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Proenkephalin as a new glomerular filtration marker for rule-out of sustained kidney injury after cardiac catheterization: main results from the prospective PANCAKE study

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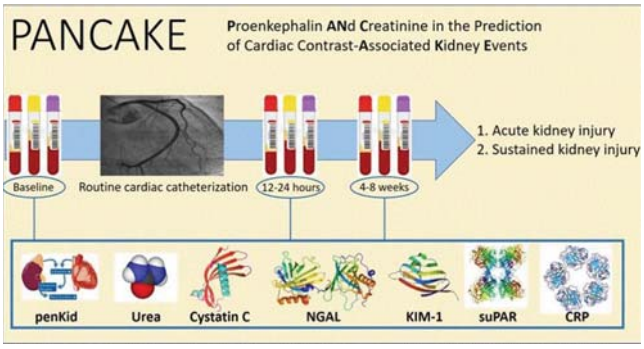
Introduction: Use of contrast media is necessary for diagnostic imaging and PCI. However, contrast-induced kidney injury has been identified as the most frequent cause of hospital-acquired acute kidney injury and is associated with poor prognosis. Currently, contrast-induced kidney injury cannot be diagnosed on the day of cardiac catheterization or on the following day, when the majority of patients who undergo elective cardiac catheterization are discharged from the hospital in the real-world setting. Recently, proenkephalin (penKid) was introduced as a new glomerular filtration marker, which is capable of identifying normal subjects at high risk of future decline in renal function. The aim of this study was to investigate whether the change in penKid level on the day following cardiac catheterization can predict kidney injury before hospital discharge and thus allows for early detection of affected patients.

Methods: A total of 214 consecutive patients who underwent routine cardiac catherization were recruited, and blood was drawn at three time-points: immediately before catherization, 12–24 hours after catheterization and 4–8 weeks after discharge. Creatinine was measured for endpoint definition, while the markers urea, CRP (C-reactive protein), NGAL (neutrophil gelatinase-associated lipocalin), KIM-1 (kidney injury marker-1), cystatin C, suPAR (soluble urokinase-type plasminogen activator receptor), and penKid were measured as biomarkers of interest. The main outcome measure was sustained kidney injury (SKI), which was defined as an increase above 20% in serum creatinine between time-points 1 and 3. The main test was whether the change in biomarkers between baseline and immediately before discharge (time-points 1 and 2) can predict the development of sustained kidney injury.

Results: While only 5.6% of subjects developed acute kidney injury as defined according to KDIGO guidelines (delta serum creatinine between time-points 1 and 2), sustained kidney injury at mid-term follow-up (4–8 weeks) was found in 28.7% of the subjects. None of the baseline biomarkers, including creatinine, reliably predicted SKI (AUC in ROC analyses between 0.50 and 0.60). In rule-out analyses, stable values of penKid (not increasing from before catherization to discharge next day) reliably ruled out SKI at a specificity of 96.0% (90.1–98.9), while specificity was lower for the other candidate biomarkers [CRP: 63.4% (53.2–72.7); NGAL: 55.3% (44.1–66.1); KIM-1: 63.9% (53.5–73.4); cystatin C: 93.0% (86.1–97.1); suPAR: 52.0% (41.8–62.1)]. Using penKid, only 7 patients were categorized as false-positive, while all other patients would have been discharged safely.

Conclusion: Change in penKid levels between cardiac catheterization and discharge reliably rules out sustained kidney injury after contrast administration. PenKid thereby holds promise as an early biomarker for contrast-induced kidney injury and should be evaluated in pilot interventional trials.



Study Flow PANCAKE-Study