Diagnostic Utility of Serial Microscopic Examination of the Urinary Sediment in Acute Kidney Injury

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Abstract

Background: Microscopic examination of the urinary sediment (MicrExUrSed) is an established diagnostic tool for acute kidney injury (AKI). However, single inspection of a urine specimen during the course of AKI is a mere snapshot affected by timing. We hypothesized that longitudinal MicrExUrSed provides information otherwise not identified in a single inspection.

Methods: MicrExUrSed was undertaken in patients with AKI stage ≥ 2 and suspected intrinsic cause of AKI seen for nephrology consultation over a 2-year period. MicrExUrSed was performed on the day of consultation and repeated at a second (2 - 3 days later) and/or third (4 – 10 days later) interval. Cast scores were assigned to each specimen. Chawla scores (CS) 3 to 4 and Perazella scores (PS) 2 to 4 were categorized as consistent with acute tubular injury (ATI), whereas CS 1 to 2 and PS 0 to 1 were categorized as non-diagnostic for ATI (non-ATI). Non-recovering AKI was defined as a rise in serum creatinine (sCr) ≥ 0.1 mg/dL between microscopy intervals.

Results: At least 2 consecutive MicrExUrSed were performed in 121 patients [46% women, mean age 61 ± 14, mean sCr at consult of 3.3 ± 1.9 mg/dL]. On day 1, a CS and PS consistent with non-ATI was assigned to 64 (53%) and 70 (58%) patients, respectively. After a subsequent MicrExUrSed, CS and PS changed to ATI in 14 (22%) and 16 (23%) patients. Thus, 20 – 24% of patients only revealed evidence of ATI after serial MicrExUrSed was performed. Patients with non-recovering AKI were more likely to change their PS to ATI category [odds ratio: 5.8 (CI:1.7-19.3; p=0.005) and positive likelihood ratio: 2.0 (CI: 1.3-2.9)].

Conclusion: Serial MicrExUrSed revealed diagnostic findings of ATI otherwise not identified in a single examination. A repeat MicrExUrSed may be warranted in cases of AKI of unclear etiology that are not recovering.
Introduction

Microscopic examination of the urinary sediment is a well-established clinical tool of diagnostic and prognostic value in the evaluation of acute kidney injury (AKI) (1-4). Specifically, the identification of renal tubular epithelial cells (RTECs) and granular casts (GCs) strongly suggest a diagnosis of acute tubular injury (ATI) (5,6), the most common cause of acquired AKI in the hospital setting (7). The abundance of “muddy” brown granular casts is considered a pathognomonic finding for ATI. Over a decade ago, the first systematic approaches to grade findings from urinary sediment microscopy were developed. The Chawla score (CS) and the Perazella score (PS) were created with the intention to standardize the identification of GCs, renal epithelial cells (RTECs) and renal epithelial cell casts (RTECCs) (2,3). These scores demonstrated diagnostic and prognostic value in the evaluation of AKI due to ATI. The CS is determined by assessing the percentage of low power fields (LPFs) with GCs and RTECCs, whereas the PS is determined by identifying the number of GCs in an LPF and the number of RTECs in a high-power field (HPF). However, these scores were designed based on a single examination of the urinary sediment. Although casts provide valuable diagnostic clues, the natural history of cast formation remains unexplored. Thus, a single inspection of a urinary sediment specimen during the course of AKI is a mere snapshot that depends on the day of inspection. Therefore, potential evidence of ATI can be missed. Therefore, we hypothesized that longitudinal MicrExUrSed can provide additional diagnostic information otherwise not identified in a single inspection.

Methods

This study was conducted with approval by the Institutional Board Review and in accordance with the Declaration of Helsinki. Urine specimens were collected from patients with AKI stage ≥ 2 (by Kidney Disease: Improving Global Outcomes) (KDIGO) who were seen on consultation in an inpatient nephrology service over a 2-year period at Ochsner Medical Center when an intrinsic etiology of AKI was suspected and members of the research staff were available (8).
Microscopic examination of the urinary sediment was performed as soon as possible and always within 1 hour of sample collection. Once collected, specimens were kept at room temperature and transferred to the laboratory. A 10 mL aliquot of urine was placed in a 15 mL high-clarity polypropylene conical tube and centrifuged at 800 g for 5 mins. The supernatant was poured off and the pellet was resuspended by manual agitation in the remaining 0.2 ml of supernatant. A plastic transfer pipette was used to place a single drop onto a standard microscope slide and a coverslip was placed over it. This process was done with and without Sternheimer-Malbin stain (Kova®, Garden Grove, California) (9). Then, each sample was examined by a trained operator using a Nikon Eclipse E200 microscope (Melville, New York) with 10x, and 40x magnification objectives and a 10x magnification eye-piece. The entirety of the slide was examined at both LPF (100x magnification) and HPF (400x magnification). Representative images of all sample slides were taken using an Apple iPhone 6S camera (Cupertino, California) and LabCam microscopy adaptor (iDu Optics, New York, New York) on a Leica CME microscope (Buffalo Grove, Illinois). At least 2 operators independently assessed and scored each specimen, 1 operator was blinded to the clinical data and 1 operator was unblinded. Operators included nephrologists, nephrology fellows, internal medicine residents, and medical students who were trained to determine both PS and CS.

Microscopic examination of the urinary sediment was first performed on the day of consult (Day 1). Then, a subsequent serial urine sediment microscopy examination was attempted to be performed at a second time interval defined as day 2 or 3 from the day of the consult, and/or at a third time interval defined as day 4 to 10 from the day of the consult. A second and third serial microscopy was not uniformly completed for all the patients in the cohort. Microscopic examination of the urinary sediment was not repeated if the patient was anuric, discharged, deceased, commenced hemodialysis, or there was an inability to collect urine due to staffing or logistics.
Urinary cast scores (CS and PS) for ATI were determined at each serial microscopy interval (Tables S1 and S2) (5,6). A CS of 3 to 4 and a PS of 2 to 3 were categorized as consistent with ATI, whereas CS of 1 to 2 and PS of 0 - 1 were categorized as non-diagnostic for ATI (Figures 1 and 2).

To evaluate for factors influencing the probability of conversion of the urine cast score from non-ATI category to ATI category, we examined the course of AKI and the timing of AKI. Thus, we defined non-recovering AKI as a rise in serum creatinine ≥ 0.1 mg/dL at the time of either the second or third serial microscopy compared to the serum creatinine on the day of the first microscopy. When the serum creatinine trends down even by 0.1 mg/dL, most clinicians interpret it as a positive trajectory and the initial diagnostic suspicion is typically not challenged. However, when the serum creatinine does not decrease, the practicing clinician might be interested in reassessing the tentative diagnosis. In addition, we arbitrarily defined early period of AKI as the first 6 days after the onset of AKI and late period of AKI as ≥ 7 days since the onset of AKI.

A presumptive etiology of AKI was determined based on available clinical information as previously reported (10): ischemic ATI was considered in cases when AKI occurred following hemodynamic instability (shock, hypotension, large fall in systolic blood pressure, tachyarrhythmia, bradyarrhythmia), volume depletion unresponsive to intravenous expansion or exposure to vasomotor drugs (angiotensin converting enzyme inhibitors, angiotensin receptor blockers, calcineurin inhibitors) that did not resolve upon drug discontinuation; toxic ATI was considered when AKI occurred following exposure to an exogenous toxin (e.g., iodinated radiocontrast, vancomycin) or endogenous toxin (e.g., myoglobin, light chains); acute glomerulonephritis was considered when it was biopsy-proven or when AKI included suggestive elements such as serological values, clinical context and/or urinary acanthocytes; hepatorenal syndrome was considered based on the established diagnostic criteria (11); prerenal azotemia was considered when AKI occurred following a history of volume depletion and the AKI resolved after some form of fluid resuscitation; cardiorenal syndrome was considered when AKI
occurred in the context of acute decompensated heart failure; and obstructive uropathy was considered when AKI occurred with radiological evidence of obstruction of the urinary outlet.

As outcome measures, we assessed the odds ratio (OR) and positive likelihood ratio (+LR) (and confidence interval) of conversion of urine cast score from a non-ATI category to an ATI category by either the CS or the PS, based on 2 exposure variables: non-recovering AKI and late period of AKI. Additionally, we assessed the effect of serial MicrExUrSed on the predictive value of urine cast scores, PS or CS, in determining the likelihood of a poor renal outcome defined as a combined endpoint of ≥ 50% increase in serum creatinine at discharge [acute kidney disease (AKD)] or need for renal replacement therapy during the course of AKI (AKI-RRT). Because hepatorenal syndrome type 1 is a functional form of AKI known to carry a high risk for poor renal outcomes without overt findings of ATI by MicrExUrSed (11), we established a prespecified subgroup of AKI in patients without end-stage liver disease (non-ESLD) for both analyses. Statistical analyses were performed using GraphPad Prism 7 software package (San Diego, California). A p value < 0.05 was deemed significant.

Results

A total of 497 microscopic examinations of the urinary sediment were performed during the study period. Of these, serial inspection was not performed in 222 patients and those were excluded. At least 2 serial microscopic examinations of the urinary sediment were performed in 121 patients with AKI that composed the cohort (Figure 3). Among them, 105 had a subsequent microscopic examination performed on the second time interval (days 2 or 3 after consultation) and 49 had subsequent microscopic examination performed on the third time interval (days 4 to 10 after consultation). Three serial examinations were performed on 33 (27%) patients. The patients who entered the cohort had a median age of 61 (25 - 88) years, 36% of them (n = 44) were female and were primarily of Caucasian (62%) and African American (31%) race. The mean serum creatinine at the time of the initial urine microscopy was 3.3 ± 1.9 mg/dL, with 80% of the patients diagnosed with stage 3 AKI, and 20% with stage 2 AKI. Preexisting chronic kidney disease stages 3A to 5 was present in 35%. The presumptive
etiology of AKI based on clinical grounds with consideration of MicrExUrSed findings was primarily ischemic ATI which accounted for 59% (n = 71) of the patients (Table 1). Dialysis was required in 46 (38%) patients during their course of AKI.

On day 1, a CS and PCS consistent with non-ATI was assigned to 64 (53%) and 70 (58%) patients, respectively. Among those 64 and 70 patients, CS and PS changed from non-ATI category to ATI in 16 (22.5%) and 14 (21.8%) (Figure 4). Thus, 14 of 71 (20%) (by CS) and 16 of 67 (24%) (by PS) of patients only revealed evidence of ATI after serial urinary sediment microscopy was performed. On the other hand, in 23/51 (45%) cases (by PS) and 20/57 (35%) cases (by CS), the initial urine sediment inspection classified the specimen under the ATI category, but it regressed to non-ATI upon subsequent serial inspection. Of note, 11/23 (55%) per PS 11/20 (47.8%) per CS had non-recovering AKI.

When the findings by microscopic examination of the urinary sediment were assessed over time, we observed that specimens categorized as ATI were identified throughout the temporal spectrum of AKI (Figure 5). While the highest number of cases on ATI were found within the 4-5 day of AKI interval, cases of AKI were found all time intervals.

Patients with non-recovering AKI were more likely to change their PS from non-ATI to ATI compared to those with stable or improved AKI [OR: 5.8 (1.7-19.3) p = 0.005 and +LR: 2.0 (CI: 1.4 – 2.9)]. Based on CS, the OR was 1.1 (CI: 0.6-3.2), not statistically significant (p=0.09) and the +LR was 1.2CI: 0.6–2.2). and Among the non-ESLD subgroup (n = 63), based on PS, OR was 12.4 (CI: 2.4-65.1), p = 0.003 and +LR was 2.5 (CI:1.5-4.2). Based on CS, OR was 1.3 (CI: 0.3-6.8), p=0.73 and +LR was 1.2 (CI: 0.5-2.7) (Figure 6).

In terms of the influence of timing of the microscopic examination of the urinary sediment, there was no significant difference in the rate of change in ATI category when the serial microscopy was performed at a late stage of AKI (≥ 7 days) compared to early AKI (< 7 days) [Based on PS, OR: 1.0 (CI: 0.4-2.8),
p=1.0 and +LR: 1.0 (CI: 0.7–1.5). Based on CS, OR: 0.8 (CI: 0.6-2.3), p=0.7 and P+LR: 0.9 (CI: 0.6–1.4)(Figure 6).

Additionally, we assessed whether serial urinary sediment microscopy improved the prognostic value of a single inspection. With findings obtained on initial microscopy alone, urine casts scores did not predict AKD/AKI-RRT. Based on PS, OR was 1.8 (CI: 0.7–4.2), p = 0.2 and +LR was 1.4 (CI: 0.8-2.5). Based on CS, OR was 1.3 (CI: 0.6–3.0), p = 0.5 and +LR was 1.2 (0.7-1.9). With the addition of serial microscopy, both the OR and +LR numerically decreased based on PS (OR: 1.5 (CI: 0.6 –3.3), p = 0.37 and +LR: 1.2 (CI: 0.8-1.8)] and numerically increased based on CS [OR of 1.8 (CI: 0.8– 4.0), p = 0.18 and +LR: 1.3 (0.9-1.9)] but remained equally non-significant (Figure 7). However, when the analyses were restricted to the non-ESLD subgroup (n = 63), serial microscopy partially altered the prognostic value of ATI cast scores. Based on PS, at initial microscopy alone, the OR was 3.1 (CI: 1.1–9.3), p = 0.04 and the +LR was 1.9 (CI: 1.0-3.8), whereas after serial microscopy, the OR was 2.6 (CI: 0.9–7.4), p = 0.09 and the +LR was 1.4 (CI: 0.9-2.2). Based on CS, at initial microscopy, the OR was 2.3 (CI: 0.8–6.4, p = 0.13 and the +LR was 1.4 (CI: 0.9-2.2), whereas after serial microscopy, the OR was strengthened to 3.3 (CI: 1.0–10.3), p = 0.04 and the +LR remained 1.4 (CI: 1.0-2.0) PS [].

When a subgroup analysis of patients with non-recovering AKI (n = 66) were assessed for prediction of AKD/AKI-RRT, we found that on initial microscopy, based on PS, OR was 1.3 (CI: 0.4-4.9), p = 0.66 and +LR 1.2 (CI: 0.6-2.3), whereas based on CS, the OR was 1.9 (CI: 0.5-7.2), p = 0.67 and +LR was 1.4 (CI: 0.7-2.7). Upon subsequent microscopy, the OR and +LR were once again numerically decreased based on PS [OR: 1.1 (CI: 0.3-4.2), p = 0.91 and +LR: 1.0 (CI: 0.6-1.7)] but numerically increased based on CS [OR: 2.2 (CI: 0.5-9.5), p = 0.28 and +LR: 1.3(CI: 0.7-2.4)]. (Figure 8)

**Discussion**

Microscopic examination of the urinary sediment is an established technique to aid in the diagnosis of AKI (12). Many practitioners use this tool in clinical practice. When an initial urinary inspection reveals a
bland sediment without relevant findings, treating providers may occasionally perform a second
inspection later in the course of AKI, particularly in scenarios where clinical suspicion for an intrinsic
cause of AKI is high. While this approach of repeating urinary sediment inspection may be customary
for a subset of nephrology providers, it lacked supporting evidence of its benefit. Thus, our report
provides a rationale for the performance of serial urinary sediment examination when clinically
indicated.

Our study evaluated the utility of serial urinary sediment microscopy and demonstrated that it is
valuable diagnostically. By repeating urinary sediment microscopy, we were able to uncover an
additional ~ 20 – 25% cases of ATI that were not identified on the initial microscopy. This accounts for ~
20 - 25% of total ATI cases (Figure 4). Thus, many cases with overt ATI could be missed with a single
inspection. Furthermore, we observed that patients with non-recovering AKI were more likely to convert
from non-ATI to ATI category as per PS. This observation is clinically meaningful in that practitioners
often encounter cases of AKI without a clear-cut etiology. In those cases, if the kidney function
improves, determining the etiology may be seen as clinically irrelevant. However, when patients exhibit
a stagnant or worsening clinical course, it may important for the practitioner to reassess the etiology of
AKI due to potential implications in management. Our results indicate that serial urinary sediment
microscopy may offer additional diagnostic clues to ascertain the etiology of AKI.

The natural history of cast formation is not fully understood (13). When microscopic examination of the
urinary sediment is performed, it has remained unclear whether the timing of the test may affect the
ability of the operator to catch relevant findings. Thus, we assessed the relationship between the
temporal spectrum of AKI and the findings on urine microscopy. We observed a wide distribution of
cases of ATI along the duration of AKI (Figure 5). In other words, cases of ATI were identified when the
inspection of a urine specimen was performed either early or late in the course of AKI. This observation
is reassuring in that the duration of AKI should not discourage against performing or repeating the test.
Interestingly, evidence of ATI appears to be clustered around days 4 to 6 from the onset of AKI, but that
observation may only reflect the higher number of examinations performed within that time period, likely due to the average timing of the inpatient nephrology consultations. Furthermore, another aspect related to timing was the observation of a small subset of patients found to have ATI on initial microscopy but not on serial microscopy. This finding suggests that a bland sediment in a single inspection late in the course of AKI could correspond to a case of ATI should the inspection had occurred earlier. Thus, clinical suspicion remains critical when interpreting findings on urine microscopy.

Aside from diagnostic capacity, CS and PS have been previously shown to be prognostic biomarkers (2,3). Urinary sediment findings have been found to correlate well with biomarkers of AKI and were associated with higher odds of poor renal outcomes (AKI-RRT) (4,14). Contrary to previous reports, in our study, ATI score was not associated with AKD/AKI-RRT, neither based on initial or serial urinary sediment microscopy (Figure 7). However, our cohort was enriched with more cases of ATI by study design compared to previous studies (4,14). Furthermore, patients with ESLD with hepatorenal syndrome type 1 were overrepresented in our cohort compared to previous reports. There are 2 considerations to take into account in patients with ESLD. Firstly, hepatorenal syndrome type 1 is a functional form of AKI that often progresses to anuria and need for dialysis without evidence of ATI by urine microscopy (11,15). Therefore, ATI scores are expected to be less predictive of poor renal outcomes in this population. Secondly, in patients with pronounced hyperbilirubinemia, RTEC and RTECC can be found even in the absence of AKI (16). Therefore, misleading ATI scores can be found in that subgroup. Consequently, we reanalyzed the data restricting it to patients without ESLD and observed a significant improvement in the prognostic value of ATI score (Figure 7). Despite the enhanced prognostic strength of ATI score for AKD/AKI-RRT in the non-ESLD subgroup, the magnitude of the OR was lesser than those observed in previous reports (4, 14). A plausible explanation for the difference in that our cohort was enriched for patients with ATI. For instance, prerenal azotemia accounted for only 3% of our cases compared to 32% in a referenced study (4).
Therefore, it is not surprising that the prediction of AKD/AKI-RRT based on ATI score was not as robust in our cohort enriched with more severe cases of AKI.

Our study is not without limitations. First, we rely on the interpretation of trained operators to score each specimen. Although each operator was thoroughly trained to assess and score each sample, variability is plausible. However, interobserver agreement has been reported to be acceptable among nephrologists and/or nephrology providers (2). There is possibility of observer bias as one operator was unblinded. In addition, we found heterogeneity in the results depending on the urine cast score used, i.e., PS versus CS. Although PS and CS have similarities, they rely on different elements. In particular, PS uses RTECs and CS uses RTECCs. Moreover, CS uses a wide range of percentage of LPFs with casts to assign a score of 3 (10 - 90%) and it is often difficult to display uniformity of a sample across all LPFs. Within that range of percentage of LPFs with casts, specimens can fall into a non-ATI or ATI score based on PS that uses the number of GC per LPF instead of the percentage of LPFs with findings. As a result, PS and CS may be seen as complementary, with PS somewhat more robust diagnostically and CS somewhat more robust prognostically. However, a larger sample size may be needed to corroborate these observations. Additionally, our study population is enriched with intrinsic causes of AKI such as ATI as they were collected from patients for whom nephrology was consulted and the team suspected an intrinsic cause of AKI. We caution generalizations regarding other populations which are predominantly prerenal in etiology. In addition, we did not adjust for confounding factors such as urine output, but we accounted for serum creatinine level and duration of AKI.

In summary, our study adds to the existing literature that indicates that microscopic examination of the urinary sediment is a useful clinical tool. Our findings expand its value by demonstrating that serial inspection may provide additional information with potential clinical relevance. We suggest considering the performance of serial urinary sediment microscopy in cases of AKI with suboptimal clinical or non-recovering course and of uncertain etiology.
Disclosures

J.C.Q.V. has participated in Advisory Board meetings for Mallinckrodt Pharmaceuticals and Retrophin and in a Speaker Bureau for Otsuka Pharmaceuticals. None of the products related to those engagements are discussed in this manuscript. All remaining authors have nothing to disclose.

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References


**Table 1. Baseline characteristics of patients included in the cohort (n = 121)**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>61 (25-88)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Female: 36% (44)</td>
</tr>
<tr>
<td>Race</td>
<td>White: 62% (75)</td>
</tr>
<tr>
<td>Primary etiology of AKI</td>
<td>Ischemic ATI: 59% (71)</td>
</tr>
<tr>
<td>Secondary etiology of AKI</td>
<td>Ischemic ATI: 8% (1)</td>
</tr>
<tr>
<td>Preexisting CKD stages 3A to 5*</td>
<td>35% (43)</td>
</tr>
<tr>
<td>Baseline serum creatinine (mg/dL)</td>
<td>AKI on CKD de novo AKI (no preexisting CKD): 1.5 (0.9 - 4.3)</td>
</tr>
<tr>
<td>Serum creatinine at first urine microscopy (mg/dL)</td>
<td>3.3 (0.8 - 12.0)</td>
</tr>
<tr>
<td>AKI KDIGO stage at first urine microscopy</td>
<td>Stage 2: 20%</td>
</tr>
</tbody>
</table>


*CKD status was determined by baseline estimated glomerular filtration rate (eGFR) prior to AKI. Patients without baseline EGFR data were considered de novo AKI.
FIGURE LEGENDS

**Figure 1.** Representative photomicrographs illustrating the application of the Perazella score (PS) to grade urinary sediment slides for elements of acute tubular injury (ATI). **Panels A-B:** PS of 1: 1 - 5 granular casts (GC) per LPF with no evidence of renal tubular epithelial cells (RTECs); **Panel C:** PS of 2: ≥ 6 GCs with no evidence of RTECs; **Panels D-E:** PS of 3: ≥ 6 GCs with 1 - 5 RTECs (blue arrows, assessed at HPF); **Panel F:** PS of 4: ≥ 6 GCs with ≥ 6 RTECs.

**Figure 2.** Representative photomicrographs illustrating the application of the Chawla score (CS) to grade urinary sediment slides for elements of acute tubular injury (ATI). **Panel A:** CS score of 1: No evidence of granular casts (GC) or renal tubular epithelial cell casts (RTECC); **Panel B:** CS of 2: At least one GC or ECC on < 10% of low power fields (LPFs); **Panel C:** CS of 3: Many GC or RTECC on 10 - 90% of LPFs (bottom left, RTECC at LPF, bottom right: RTECC at high power field, both with Sternheimer-Malbin stain); **Panel D:** CS score of 4: Sheets of muddy brown granular casts with GC on > 90% of LPFs.

**Figure 3.** Flow chart illustrating the patient selection and study methods.

*Patients did not receive serial microscopy due to anuria, discharge, death, commencement of hemodialysis, or inability to collect urine due to staffing or logistics.

**Figure 4.** **Panel A:** Distribution non-ATI or ATI categorization based on Perazella score at initial and subsequent microscopy, showing rate of conversion from non-ATI to ATI score. **Panel B:** Distribution non-ATI or ATI categorization based on Chawla score at initial and subsequent microscopy, showing rate of conversion from non-ATI to ATI score. **Panel c-d:** case example of findings consistent with non-ATI on initial microscopy (c) and subsequent evidence of ATI based on serial (second) microscopy (d) performed 48 hours later. ATI: acute tubular injury.
**Figure 5. Panel A-B:** Temporal distribution of Perazella and Chawla scores throughout the course of acute kidney injury. **Panel C-D:** Temporal distribution of either stable or worsening Perazella and Chawla scores throughout the course of acute kidney injury.

**Figure 6.** Forest plots of odds ratio (OR) and positive likelihood ratio (+LR) for conversion of non-ATI to ATI grading of the urinary sediment findings when examined by serial microscopy using Perazella Score or Chawla Score at **panel A:** among the entire cohort and **panel B:** among non-end stage liver disease (non-ESLD) subgroup. **Panel C:** OR assessed based on either change in kidney function (non-recovery or worsening of AKI vs. recovery of AKI) or timing of AKI [late period (day ≥ 7) vs. early period (day 1 - 6) since onset of AKI].

**Figure 7.** Forest plots of odds ratio (OR) and positive likelihood ratio (+LR) for combined endpoint of ≥ 50% increase in sCr from baseline or need for RRT. OR assessed based on urine sediment score (ATI or non-ATI) at **panel A:** initial microscopy among the entire cohort, **panel B:** serial microscopy among the entire cohort **panel C:** initial microscopy among non-end stage liver disease (non-ESLD) subgroup, and **panel D:** serial microscopy among non-end stage liver disease (non-ESLD) subgroup.

**Figure 8.** Forest plots of odds ratio (OR) and positive likelihood ratio (+LR) for combined endpoint of ≥ 50% increase in sCr from baseline or need for RRT among patients with non-recovering acute kidney injury (AKI). OR assessed based on urine sediment score (ATI or non-ATI) at **panel A:** initial microscopy among the entire cohort, **panel B:** serial microscopy among the entire cohort **panel C:** initial microscopy among non-end stage liver disease (non-ESLD) subgroup, and **panel D:** serial microscopy among non-end stage liver disease (non-ESLD) subgroup.
Figure 2
Urinary sediment microscopic examination
(n = 497 in 343 patients with AKI)

Single urinary sediment* microscopic examination
(n = 222 in 222 patients with AKI)

Serial urine sediment microscopic examination
(n = 275 in 121 patients with AKI)

Initial urinary sediment microscopic examination
(n = 121 in 121 patients with AKI)

Day 1
(n = 121)

Subsequent urinary sediment microscopic examination
(n = 154 in 121 patients with AKI)

Day 2 - 3
(n = 105)

Day 4+
(n = 49)
Remained non-ATI
54 (44.6%)

ATI on initial microscopy
51 (42.2%)

ATI on second microscopy
13 (10.7%)

ATI on third microscopy
3 (2.5%)

ATI on initial microscopy
57 (47.1%)

Remained non-ATI
50 (41.3%)

ATI on second microscopy
10 (8.3%)

ATI on third microscopy
4 (3.3%)

a Perazella Score
16 of 70 (23%) initially non-ATI converted from to ATI

b Chawla Score
14 of 64 (22%) initially non-ATI converted from to ATI

16 of 70 (23%)

14 of 64 (22%)

Figure 4
Figure 5

(a) Perazella Score 0
(b) Perazella Score 1
(c) Perazella Score 2
(d) Perazella Score 3
(e) Perazella Score 4

Number of cases

Day of AKI (3-day intervals)

Perazella Score

Stable ATI score
Worsening ATI score

Chawla Score

Stable ATI score
Worsening ATI score

n=55
n=99
n=54
n=67

n=55
n=99
n=54
n=67

n=11
n=33
n=19
n=17
n=11
n=33
n=19
n=17
OR and +LR for conversion to ATI if non-recovering AKI

Entire cohort (n = 121)

- Perazella OR: 5.8 (1.7-19.3) p=0.005
- Perazella +LR: 2.0 (1.4-2.9)
- Chawla OR: 1.1 (0.5-3.2) p=0.09
- Chawla +LR: 1.2 (0.6-2.2)

Non-ESLD subgroup (n = 63)

- Perazella OR: 12.4 (2.4-65.1) p=0.003
- Perazella +LR: 2.5 (1.5-4.2)
- Chawla OR: 1.3 (0.3-6.8) p=0.09
- Chawla +LR: 1.2 (0.5-2.7)

Entire cohort (n = 121)

- Perazella OR: 1 (0.4-2.8) p=1.00
- Perazella +LR: 1 (0.7-1.5)
- Chawla OR: 0.8 (0.6-2.3) p=0.7
- Chawla +LR: 0.9 (0.7-1.4)
OR and +LR for AKD/AKI-RRT

**Entire cohort (n = 121)**

- Perazella OR: 1.8 (0.7-4.2)  \( p = 0.2 \)
- Perazella +LR: 1.4 (0.8-2.5)
- Chawla OR: 1.3 (0.6-3.0)  \( p = 0.5 \)
- Chawla +LR: 1.2 (0.7-1.9)

**Single Microscopy**

**Serial Microscopy**

**Non-ESLD subgroup (n = 63)**

- Perazella OR: 2.1 (1.1-9.3)  \( p = 0.04 \)
- Perazella +LR: 1.9 (1.0-3.8)
- Chawla OR: 2.3 (0.8-6.4)  \( p = 0.4 \)
- Chawla +LR: 1.4 (0.9-2.2)

**Single Microscopy**

**Serial Microscopy**

**Non-ESLD subgroup (n = 63)**

- Perazella OR: 2.6 (0.9-7.4)  \( p = 0.03 \)
- Perazella +LR: 1.4 (0.9-2.2)
- Chawla OR: 3.3 (1.0-10.3)  \( p = 0.04 \)
- Chawla +LR: 1.4 (1.0-2.0)
**Figure 8**

**A**

Non-recovering AKI (n = 66)

<table>
<thead>
<tr>
<th>Test</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perazella OR</td>
<td>1.3 (0.4-4.9)</td>
<td>0.7</td>
</tr>
<tr>
<td>Perazella +LR</td>
<td>1.2 (0.6-2.3)</td>
<td></td>
</tr>
<tr>
<td>Chawla OR</td>
<td>1.9 (0.5-7.2)</td>
<td>0.7</td>
</tr>
<tr>
<td>Chawla +LR</td>
<td>1.4 (0.7-2.7)</td>
<td></td>
</tr>
</tbody>
</table>

**B**

Non-recovering AKI (n = 66)

<table>
<thead>
<tr>
<th>Test</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perazella OR</td>
<td>1.1 (0.3-4.2)</td>
<td>0.9</td>
</tr>
<tr>
<td>Perazella +LR</td>
<td>1.0 (0.6-1.7)</td>
<td></td>
</tr>
<tr>
<td>Chawla OR</td>
<td>2.2 (0.5-9.5)</td>
<td>0.3</td>
</tr>
<tr>
<td>Chawla +LR</td>
<td>1.3 (0.7-2.4)</td>
<td></td>
</tr>
</tbody>
</table>

**C**

Non-ESLD subgroup (n = 35)

<table>
<thead>
<tr>
<th>Test</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perazella OR</td>
<td>2.7 (0.6-12)</td>
<td>0.2</td>
</tr>
<tr>
<td>Perazella +LR</td>
<td>1.6 (0.7-3.6)</td>
<td></td>
</tr>
<tr>
<td>Chawla OR</td>
<td>4 (0.8-19.4)</td>
<td>0.9</td>
</tr>
<tr>
<td>Chawla +LR</td>
<td>1.8 (0.8-3.1)</td>
<td></td>
</tr>
</tbody>
</table>

**D**

Non-ESLD subgroup (n = 35)

<table>
<thead>
<tr>
<th>Test</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perazella OR</td>
<td>2.7 (0.5-13.2)</td>
<td>0.2</td>
</tr>
<tr>
<td>Perazella +LR</td>
<td>1.3 (0.8-2.3)</td>
<td></td>
</tr>
<tr>
<td>Chawla OR</td>
<td>7.5 (1.3-57.1)</td>
<td>0.05</td>
</tr>
<tr>
<td>Chawla +LR</td>
<td>1.5 (0.9-2.6)</td>
<td></td>
</tr>
</tbody>
</table>