QUANTIFICATION OF CIRCULATING NUCLEOSOMES USING NOVEL ASSAYS SHOWS ELEVATED LEVELS IN PATIENTS AFTER TRAUMATIC INJURY: A PILOT STUDY

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BACKGROUND

- The identification of reliable biomarkers to predict symptomatic VTE in trauma patients remains a clinical challenge. Citrullinated histones are elevated in trauma patients after injury; however, standardization of an assay for this biomarker is limited by its transient nature.[1,2]
- Nucleosomes have also been investigated, and by contrast, are stable in blood.[3] Quantification of nucleosomes, which are DNA wrapped around a histone protein core, has been shown to be a biomarker of sepsis, acute respiratory distress syndrome, and malignancy.[4,5,6]
- We hypothesized that levels of circulating nucleosomes quantified after traumatic injury, specifically histone H3.1 and its citrullinated R8 post-translation modification, would be greater in trauma patients than in healthy volunteers, and would be greater in those who develop VTE compared to those who did not.

METHODS

- Trauma patients (pts) presenting to a Level I trauma center were evaluated for inclusion in a prospective case-cohort study. A subset of pts who developed incident, symptomatic VTE and of those who did not develop VTE within 90 days of discharge were selected in a 1:3 ratio, had samples collected within 12 hours injury, and were compared to pre-COVID-19 healthy volunteer samples as a non-trauma reference group. Circulating nucleosomes were quantified using Nu.Q® H3.1 and Nu.Q® H3R8 Cit assays, which has high consistency across lots, promoting standardization for translational use.
- Data were presented as median [IQR] or n (%), with Wilcoxon Rank-Sum or chi-squared test, with p-value <0.05 as statistically significant.

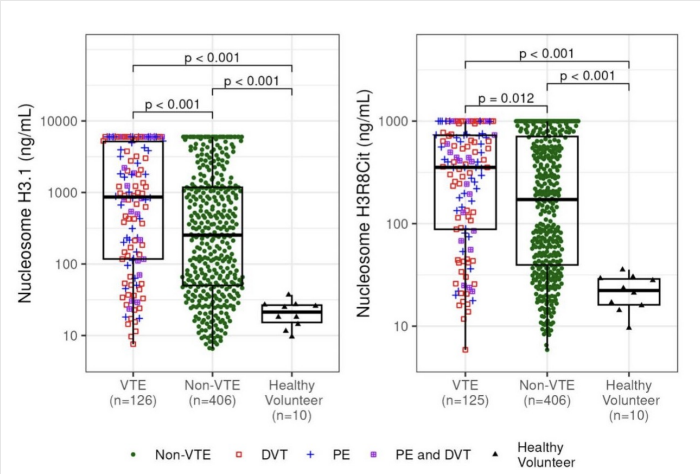
RESULTS

- A total of 532 trauma pts were analyzed (52 years [32, 65], 70.7% male, 94.5% blunt, ISS 17 [9,27]): 126 pts with VTE to 406 with non-VTE. No significant differences were found in age, sex, or mechanism between pts with VTE and those without. However, VTE pts had greater ISS scores (14 [9,24], 2 [13, 34], p<0.001) and BMI (29.1 [24.0, 34.4], 27.6 [23.8, 32.2], p=0.030). A greater percentage of VTE pts underwent surgery (57.1%, 33.0%, p<0.001) and received blood transfusions within 24 hours of injury (52.4%, 23.6%, p<0.001).
- Both H3.1 and H3R8 Cit levels were greater in both groups of trauma patients than healthy volunteers (p<0.001). H3.1 levels were significantly greater in trauma patients who developed VTE compared to those who did not (p < 0.001), as were H3R8 Cit levels (p=0.012), Figure.

CONCLUSION

- These findings suggest that neutrophil extracellular traps may contribute to the development of VTE observed after injury. Nucleosome levels of Nu.Q® H3.1 and Nu.Q® H3R8 Cit needs to be further investigated as an early biomarker potentially predictive of VTE.

FIGURE: NUCLEOSOME LEVELS IN VTE VS NON-VTE PATIENTS



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