Clinical utility of the Nucleosome levels in septic Acute Kidney Injury: improved classification and targeted intervention?

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INTRODUCTION

NETosis serves as a swift and efficient immunological reaction to mitigate and contain infections. Both basic and clinical research underscore the significance of innate immune cells like neutrophils in the onset and advancement of renal ailments.

OBJECTIVES

We evaluated levels of circulating H3.1 nucleosomes, a surrogate of NETosis, to examine if there was an association between the development of acute kidney injury (AKI) and its severity in patients with confirmed sepsis and septic shock.

METHODS

Frozen plasma citrate samples at randomization, day 2 and 7 were evaluated from 881 patients of the SISPCT cohort with either new-onset acute kidney injury (AKI) or no AKI (defined by KDIGO). Circulating H3.1 nucleosomes were measured using Nu.Q® H3.1-nucleosome ELISA.
Patients with preexisting impaired renal function already in the screening process who did not progress to AKI were evaluated to provide a comparator.

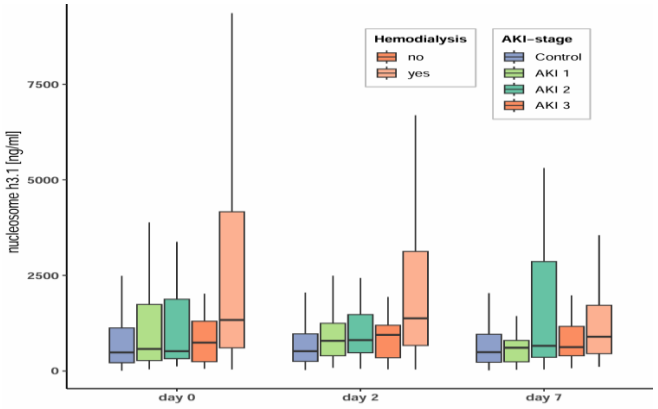

Figure 1: H3.1 Nucleosome levels over time

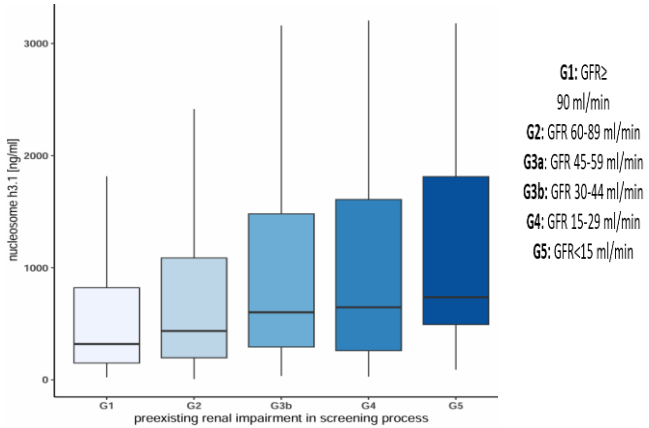

Figure 2: H3.1 levels in patients with preexisting impaired kidney function without evolving AKI (p<0.001)

RESULTS

- AKI 1: n=67 (7.6%)
- AKI 2: n=28 (3.2%)
- AKI 3: 219 (24.8%) , 189 (86%) of them required RRT

Nu.Q® H3.1 levels were significantly higher in those who developed severe AKI when compared to patients who did not develop AKI (1151 ng/ml [509-3797] vs 484ng/ml [216- 1127]); (p<0.001).
In patients who remained in RRT demonstrated a significant reduction in Nu.Q® H3.1 levels over 7 days compared to patients with AKI 3 who did not require RRT, (1335 ng/ml [604-4165] to 898 ng/ml [447-1778]; (p<0.001) compared to patients with AKI 3 and without RRT (741 pg/ml [242-1362] to 625 pg/ml [399-1166]; p=0.924).
Baseline values of H3.1 levels also differ in patients without evolving AKI but preexisting renal impairment (at screening process). The more pronounced the reduction in GFR at baseline, the higher the levels of H3.1 at baseline (p<0.001).
In terms of prediction of AKI they are not superior (AUC 0.695) to serum creatinine (AUC 0.755) or the glomerular filtration rate (AUC 0.754).
High initial H3.1 nucleosome levels were also negatively associated with 28-day survival and need for 28-day RRT.

CONCLUSIONS

NETosis represents a significant element in the pathogenesis of septic AKI. Subsequent investigations are imperative to elucidate the involvement of NETosis in both AKI and chronic kidney disease, facilitating the assessment of potential therapeutic strategies aimed at modulating these mechanisms.

ACKNOWLEDGEMENTS

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