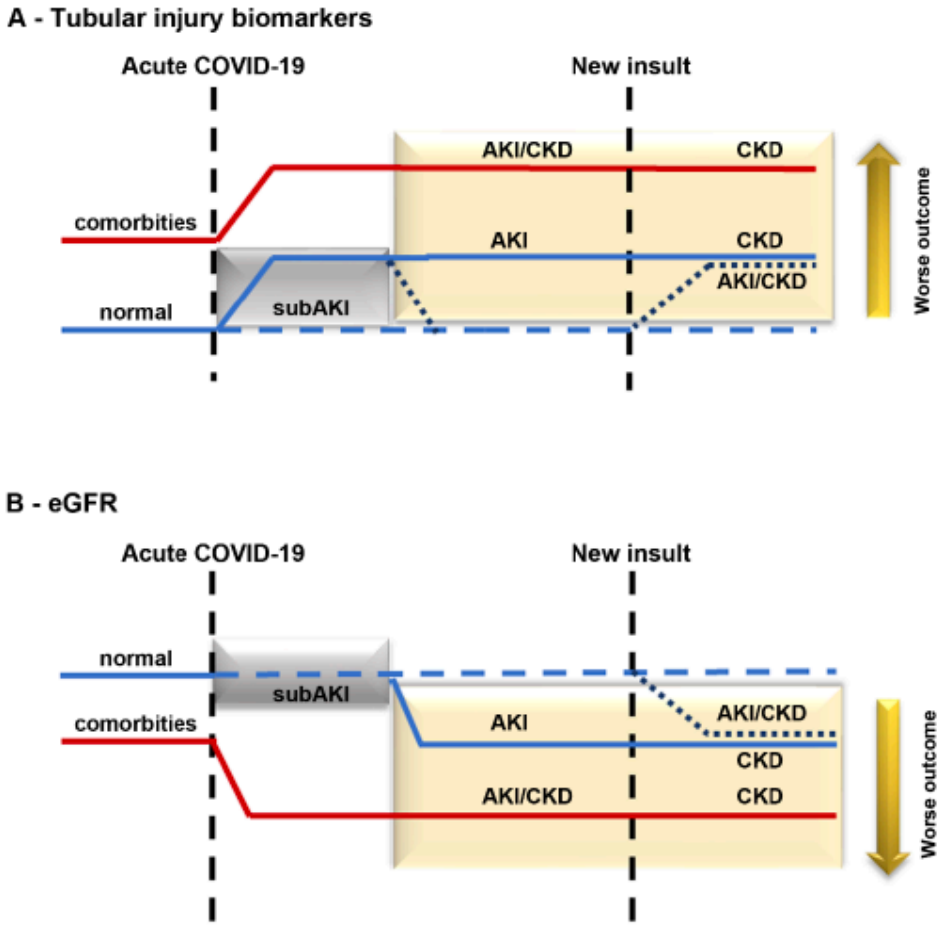
MDPI

Review

Subclinical Acute Kidney Injury in COVID-19: Possible Mechanisms and Future Perspectives

Rodrigo P. Silva-Aguiar [1], Douglas E. Teixeira [1], Rodrigo A. S. Peres [1], Diogo B. Peruchetti [1], Carlos P. Gomes [2,3], Alvin H. Schmaier [4,5], Patricia R. M. Rocco [1,6,7], Ana Acacia S. Pinheiro [1,7] and Celso Caruso-Neves [1,6,7,*]





JAMA Network Open

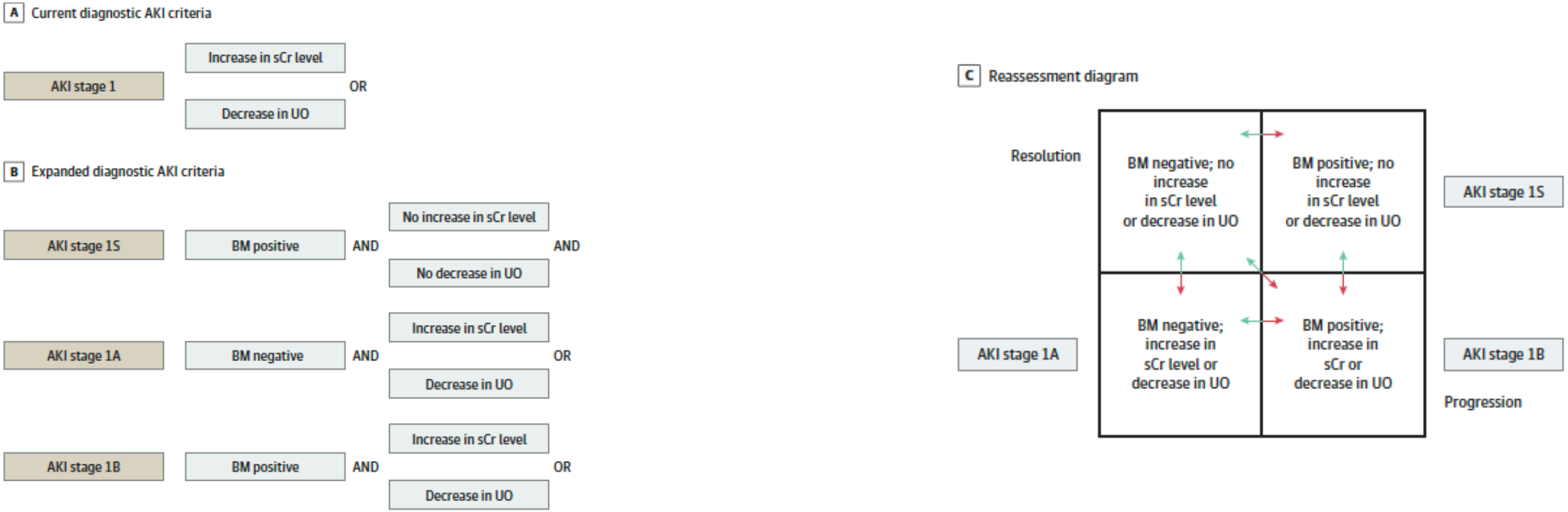
Consensus Statement | Critical Care Medicine

Recommendations on Acute Kidney Injury Biomarkers From the Acute Disease Quality Initiative Consensus Conference

A Consensus Statement

Marlies Ostermann, MD, PhD; Alexander Zarbock, MD; Stuart Goldstein, MD; Kianoush Kashani, MD, MSc; Etienne Macedo, MD, PhD; Raghavan Murugan, MD; Max Bell, MD, PhD; Lui Forni, PhD, MBBS; Louis Guzzi, MD; Michael Joannidis, MD, PhD; Sandra L. Kane-Gill, PharmD, MSc; Matthieu Legrand, MD, PhD; Ravindra Mehta, MD; Patrick T. Murray, MD; Peter Pickkers, MD, PhD; Mario Plebani, MD; John Prowle, MD; Zaccaria Ricci, MD; Thomas Rimmelé, MD, PhD; Mitchell Rosner, MD; Andrew D. Shaw, MB; John A. Kellum, MD; Claudio Ronco, MD

Figure 1. Refined Staging System for the Diagnosis of Acute Kidney Injury (AKI)



Kidney360

Biomarkers for Early Diagnosis of AKI: Could It Backfire?

Rolando Claure-Del Granado,[1,2] *Etienne Macedo*,[3] *and Jonathan S. Chávez-Íñiguez*[4,5]

KIDNEY360 3: 1780–1784, 2022. doi: https://doi.org/10.34067/KID.0001012022

Table 1. Serum creatinine, biomarkers, and its relationship between different AKI scenarios

AKI Scenarios	Serum Creatinine	Biomarker	Example
Kidney stress	✓	✓	Cr: identifies patients with mild CKD who are most at risk for developing AKI Biom: revealed when at risk of AKI
Subclinical AKI	×	✓	Cr: after the insult it takes up to 48 h to rise Biom: some rises in the first hours
AKI diagnosis	✓	×	Cr: the diagnosis of AKI by KDIGO is made by an increase in serum creatinine and a decrease in urinary output Biom: the ADQI group proposes to add biomarkers to the classification, not yet incorporated into KDIGO guideline
Prediction of severe AKI (2,3)	×	✓	Cr: does not identify which patient progressed to severe AKI Biom: Nephrochek >0.3 and NGAL >450 ng/ml predicts AKI severity

Figure 1. | Biomarker competition in AKI. There may be successful biomarkers among the current candidates for becoming an ideal biomarker and help improve early detection, management and outcomes of AKI. However, there are many barriers for their implementation like: availability, costs, unique set of AKI case-mix presentation and pathophysiology, the need of individualized panel of biomarkers for each setting, etc. Further research is needed to advance biomarkers to bedside.

AJKD
Editorial

Urine Microscopy in Acute Kidney Injury: Time for a Change

Claure-Del Granado, Macedo, and Mehta

Table 1. Recent Studies Evaluating Urinary Microscopy in AKI

Reference	Standardized Method of Sample Preparation	Score System Used	Reference Test for Diagnosis of AKI	Differential Diagnosis (prerenal vs ATN)	Prediction of Outcomes	Comments
Bagshaw et al,[11] 2006	None	Based on 7 studies, description of common findings in urine sediment of patients with sepsis; specifically, presence of muddy brown or ECCs, RTECs, and variable trace hematuria and pyuria	No gold standard used for assessing urinary sediment performance, study only summarizes common findings	Not assessed	Not assessed	Only 7 of 27 studies (26%) in the systematic review reported urinary microscopy or sediment findings
Chawla et al,[17] 2008	10 mL collected; centrifuged 5 min at 2,000 rpm; 9.5 mL of supernatant decanted; 0.5 mL of residual left, which was resuspended by hand; using a pipette, 1 drop of sediment dispensed to a glass slide and 24 × 30-mm coverslip gently applied	Grade 1: none (no evidence of GCs or ECCs); grade 2: rare (rare GCs or ECCs; at least 1 GC or ECC seen on the entire slide, but 10% of LPFs); grade 3: moderate (many GCs or ECCs, but not seen on every LPF; casts seen on >10% but <90% of LPFs); grade 4: sheets (sheets of muddy brown cast; GCs or ECCs seen on >90% of LPFs)	Clinical syndrome consistent with ATN determined by the renal consult service	Not assessed	Non–renal recovery (need of RRT or death while SCr trended upward): CSI score, 2.55 ± 0.93; recovery: CSI score, 1.57 ± 0.79; CSI AUROC = 0.79	Standardized urine sediment processing method; score system for predicting outcomes
Perazella et al,[18] 2008	10 mL collected, centrifuged 5 min at 2,000 rpm; 9.5 mL of supernatant removed by suction; 0.5 mL of residual left, which was resuspended by hand; using a pipette, 1 drop of sediment dispensed to a glass slide and coverslip gently applied	Score of 1 for 0 RTEC & 0 GC; score of 2 for 0 RTEC & 1-5 GCs or 1-5 RTECs & 0 GC; score of 3 for 1-5 RTECs & 1-5 GCs or 0 RTEC & 6-10 GCs or 6-20 RTECs & 0 GC	Final diagnosis of type of AKI at discharge (ATN, prerenal AKI, or other) as determined by renal consult service	Score 1: OR, 9.7 (95% CI, 5.3-18.6); Score ≥2: OR, 74 (95% CI, 16.6-329.1)	Not assessed	Standardized urine sediment processing method; score system for differential diagnosis
Perazella et al,[19] 2010	10 mL collected, centrifuged 5 min at 2,000 rpm; 9.5 mL of supernatant removed by suction; 0.5 mL of residual left, which was resuspended by hand; using a pipette, 1 drop of sediment dispensed to a glass slide and coverslip gently applied	Score based on RTECs/HPF (0 points for none, 1 point for 1-5, 2 points for ≥6) and GCs per LPF (0 points for none, 1 point for 1-5, 2 points for ≥6)	Final diagnosis of type of AKI at discharge (ATN, prerenal AKI, or other) as determined by renal consult service	Score not used for differential diagnosis	Adjusted RR of worsening AKI (increase in AKIN stage, need of RRT, or in-hospital death): 0 points, 1.0 (ref); 1 point, 3.4 (95% CI, 1.3-6.5); 2 points, 6.6 (95% CI, 3.4-9.1); ≥3 points, 7.3 (95% CI, 3.8-9.6)	Standardized urine sediment processing method; score system for predicting outcomes

Abbreviations: AKI, acute kidney injury; AKIN, Acute Kidney Injury Network; ATN, acute tubular necrosis; AUROC, area under the receiver operating characteristic curve; CI, confidence interval; CSI, cast scoring index; ECCs, epithelial cellular casts; GCs, granular casts; HPF, high-power field; LPF, low-power field; OR, odds ratio; ref, reference; rpm, revolutions per minute; RR, risk ratio; RRT, renal replacement therapy; RTECs, renal tubular epithelial cells; SCr, serum creatinine.

Acute Kidney Injury: Gaps and Opportunities for Knowledge and Growth

Rolando Claure-Del Granado, MD[*†] Javier A. Neyra, MD[‡] and Rajit K. Basu, MD, MS[§]

From: **Acute Kidney Injury Risk Assessment and the Nephrology Rapid Response Team**

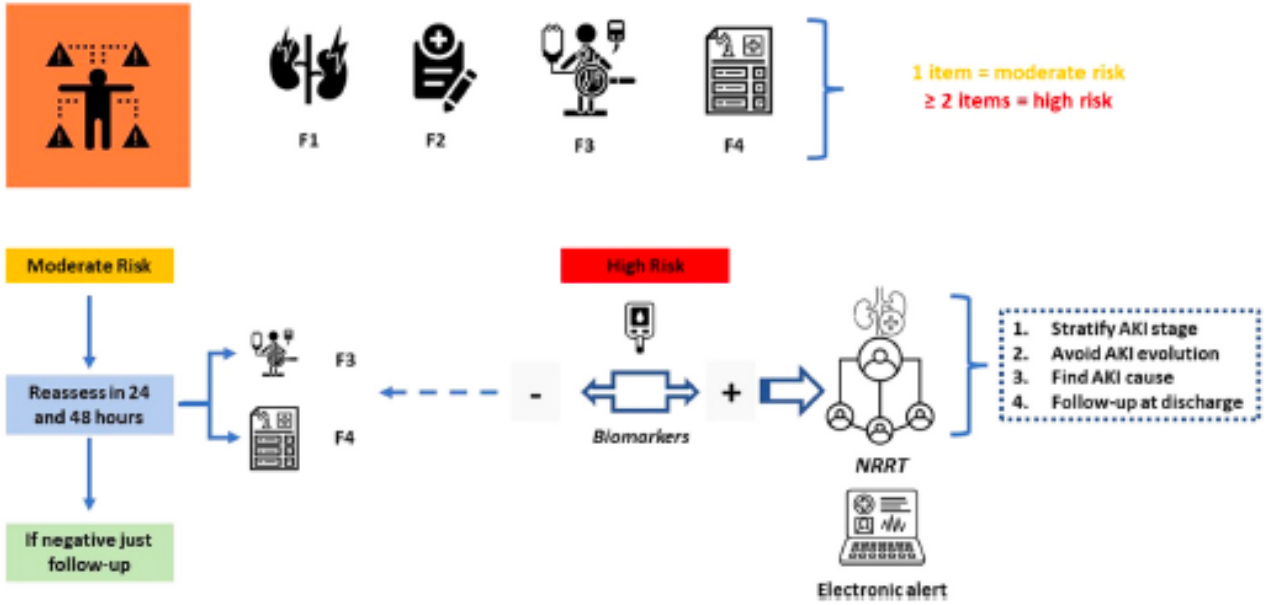
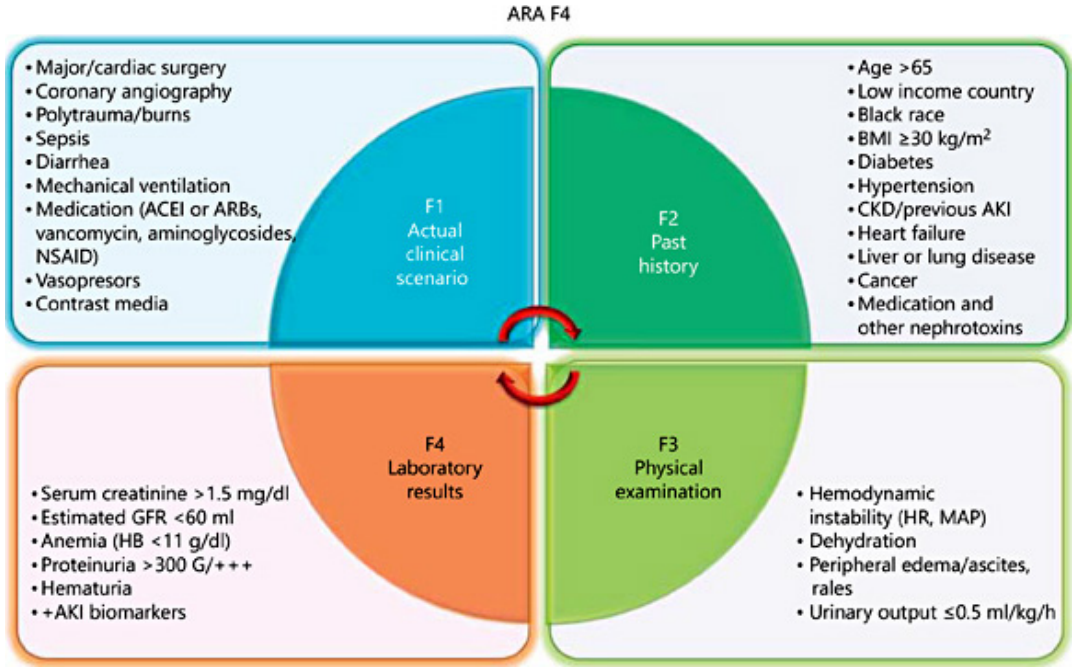
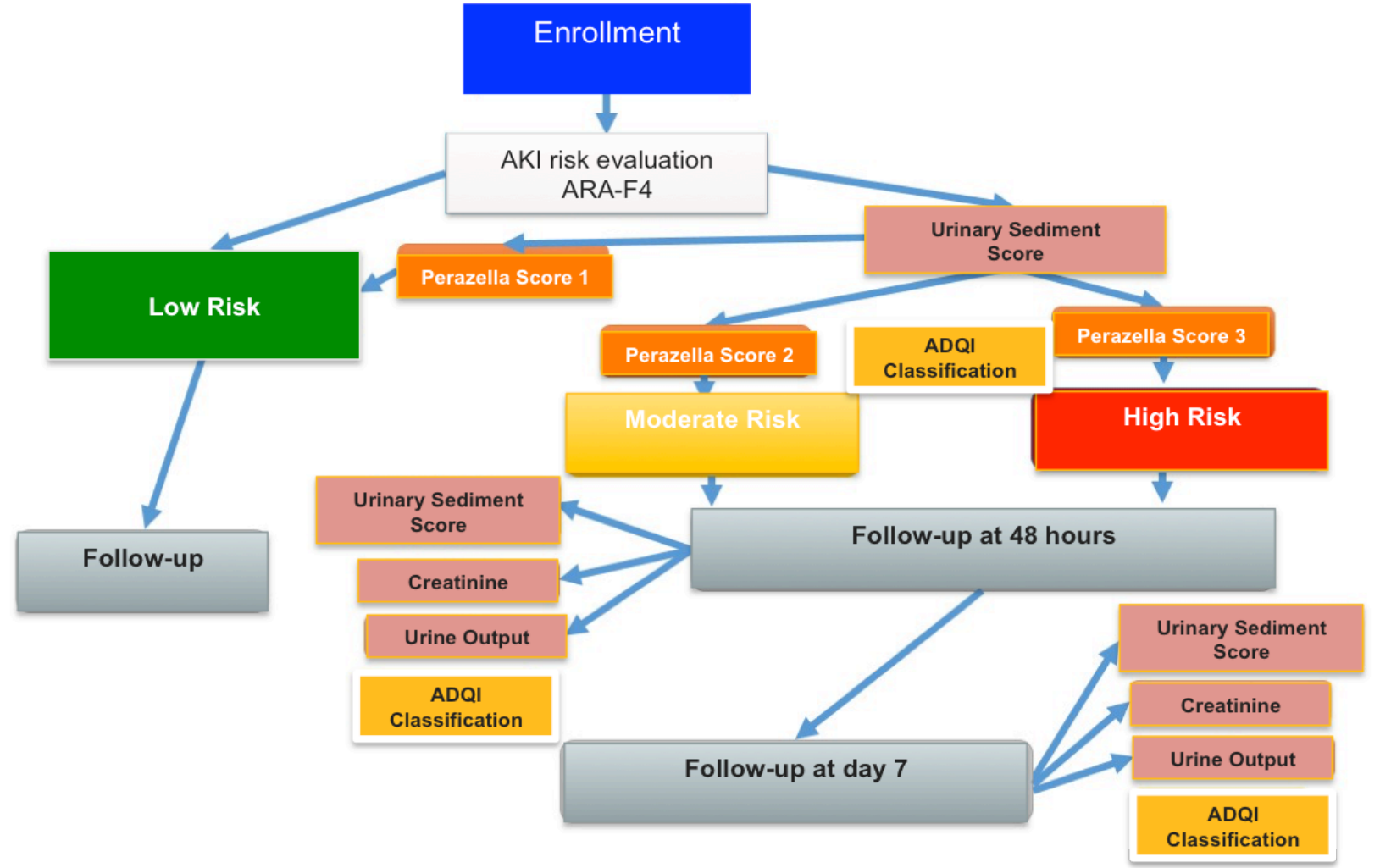


Figure 3. Stepwise approach to the patient at risk of acute kidney injury (AKI). F1: Consider the clinical scenario in which the patient's signs and symptoms and the surrounding circumstances and risks are reviewed and considered. F2: Interview the patient or his/her relatives and review the past history with a goal of identifying the level of susceptibility and intensity of exposures. F3: Physical examination that aims to characterize hemodynamic instability, volume depletion or fluid overload, and signs/source of infection, if any. F4: Analyze laboratory results including possible AKI biomarkers to complete the patient risk stratification. If biomarkers are positive an E-alert is triggered and the nephrology rapid response team (NRRT) is activated.



Blood Purif. 2016;43(1-3):82-88. doi:10.1159/000452402

Study Flowchart



Diagnostic Value of Urine Microscopy for Differential Diagnosis of Acute Kidney Injury in Hospitalized Patients

Mark A. Perazella, Steven G. Coca, Mehmet Kanbay, Ursula C. Brewster, and Chirag R. Parikh

Section of Nephrology, Yale University School of Medicine, New Haven, Connecticut

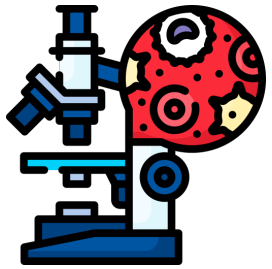


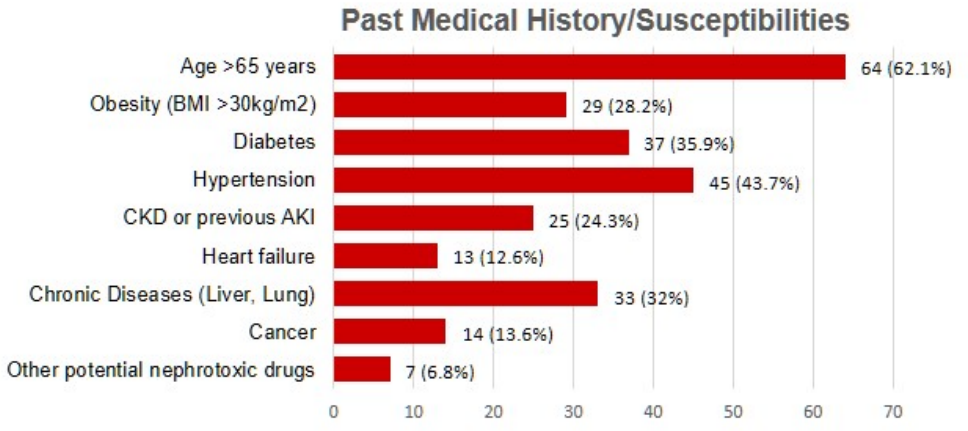
Table 1. Scoring system based on number of granular casts and RTEC seen per high-power field for differentiating ATN from prerenal AKI[a]

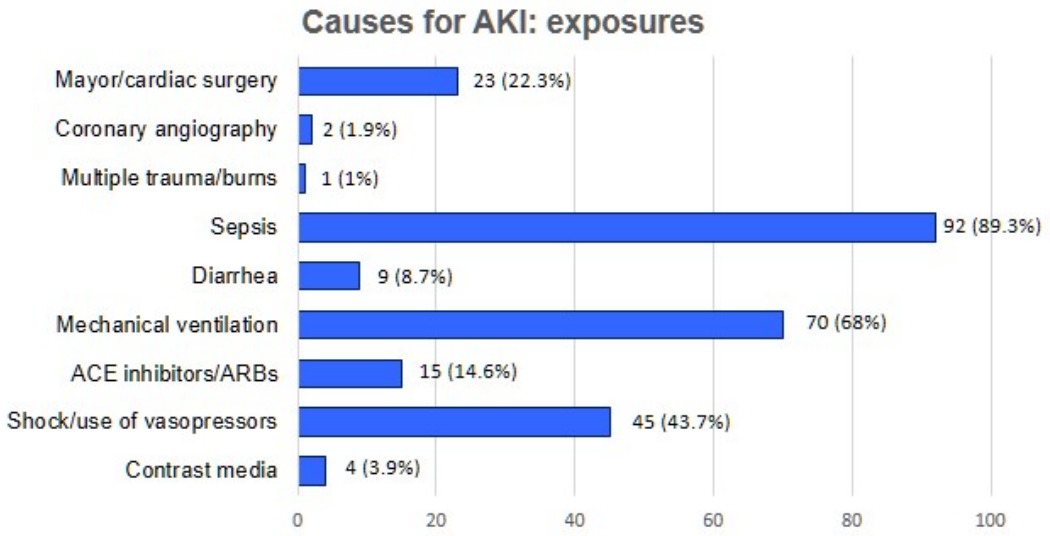
Score	Description
1	RTE cells 0 and granular casts 0
2	RTE cells 0 and granular casts 1 to 5 or RTE cells 1 to 5 and granular casts 0
3	RTE cells 1 to 5 and granular casts 1 to 5 or RTE cells 0 and granular casts 6 to 10 or RTE cells 6 to 20 and granular casts 0

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

Clin J Am Soc Nephrol 3: 1615–1619, 2008. doi: 10.2215/CJN.02860608

Baseline characteristics of patients, and etiology of AKI





Characteristics	Results %,(n)		95 % CI	*p*
Age	65,57	(28-92)		
Gender,%(n)				
Female	53,4	(55)	-6.7509% a 20.0052%	0.3302
Male	46,6	(48)		
Baseline sCr, mg/dl, median(range)	0,91	(0,6-2)		
Baseline eGFR (CKD-EPI 2021)	82,36	(25-126)		
Admission sCr, mg/dl, median(range)	1	(0,6-2,1)		
Admission eGFR (CKD-EPI 2021)	75	(24-126)		
Perazella urinary sediment score admission %,(n)				
1	62,1	(64)	10.5608% a 36.6087%	0.0005
≥2	37,9	(39)		
ADQI AKI classification,%,(n)				
1 S	37,9	(39)	10.5608% a 36.6087%	0.0005
No IRA	62,1	(64)		

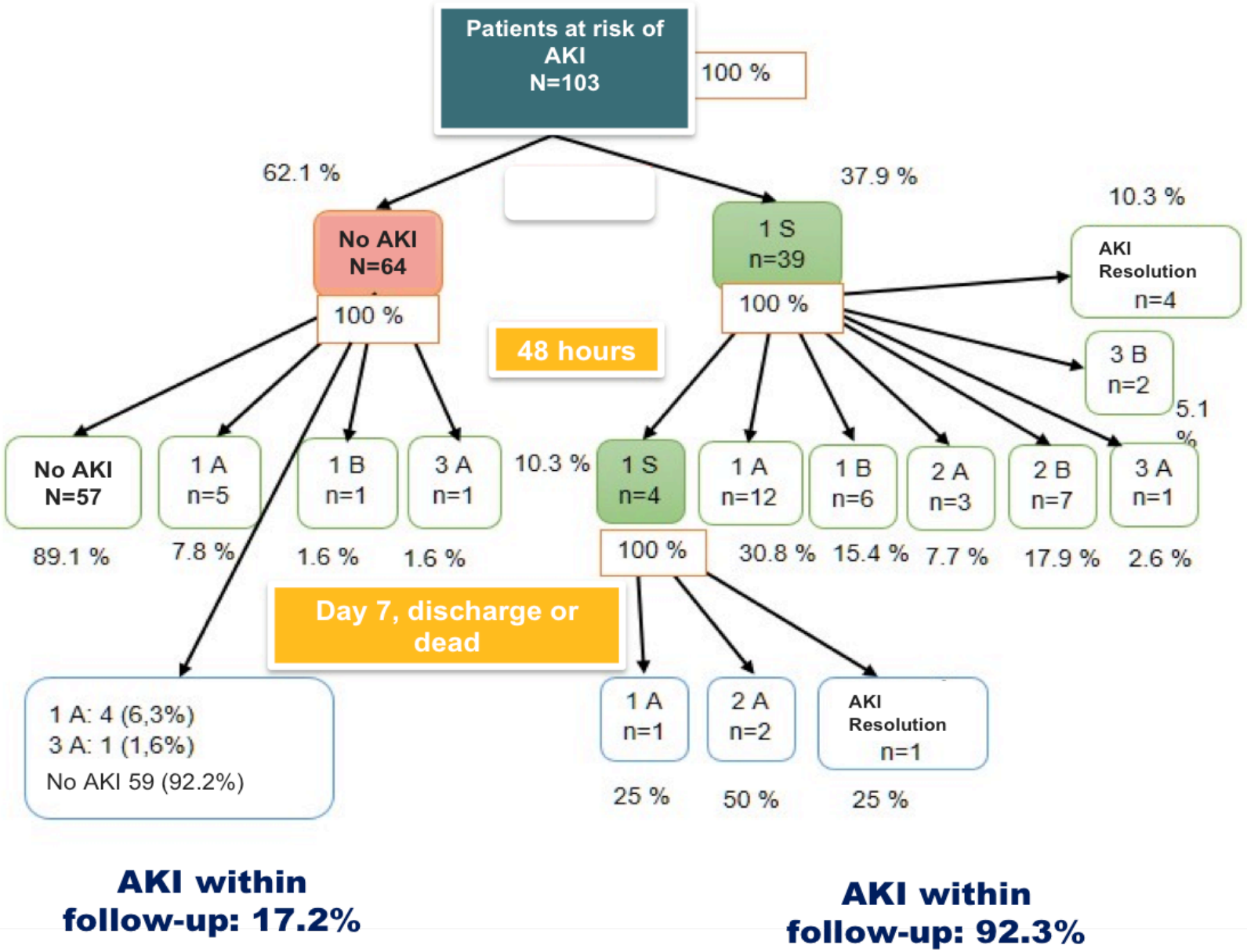
Subclinical AKI (1S) and its progression

At admission 37.9%

At 48 hours, 79.5% (31/39) **1S patients** developed **clinical AKI**

Only 11% (7/64) of **no AKI** group developed clinical AKI ($p < 0.0001$)

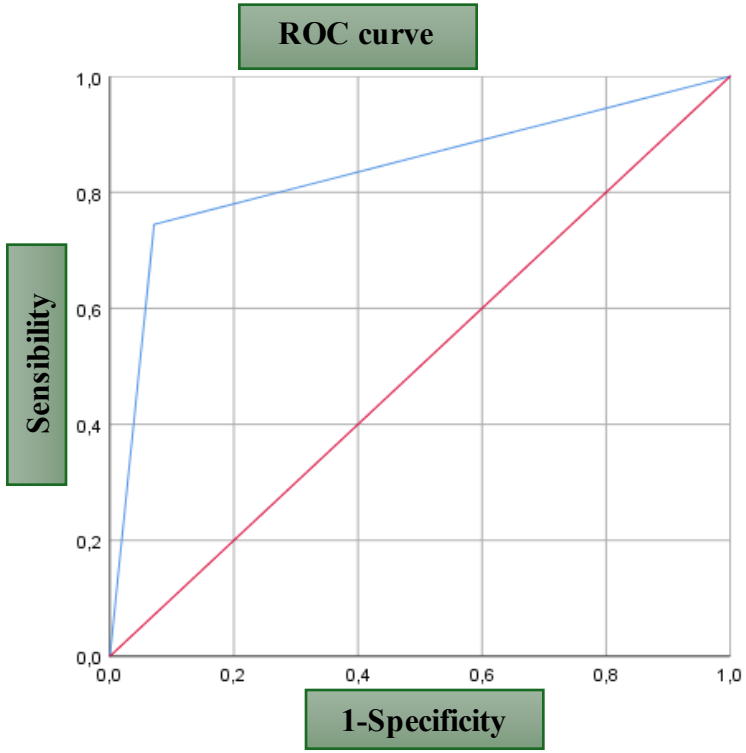
At 7 days, only 7,9 % of patients with a USS ≤1 developed **clinical AKI** vs. 75% of **AKI-1S patients**; $p < 0.0001$



Urinary Sediment Score/Subclinical AKI

A USS ≥2 points was associated with AKI (odds ratio (OR), 37.9; 95% CI, 11.3 to 127.2; p < 0.0001).

A USS ≥2 at admission have a good performance in predicting clinical AKI with a ROC-AUC 0.84 (95% CI 0.75-0.92); p < 0.0001.



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AKI 1S 10.3%

No AKI 1.6%

p = 0.05

The image part with relationship ID rId11

AKI 1S 43.6%

No AKI 14.6%

p = 0.008

Conclusions

- Subclinical AKI is still AKI
- Urine sediment score can identify this early phase of AKI.
- USS is a useful tool to refine the diagnostic and staging criteria for AKI especially in resource-limited settings.
- Patients will subclinical AKI (ADQI 1S) had a higher risk of:
  - Developing clinical AKI (KDIGO criteria)
  - Higher need of RRT
  - Higher mortality