Admission Urine Olfactomedin 4 Can Predict Furosemide Response and Receipt of Renal Replacement Therapy

Imogen Clover-Brown, MD; Denise C. Hasson, MD; Kristalynn M. Kempton, MS; Kelli A. Krallman, RN, BSN, MS; Stuart L. Goldstein, MD; Matthew N. Alder, MD, PhD

Background

Acute kidney injury (AKI) is associated with increased mortality and morbidity. Many novel AKI biomarkers are being investigated but no current biomarkers are specific to the Loop of Henle.

Furosemide stress test (FST) is another tool to evaluate AKI. Insufficient urine output after furosemide can predict progression of AKI and receipt of renal replacement therapy (RRT). However, providers may avoid FST in critically ill patients given concerns about fluid status and hemodynamic stability. Because furosemide acts in the Loop of Henle, a Loop of Henle specific biomarker may predict FST response without giving diuretics.

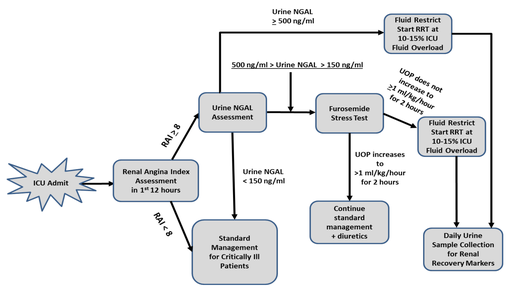
Olfactomedin 4 (OLFM4) is a glycoprotein produced by neutrophils and epithelial cells under stress. It has been under investigation as a sepsis biomarker but was found to have increased expression in the Loop of Henle during AKI.

Objective

To assess urine olfactomedin 4 (uOLFM4) as a Loop of Henle specific AKI biomarker to predict need for RRT

Methods

All PICU patients are enrolled in TAKING FOCUS 2 (Trial in AKI using NGAL and Fluid Overload to Optimize CRRT Use). Patients have a Renal angina index (RAI) calculated 12 hours after admission. If RAI is >8, urine NGAL (uNGAL) is measured.



Urine samples were collected from uNGAL residuals or bladder catheter waste for up to 7 days

uOLFM4 levels were measured via Abcam ELISA

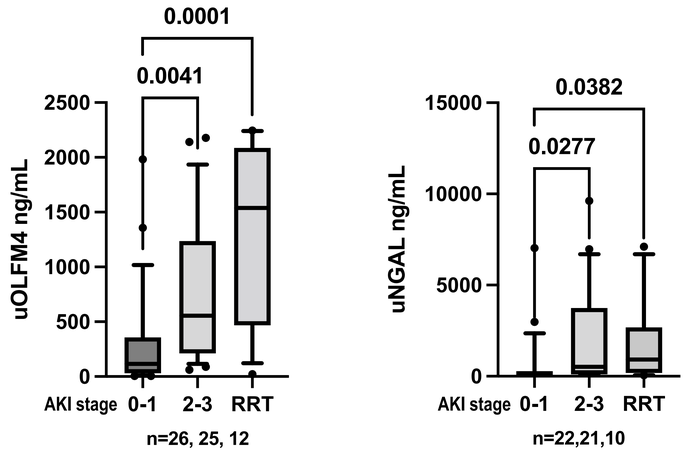
AKI was staged using KDIGO criteria. Severe AKI was defined as >2x increase in serum creatinine from baseline. Baseline creatinine was determined by the lowest level measured in the 3 months prior to admission or calculated with the revised Schwartz equation if prior creatinine was not available.

Between May 2022 and February 2023, 114 patients with RAI >8 were assessed for eligibility. 51 patients were excluded for lack of urine samples. 63 patients were included.

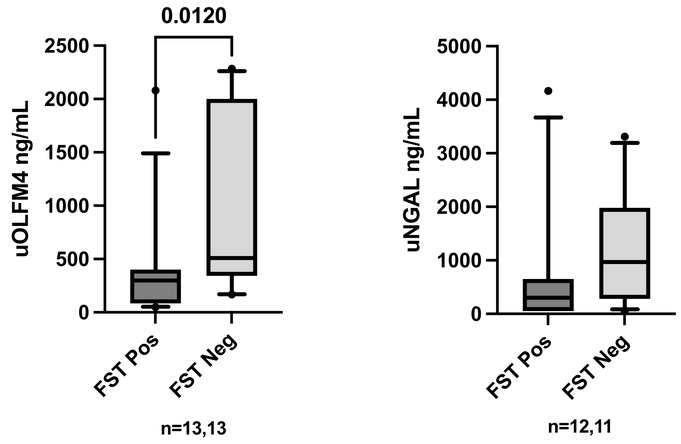
Patients were grouped by peak AKI stage/RRT status in the 7-day study period. Day 0-2 uOLFM4 levels were used.

Results

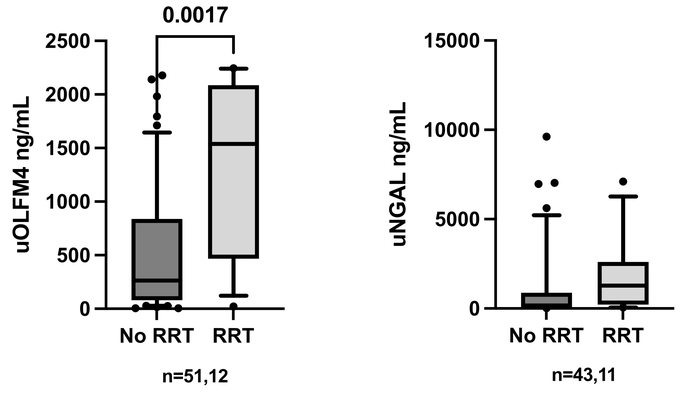
uOLFM4 is Higher in Patients with Significant AKI



uOLFM4 is Higher in Patients Who Do Not Respond to Furosemide



uOLFM4 is Higher on Admission in Patients who Receive RRT



Limitations

Patients with the significant AKI and those who receive RRT are more likely to be anuric so, uOLMF4 cannot be measured

OLFM4 is expressed in neutrophils as well as endothelial cells. Patients with UTIs may have falsely elevated uOLFM4 levels because of neutrophils in their urine. A separate analysis excluding patients with moderate or large leukocyte esterase that did not change the results, so these patients were included.

Few patients received RRT or underwent FST

Strengths

Prospective studies in pediatric patients

Strong infrastructure within the Cincinnati Children's Center for Acute Care Nephrology

Recruited a significant number of high acuity patients

Multiple time/data points for patients for post-hoc analyses

Conclusions

uOLFM4 identified patients with severe AKI

uOLFM4 outperformed uNGAL in identifying patients who received RRT and who failed FST

uOLFM4 could be an additional tool to help identify patients who require RRT. uOLFM4 could potentially be included in a future clinical decision algorithm to augment FST

Next Steps

Enrollment is ongoing with plans to expand to multiple centers

Will assess uOLFM4 levels in the days prior to FST or initiation of RRT to determine if it can identify AKI earlier in the course

References

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