



Letter to Editor

[TIMP-2]*[IGFBP7] for Predicting Early AKI



We would like to congratulate Zaouter and colleagues for researching into the important clinical problem of Cardiac Surgery Associated-Acute Kidney Injury (CSA-AKI) that was published in a recent issue of the journal [1]. Herein, one of the objectives was to measure concentration of two urinary G1 cell cycle arrest proteins, the insulin-like growth factor binding protein 7 (IGFBP7) and the tissue inhibitor of metalloproteinases- 2 (TIMP-2) expressed as [TIMP-2]*[IGFBP7], for possible early prediction/diagnosis of CSA-AKI. To determine the earliest rise of the markers tested, data were collected before induction of general anaesthesia, and then at 1, 4, 12 and 24-hours post-operatively.

The authors noted that values of [TIMP-2]*[IGFBP7] were similar between patients with and without AKI at all times, except 12 hours. It was concluded that [TIMP-2]*[IGFBP7] has a poor discrimination for predicting AKI at all measured times. We wish to express our concern with certain aspects of the methodology that we feel could affect the interpretation of these results.

Firstly, the prediction of AKI has been validated only for 12 hours following the assessment of [TIMP-2]*[IGFBP7] [2–5]. Zaouter and colleagues however, used it for evaluating AKI that developed anytime over next 7 postoperative days. The temporal association of urinary TIMP-2 and IGFBP7 beyond 12 hours has not been proven for AKI. Thus we feel its evaluation for CSA-AKI developing over 7 days postoperatively is not methodologically correct. Secondly, the section of “outcome data” mentions that the urinary [TIMP-2]*[IGFBP7] combination was evaluated for utility as a reliable “diagnostic” strategy. Urinary [TIMP-2]*[IGFBP7] levels are known to rise early after renal injury that is distinct from renal functional impairment. The combination is thus validated for prediction of AKI only and not for its diagnosis as mentioned in this section by the authors. Thirdly, urinary [TIMP-2]*[IGFBP7] can predict only stage 2 and 3 AKI. The authors however evaluated the combination for prediction of all stages of AKI (1/2 or 3). We feel this would almost amount to using a laboratory investigation for diagnosing a condition that is known to be not associated with it. Thus, we feel that the results regarding urinary [TIMP-2]*[IGFBP7] for “predicting” CSA-AKI in these

settings may not be entirely correct. Maybe for these reasons, the 12 hours [TIMP-2]*[IGFBP7] despite being significantly greater amongst those with AKI failed to be useful predictor and had a low Area Under Curve (0.65; 95% CI: 0.53–84) for CSA-AKI. Indeed, on closer observation the results did show a lower baseline [TIMP-2]*[IGFBP7] in patients without AKI; followed by a rise later such that it was higher in those with AKI at all subsequent time points (though statistical significance was lacking at all times except the 12 hours reading).

Another observation made by the authors that could need some clarification includes a significantly higher preoperative serum creatinine in patients who did not develop CSA-AKI.

Disclosure of interest

The authors declare that they have no conflict of interest.

References

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