



Development of approaches to promote personalized medicine in trauma care

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Abstract

This research aims to provide personalized medicine of trauma care by identifying potential subgroups in multiple trauma, which are complicated by factors such as age, sex and pre-existing medical conditions. Traditional studies have not accounted for the heterogeneity of trauma patients. This research used machine learning on the Japan Trauma Data Bank to create a model that identifies individualized trauma patterns (trauma phenotypes) and performed proteomic profiles to evaluate the biological characteristics of high-mortality phenotypes.

Background & Results

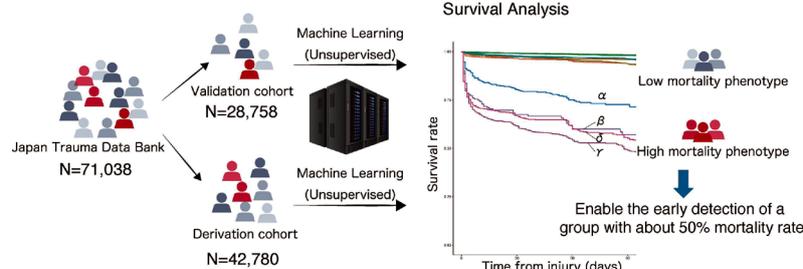
Despite the standardization of trauma care globally, there are still approximately 4.5 million trauma-related deaths annually, posing a significant challenge. The pathophysiological importance of coagulation-fibrinolysis and immune responses in trauma is well-known, but their clinical application as treatment targets remains limited. This complexity arises from the combination of patient background and the nature and extent of injuries. Previous studies have indicated that the combination of injured organs in polytrauma can affect patient outcomes and potentially indicate a risk of trauma death (J. Tachino et al. *J Trauma Acute Care Surg.* 2021).

Our research aimed to develop novel approaches to trauma care by identifying potential subgroups (phenotypes) in heterogeneous trauma patients using machine learning, followed by pathophysiological analysis. Proteomic analysis using patient serum (mass spectrometry) was performed for this purpose.

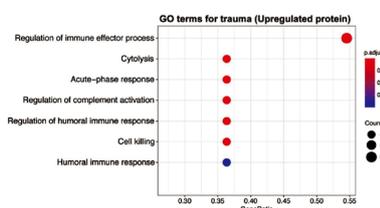
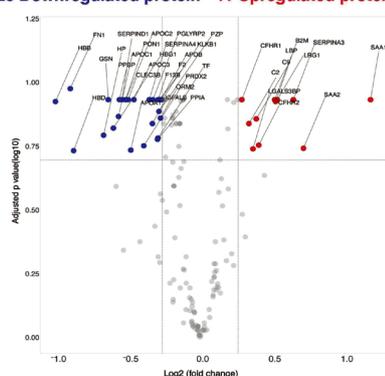
The study analyzed data from 71,038 blunt trauma patients in the JTDB, identifying eight trauma phenotypes. One phenotype exhibited a high mortality rate of about 50%. Latent class analysis further subdivided this phenotype into four subtypes (α to δ): " α represented younger patients with polytrauma", " β involved head injuries with low body temperature", " γ was seen in elderly patients with severe head injuries" and " δ characterized polytrauma patients with a higher actual mortality rate than predicted". Subsequently, this phenotyping was applied to 90 patients at the Osaka University Advanced Critical Care Center, and serum proteomic profile was performed. The high-mortality phenotype showed enhanced acute inflammatory response, dysregulation in the complement activation pathway, and reduced regulation in coagulation and platelet degradation pathways, indicating coagulopathy.

Significance of the research and Future perspective

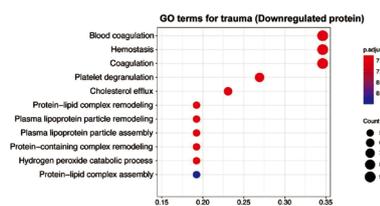
This research is significant in two main points. First, it utilizes early trauma care data to identify clinical states with high mortality, allowing for the identification of populations for early intervention, leading to potential revisions and development of new treatment strategies. Second, the molecular pathology of phenotypes derived from proteomic analysis identifies coagulation disorders and excessive inflammation in high-mortality phenotypes. These findings may lead to breakthroughs in new trauma care strategies and drug development. Currently, an application is being developed to identify trauma phenotypes in real-time. Future developments aim to integrate this system with electronic health records and diagnostic imaging, facilitating natural identification of phenotypes during clinical care.



26 Downregulated protein 11 Upregulated protein



11 proteins are up-regulated in high mortality phenotypes, and pathways involved in immune system regulation, complement pathways and cytolysis are activated.



26 proteins are down-regulated in high mortality phenotypes, and inactivation of pathways involved in blood coagulation and platelet function.

Patent Japanese Patent Application No.2022-009695, No.2023-120246

Treatise Tachino, Jotaro; Matsumoto, Hisatake et al. Development of clinical phenotypes and biological profiles via proteomic analysis of trauma patients. *Critical Care.* 2022, 26, 241. doi: 10.1186/s13054-022-04103-z

U R L Tachino, Jotaro; Katayama, Yusuke et al. Assessment of the interaction effect between injury regions in multiple injuries: A nationwide cohort study in Japan. *J. Trauma Acute Care Surg.* 2021, 90(1), 185-190. doi: 10.1097/TA.0000000000002969

U R L <https://www.med.osaka-u.ac.jp/eng/activities/results/2022year/matsumoto2022-08-10>

Keyword trauma, phenotype, inflammatory response, personalized medicine