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DIAGNOSTIC VALUE OF KIDNEY INJURY MOLECULE-1 AND INTERLEUKIN-18 FOR EARLY DETECTION OF CONTRAST-ASSOCIATED ACUTE KIDNEY INJURY FOLLOWING CORONARY ANGIOGRAPHY AND PERCUTANEOUS CORONARY INTERVENTION: AN EVIDENCE-BASED NARRATIVE REVIEW

Khujakov Murodbek Oybekovich
Assistant, Department of Medical Radiology, Interventional Cardiology, Nephrology and Hemodialysis, and Clinical Laboratory Diagnostics, Faculty of Advanced Medical Education, Andijan State Medical Institute, Andijan, Uzbekistan

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Abstract: Contrast-associated acute kidney injury (CA-AKI) remains a significant complication after coronary angiography and percutaneous coronary intervention (PCI), with traditional diagnosis relying on delayed rises in serum creatinine (SCr). Kidney injury molecule-1 (KIM-1) and interleukin-18 (IL-18) are tubular injury biomarkers that rise earlier and may improve early detection. Urinary KIM-1, a proximal tubular transmembrane protein upregulated after ischemic or toxic injury, typically increases within 6 hours post-contrast, with areas under the receiver operating characteristic curve (AUC) reported around 0.79–0.85 in meta-analyses and umbrella reviews. Urinary IL-18, a pro-inflammatory cytokine released from proximal tubules, also elevates early (often by 6 hours) and shows AUCs of approximately 0.75–0.79 for predicting CA-AKI. Both markers demonstrate good sensitivity and specificity at early time points and complement functional markers such as cystatin C or structural markers such as NGAL. Combined panels improve discrimination. While promising for early risk stratification, especially in intermediate-to-high-risk patients, limitations include assay variability, heterogeneous cut-offs, and limited outcome data on biomarker-guided management. Current evidence supports their potential role alongside established biomarkers for earlier identification of CA-AKI after coronary procedures.

Keywords: contrast-associated acute kidney injury; KIM-1; interleukin-18; urinary biomarkers; coronary angiography; percutaneous coronary intervention; early detection; narrative review

1. Introduction

CA-AKI after coronary angiography and PCI is associated with increased morbidity, prolonged hospital stay, and higher mortality. Incidence varies from roughly 7–15% in unselected cohorts and is substantially higher in patients with chronic kidney disease, diabetes, hemodynamic instability, or large contrast volumes. Diagnosis is still predominantly based on SCr changes (KDIGO criteria: ≥0.3 mg/dL within 48 hours or ≥1.5× baseline within 7 days), which peak late and delay intervention.

Novel urinary biomarkers reflecting tubular injury can detect damage hours after contrast exposure. Among the most studied are kidney injury molecule-1 (KIM-1) and interleukin-18 (IL-18). This evidence-based narrative review evaluates their diagnostic performance for early detection of CA-AKI following coronary procedures, synthesizing data from prospective studies, meta-analyses, and umbrella reviews.

2. Biology and Kinetics of KIM-1

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KIM-1 is a type I transmembrane glycoprotein expressed at low levels in normal proximal tubular epithelium. After ischemic or toxic injury it is markedly upregulated, shed into the urine, and serves as a sensitive marker of proximal tubular damage. Urinary KIM-1 concentrations rise within hours of injury and correlate with histologic severity in experimental models.

In the setting of contrast exposure, urinary KIM-1 typically increases by 6 hours post-procedure in patients who later develop CA-AKI. Absolute levels and delta (change from baseline) values have both shown discriminative ability. Serum KIM-1 has been studied less frequently and generally shows weaker or delayed changes compared with the urinary fraction.

3. Diagnostic Performance of KIM-1

Prospective studies after coronary angiography/PCI report significant elevations of urinary KIM-1 at 6 hours in CA-AKI patients versus controls. In one cohort, a 6-hour urinary KIM-1 threshold of approximately 0.56 ng/mL yielded an AUC of 0.81 (sensitivity 78%, specificity 82%). Larger meta-analyses and umbrella reviews of biomarkers for contrast nephropathy place urinary KIM-1 with an AUC of approximately 0.79–0.85, sensitivity around 0.76–0.84, and specificity around 0.76–0.84. In a comprehensive umbrella review of meta-analyses, urinary KIM-1 ranked immediately after NGAL and cystatin C (AUC 0.85), with a positive likelihood ratio of 3.58 and negative likelihood ratio of 0.25.

A 2024 systematic review specifically examining KIM-1 after invasive cardiac procedures concluded that it shows promise as an early marker of renal injury, correlating with injury severity and participating in tissue repair pathways. Performance is generally best at 6–12 hours and declines relative to SCr by 48 hours. Normalization to urinary creatinine can modestly improve specificity in some datasets.

4. Biology and Kinetics of IL-18

IL-18 is a pro-inflammatory cytokine constitutively expressed in the intercalated cells of the collecting duct and upregulated in proximal tubules after ischemic or toxic injury. It is released into urine early after tubular stress and has been implicated in the inflammatory cascade of AKI. Urinary IL-18 rises within 6 hours after contrast exposure in patients destined to develop CA-AKI, while serum levels show less consistent early changes.

5. Diagnostic Performance of IL-18

Urinary IL-18 has demonstrated moderate but clinically useful early diagnostic accuracy. In a prospective study of 95 patients undergoing coronary angiography/PCI, 6-hour urinary IL-18 >118 pg/mL had an AUC of 0.75 (sensitivity 56%, specificity 88%); delta IL-18 also differed significantly between CA-AKI and non-CA-AKI groups. Meta-analyses of urinary biomarkers after PCI report a pooled AUC of approximately 0.79 for IL-18. Comparative accuracy analyses of hospital-acquired AKI biomarkers place IL-18 with sensitivity around 68% and specificity around 80%, yielding a diagnostic odds ratio lower than NGAL but still informative.

IL-18 has also shown prognostic associations with later cardiac events in some older studies. Its performance is protocol-dependent and can be influenced by concurrent inflammation or infection.

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6. Comparative and Combined Performance

In head-to-head and pooled analyses, both KIM-1 and IL-18 rise earlier than SCr but generally exhibit lower overall AUCs than NGAL (typically 0.91) or cystatin C (0.89–0.93). In the 2022 meta-analysis by Lin et al. of biomarkers after PCI, urinary KIM-1 and IL-18 each had pooled AUCs of 0.79, while urinary NGAL reached 0.91. Umbrella reviews similarly rank urinary KIM-1 (AUC 0.85) behind NGAL and cystatin C but ahead of several other candidates.

Combination of early urinary KIM-1 or IL-18 with NGAL, cystatin C, or clinical risk scores (e.g., Mehran score) improves specificity and overall discrimination. Joint assessment of 6-hour urinary biomarkers with Doppler renovascular indices has produced AUCs approaching 0.96 in single-center data. Neither marker alone is sufficient for definitive diagnosis or staging; they are best viewed as complementary early signals of tubular injury.

7. Clinical Implications, Limitations, and Future Directions

Potential applications include early post-PCI urinary sampling (4–6 hours) in intermediate- or high-risk patients to identify those who may benefit from intensified monitoring or renoprotective measures before SCr rises. High negative predictive value in some protocols supports rule-out utility.

Limitations are significant: lack of standardized commercial cut-offs, inter-assay variability, influence of baseline urinary abnormalities or systemic inflammation, high heterogeneity across studies in CA-AKI definitions and timing, and sparse evidence that biomarker-guided care changes hard clinical outcomes. Cost and availability further restrict routine use.

Future priorities include standardized assay platforms, larger multicenter validation of absolute and relative thresholds, evaluation of multi-biomarker panels, and randomized trials assessing whether early detection with KIM-1/IL-18 improves patient-centered outcomes.

8. Conclusion

Urinary KIM-1 and IL-18 are evidence-supported early biomarkers of tubular injury that rise within 6 hours after contrast exposure during coronary angiography and PCI. They demonstrate moderate-to-good diagnostic accuracy (AUCs generally 0.75–0.85) for predicting subsequent CA-AKI and complement more extensively validated markers such as NGAL and cystatin C. While not yet ready for standalone clinical decision-making, they add incremental value in research and selected high-risk settings. Continued standardization and outcome-oriented studies will clarify their precise role in post-procedural care pathways.

Selected Key References

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