ICU
MANAGEMENT & PRACTICE

Transforming Research to Improve Therapies for Trauma

The impact of trauma on global health is significant, resulting in millions of deaths and disabilities annually, with a particularly high toll on young people. However, the elderly are also increasingly affected. Variances in trauma-related death patterns worldwide are influenced by factors such as prompt treatment availability and the prevalence of older age and comorbidities. The complexities of trauma extend beyond immediate bleeding to include dysregulated immune and coagulation responses, leading to long-term complications and mortality, especially when traumatic brain injury (TBI) is involved.

A recent review outlines steps to advance research and introduce enhanced or novel therapies for trauma patients. The focus is on improving initial resuscitation and long-term care, addressing complications such as nosocomial infections and thromboembolic events resulting from the dysregulated host response.

Acute traumatic coagulopathy arises early after injury due to a combination of tissue damage and systemic hypoperfusion, worsened by resuscitation efforts. These coagulation disturbances contribute to both immediate haemorrhagic deaths and complications like multiple organ dysfunction and thrombotic events. However, gaps persist in understanding the initiation, evolution, and transition of coagulopathy. Factors such as injury severity, shock depth, and endogenous catecholamine release influence its complexity. Effective treatments for major haemorrhage require a detailed understanding of coagulopathy at various time points.

Aside from tranexamic acid, current therapies focus on replacing consumed or inhibited coagulation factors. However, the optimal timing, dose, and components of plasma or platelet transfusions remain uncertain. Moreover, the inactivation of these treatments by trauma-induced processes limits their effectiveness. Specific inhibitors targeting dysregulated processes like activated protein C pathway activation are lacking, highlighting the need for coordinated drug discovery efforts.

A critical challenge in TBI care is the lack of a standardised classification system, hindering research and treatment advances. Proposed systems should incorporate traditional measures like the Glasgow Coma Scale (GCS), brain imaging, prognostic biomarkers, and injury-related conditions. Despite the majority of TBIs being mild, with half not fully recovering within six months, those with low-energy mechanisms often receive less critical care. However, even mild TBI carries significant morbidity, including chronic headache and depression, yet follow-up rates remain low, limiting early identification of at-risk patients.

In severe TBI, acute interventions have shown limited success in improving survival rates, emphasising the need for individualised therapies. Treatments like early administration of tranexamic acid and viscoelastic assays to guide haemostatic interventions have shown promise. Precision medicine approaches, utilising dynamic blood and intracranial pressure analyses, aim to identify subgroups benefiting from specific therapies. Blood-based protein biomarkers hold potential for TBI evaluation and monitoring, though regulatory clearance for clinical decision-making remains limited.

Recent efforts, such as the second Lancet Neurology Commission on TBI, highlight existing knowledge gaps and provide recommendations for TBI research, clinical care, and policy development . However, further refinement and collaboration are necessary to address the evolving challenges of TBI management effectively.

Optimising trauma trial design is essential for identifying effective interventions. Biologically-driven inclusion criteria based on targeted pathways can enhance trial efficiency and reduce the risk of therapy ineffectiveness. Adaptive trial designs, incorporating response-adaptive randomisation and Bayesian analyses, offer flexibility and efficiency in evaluating trauma therapies. These designs are particularly suitable for trauma research,

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given the rapid accrual of patient-centred outcomes.

Recent recommendations emphasise the importance of selecting appropriate primary outcomes for trauma trials, such as all-cause mortality or patient-centred clinical outcome scales. Biorepositories from RCTs provide valuable resources for identifying patient cohorts benefiting from interventions and assessing treatment effects on clinical outcomes.

Advancing trauma research requires bridging the gap between animal studies and clinical trials, optimising trial design, and selecting relevant primary outcomes. Improving trauma outcomes requires a multidisciplinary approach and an understanding of the evolving trajectory of trauma care. Key research priorities include identifying dysregulated pathways and using biomarker-driven adaptive clinical trials to inform personalised treatment approaches. Ultimately, the future of trauma research lies in delivering the right therapy to the right patient at the right time.

Source: Critical Care

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