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## Clinical significance of uNGAL, uKIM-1, and uL-FABP in patients with acute pulmonary edema

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**Introduction:** Novel urinary biomarkers such as urinary neutrophil gelatinase-associated lipocalin (u-NGAL),urinary kidney injury molecule-1 (u-KIM-1), and urinary liver-type fatty acid-binding protein (uL-FABP) are proposed to be reliable markers for acute heart failure (AHF). Acute pulmonary edema (APE) is one of the vascular phenotypes of AHF, such as 'vascular failure", often with high blood pressure at admission. We aimed to investigate the differences in the clinical impact and prognostic utility of urinary biomarkers in AHF patients with and without APE.

**Methods and results:** This prospective observational study included 203 AHF patients (mean age: 77 years, 52% male). uL-FABP, u-NGAL, and u-KIM-1 were measured at admission and before discharge, with correction for urinary creatinine. APE was defined as acute-onset dyspnea and radiographic alveolar edema requiring non-invasive positive pressure ventilation. The primary outcome was a composite of all-cause death and AHF rehospitalization for 1 year. The median uL-FABP levels at admission were higher in APE (n=42) than in non-APE patients (n=161; 10.8 [4.5–23.7] vs. 20.7 [5.9–63.5] μg/gCr, p=0.017), whereas u-KIM-1, u-NGAL, and serum creatinine did not significantly differ between AHF patients with and without APE. The primary outcome did not differ between patients with and without APE. However, among patients with APE, Kaplan–Meier analysis showed that higher uL-FABP (≥median: 20.7 μg/gCr) was associated with adverse events (log-rank: p=0.019). After adjusting for age, sex, serum creatinine, and brain natriuretic peptide, multivariable Cox hazard analysis showed that higher uL-FABP is an independent predictor of adverse events (HR: 4.0 [1.2–18.2], p=0.023).

**Conclusion:** Unlike u-NGAL and u-KIM-1, uL-FABP was higher in APE patients than in non-APE patients. Further, among patients with APE, higher uL-FABP was predictive for poor prognosis.