Hypercoagulability and Systemic Inflammation Contribute to Venous Thromboembolism in Orthopaedic Surgery Patients With Metastatic Bone Disease

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Purpose: Patients with metastatic bone disease (MBD) are at high risk for potentially life-threatening venous thromboembolism (VTE) following orthopaedic surgery. Hypercoagulability and inflammation promote clot formation; however, their contribution to VTE pathophysiology in patients with MBD remains unknown. This pilot study aimed to address this knowledge gap by: (1) evaluating extent and duration of hypercoagulability using serial thromboelastography (TEG), a whole-blood viscoelastic hemostatic assay; and (2) quantifying temporal changes in plasma cytokine concentrations. We hypothesized that VTE would be associated with TEG parameters of hypercoagulability and increased systemic inflammation.

Methods: Consecutive adults with MBD who required orthopaedic surgery for pathologic fracture treatment were enrolled into this single-center, prospective cohort study. Analyses for serial TEG (TEG6s Hemostasis Analyzer) and 17 relevant inflammatory cytokines (MESO QuickPlex) were performed preoperatively and at 6 time points over a 12-week postoperative follow-up period. Patients used pharmacological thromboprophylaxis for 4 weeks postoperatively, and incidence of VTE was monitored. Maximal amplitude (MA), which indicates clot strength, was evaluated using TEG, with hypercoagulability defined as MA ≥65 mm. Mean MA values were compared with the 65-mm threshold using 1-sample t-tests, and cytokine levels in patients with and without VTE were compared using 2-sample t-tests.

Results: 35 patients participated, with a mean age of 68 years (standard deviation = 11) and 60% being female. Five patients (14.3%) developed VTE (1 pulmonary embolism, 4 proximal deep vein thromboses). Preoperatively, patients with VTE complications demonstrated hypercoagulability above the 65-mm threshold (P = 0.03), and significantly elevated concentrations of interferon gamma-inducible protein-10 (IP-10) and interleukin-17A (IL-17A), compared to patients without VTE (P = 0.02 and P = 0.03, respectively). In patients without VTE, 51.9% remained hypercoagulable at 6 weeks postoperatively. Concomitant with TEG-defined hypercoagulability, IP-10 and IL-17A levels were elevated at 6 weeks postoperatively.

Conclusion: Patients who developed VTE demonstrated significant hypercoagulability and increased systemic inflammation preoperatively compared to patients without VTE. Persistently elevated IP-10 and IL-17A, which are linked to endothelial dysfunction and platelet activation, suggest that prolonged postoperative hypercoagulability may, in part, be inflammatory-mediated. This warrants future investigation into thromboprophylaxis agents with both anti-platelet and anti-inflammatory effects (ie, acetylsalicylic acid).