

論 文 要 旨

Damage-associated molecular patterns and fibrinolysis perturbation
are associated with lethal outcomes in traumatic injury

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Background

Upon cellular injury, damage-associated molecular patterns (DAMPs) are released into the extracellular space and evoke proinflammatory and prothrombotic responses in animal models of sterile inflammation. However, in clinical settings, the dynamics of DAMP levels after trauma and links between DAMPs and trauma-associated coagulopathy remain largely undetermined.

Methods

Thirty-one patients with severe trauma, who were transferred to Kagoshima City Hospital between June 2018 and December 2019, were consecutively enrolled in this study. Blood samples were taken at the time of delivery, and 6 and 12 h after the injury, and once daily thereafter. The time-dependent changes of coagulation/fibrinolysis markers, including thrombin-antithrombin complex, $\alpha 2$ -plasmin inhibitor ($\alpha 2$ -PI), plasmin- $\alpha 2$ -PI complex, and plasminogen activator inhibitor-1 (PAI-1), and DAMPs, including high mobility group box 1 and histone H3, were analyzed.

The relationship between coagulation/fibrinolysis markers, DAMPs, Injury Severity Score, in-hospital death, and amount of blood transfusion were analyzed.

Results

The activation of coagulation/fibrinolysis pathways was evident at the time of delivery. In contrast, PAI-1 levels remained low at the time of delivery, and then were elevated at 6–12 h after traumatic injury. Histone H3 and high mobility group box 1 levels were elevated at admission, and gradually subsided over time. PAI-1 levels at 6 h were associated with serum histone H3 levels at admission. Increased histone H3 levels and plasmin- $\alpha 2$ -PI complex levels were associated with in-hospital mortality. $\alpha 2$ -PI levels at admission showed the strongest negative correlation with the amount of blood transfusion.

Conclusion

The elevation of histone H3 levels and fibrinolysis perturbation are associated with fatal outcomes in patients with traumatic injury. Patients with low $\alpha 2$ -PI levels at admission tend to require blood transfusion.

Keywords Damage-associated molecular patterns (DAMPs), Trauma-induced coagulopathy, Histone H3, Plasmin- $\alpha 2$ -PI complex (PIC), Plasminogen activator inhibitor-1 (PAI-1)