Patients with Acute or Impending Pathological Fractures Demonstrate Platelet-Mediated Hypercoagulability and High Venous Thromboembolism Rates

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Purpose: Patients with metastatic bone disease (MBD) are at a 7-fold increased risk for venous thromboembolism (VTE) compared to patients without cancer. Platelet mapping (PLM) analysis can be used to activate platelets at the adenosine diphosphate (ADP) receptor or the thromboxane A2 (AA) receptor, to evaluate clot strength. This study aimed to evaluate platelet contribution to hypercoagulability via the AA and ADP pathways.

Methods: Consecutive adults with MBD undergoing orthopaedic surgery for acute or impending pathological fractures (APF [acute pathological fracture] or IPF [impending pathological fracture) were enrolled in this single-center, prospective cohort study. Whole blood samples collected preoperatively; on postoperative day (POD) 1, 3, and 5; and 2, 6, and 12 weeks postoperatively were analyzed using TEG 6s haemostasis analyzers (Haemonetics Corporation). Bilateral lower extremity Doppler ultrasound was performed on POD3 for deep vein thrombosis (DVT) screening, and incidence of image-confirmed DVT or pulmonary embolism (PE) was recorded. All patients received thromboprophylaxis postoperatively. Platelet hyperactivity was defined as maximal amplitude (MA; a measure of clot strength) over 55 mm. Student t tests were used to compare MA values with this threshold and between those with and without VTE.

Results: 19 participants (10 female; 52.6%), with a mean age of 68 (± 12) years were enrolled. VTE incidence was 21.1% (n = 4; 1 PE and 3 DVTs). PLM (polarized light microscopy) analysis demonstrated prolonged platelet hyperactivity based on elevated ADP-MA and AA-MA that extended to 6 weeks postoperatively for the AA pathway and even further for the ADP pathway (Figure 1). Increased platelet hyperactivity was measured in those who experienced VTE complications.

Conclusion: This study supports further investigation into the safety and efficacy of prolonged thromboprophylaxis for some patients and the investigation of mechanisms for platelet activation following surgery for MBD.

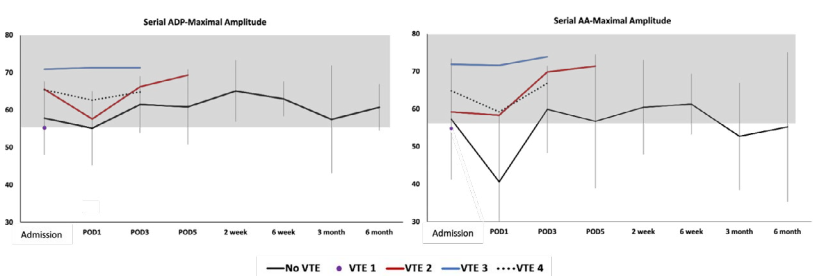

Figure 1: Serial Platelet Mapping demonstrates platelet hyperactivity (above 55 mm; grey shaded area) in both the ADP-pathway (left) and AA-pathway (right) for three of four patients with VTE. Prolonged platelet hyperactivity is demonstrated and is more pronounced in the ADP-pathway for patients with metastatic bone disease requiring surgical treatment for acute or impending pathological fractures.