

Δ Defining the ‘Second Hit’: Does Intramedullary Nail Fixation of Femoral Shaft Fractures Hijack the Acute Phase Response in Severely Injured Patients?

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Purpose: A pathologic acute phase response to major trauma can lead to a maladaptive interaction between inflammatory and coagulation systems resulting in increased morbidity and mortality. Known as the “second hit hypothesis,” orthopaedic surgical intervention may exacerbate this maladaptive response. Two processes thought to contribute to this phenomenon include excessive plasmin activation with resultant hyperfibrinolysis, and dysregulated activation of neutrophils and the innate immune system. Our aim is to investigate the biomolecular acute phase response to intramedullary nail (IMN) fixation of femoral shaft fractures in patients with isolated vs polytraumatic injuries.

Methods: Trauma patients >16 years with a femur fracture undergoing IMN fixation were prospectively enrolled. Five blood samples were obtained: preoperatively, immediately after intramedullary reaming (post-ream), in the immediate postoperative area (postoperative day 0), and at postoperative days 1 and 2. Measures of plasmin activation and fibrinolysis included D-dimer, p11, and plasmin-antiplasmin complex (PAP). Measures of neutrophil activation included calprotectin and myeloperoxidase (MPO). Assays consisted of multiplex or standard ELISA (enzyme-linked immunosorbent assay). Statistical analyses were performed with GraphPad Prism.

Results: 22 patients were enrolled. 10 patients had polytraumatic injuries (ISS 28.5 ± 11.7) and 12 had isolated femur fractures (ISS 13 ± 9.4). PAP was increased in polytrauma patients only on postoperative day 0. Both cohorts exhibited a sharp and significant increase in d-dimer post-operatively with normalization by postoperative day 1. IL (interleukin)-6 was significantly elevated preoperatively in polytrauma patients only. All patients trended toward elevated plasma levels of calprotectin and MPO as compared to control pooled plasma. Polytrauma patients trended toward elevated levels of calprotectin relative to isolated injuries. Preoperative calprotectin levels were significantly positively correlated with hospital length of stay and ISS.

Conclusion: Markers of increased plasmin activation and subsequent fibrinolytic activity (PAP, D-dimer) demonstrated sharp increases after reamed IMN placement, with greater effects in polytrauma patients. Plasma markers of neutrophil activation demonstrated prognostic value relative to injury severity. These findings suggest that targeted antifibrinolytics (ie, tranexamic acid) warrant investigation for their potential to reduce plasmin activation, hyperfibrinolysis, and subsequent risk of adverse outcomes following IMN fixation in trauma patients.

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See the meeting website for complete listing of authors’ disclosure information. Schedule and presenters subject to change.