Increased Prothrombotic Cytokine Levels Are Associated With Hypercoagulability Following Hip Fracture

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Purpose: Venous thromboembolism (VTE) risk after hip fracture surgery (HFS) remains a concern, despite thromboprophylaxis prescription. There is increasing evidence supporting the interplay between hypercoagulability and inflammation during clot formation, as inflammatory cytokines can promote thrombus formation (interleukin [IL]-6, IL-9, IL-17A) or resolution (IL-4, IL-8, IL-10). Thromboelastography (TEG) is a whole-blood assay that provides a comprehensive analysis of hemostasis and can identify trauma patients at increased risk for VTE. This study aimed to describe the relationship between pro- and anti-inflammatory cytokines and hypercoagulability after HFS for the first time.

Methods: This is a single-center prospective cohort study of patients requiring HFS. Participants underwent serial blood draws until 6-week follow-up for TEG and plasma cytokine analysis. Patients were prescribed pharmacological thromboprophylaxis for 28 days. Incidence of VTE (proximal deep vein thrombosis [DVT] or pulmonary embolism [PE]) was monitored. Hypercoagulability was defined as maximal amplitude (MA, a measure of clot strength) of 65 mm or greater. Mann-Whitney U tests were used to compare cytokine levels between the hypercoagulable and non-hypercoagulable groups. Spearman correlations were calculated between MA and cytokine levels.

Results: A total of 87 patients were included in this analysis with a median age of 78 years (interquartile range [IQR] 71.0-85.3), with 67% being female. There were 2 symptomatic VTE events (2%), with both participants having elevated MA within 24 hours of VTE diagnosis (VTE 1: MA = 66.1 on postoperative day [POD]2 and VTE 2: MA = 66.7 on POD3). IL-17A and IL-2 receptor antagonist (IL-2Ra) were statistically significantly elevated at admission and on POD1 in patients who were hypercoagulable. Additionally, IL-22 was significantly elevated on POD3 in the hypercoagulable group.

Conclusion: This large prospective cohort of patients requiring HFS demonstrated significantly elevated early IL-17A levels, which has been linked to thrombus formation, supporting that hypercoagulability may be, in part, inflammatory-mediated. These novel data also suggest that there is weak monotonic relationship between IL-2Ra and IL-9 and hypercoagulability. Further research is warranted to investigate inflammatory-mediated hypercoagulability, especially with respect to IL-17A and IL-2Ra, which may help inform future novel therapeutic targets for VTE risk reduction.