Evaluating the Platelet Contribution to Hypercoagulability in Patients with Metastatic Bone Disease After Orthopaedic Surgery

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Background

- Patients with cancer that has spread to bone (metastatic bone disease, MBD) are at 7-fold higher venous thromboembolism (VTE) risk after orthopaedic surgery than non-cancer patients[1]
- Malignancy induces hypercoagulability[2], yet the extent of hypercoagulability and the platelet contribution to this is unknown in patients with MBD
- Thrombelastography (TEG) is a point-of-care test of whole blood which can identify hypercoagulablity through measurement of clot strength (maximal amplitude, MA)
- TEG-based platelet mapping (PLM) measures platelet activity via activation of adenosine diphosphate (ADP) and arachidonic acid (AA) platelet receptor pathways

Primary Objective

- To quantify hypercoagulability and to evaluate platelet activity in patients with MBD who have undergone orthopaedic surgery to treat pathologic fractures

Methods

- Single-centre, prospective cohort study of adults (≥18 years) with MBD or haematological malignancy of bone who required orthopaedic surgery for pathologic fracture
- Exclusion: Primary bone cancer; pregnant; current treatment for deep vein thrombosis (DVT) or pulmonary embolism (PE)
- Serial TEG and PLM analyses were performed at seven timepoints using TEG®6s haemostasis analyzers (Haemonetics Corp, Boston, MA)
- MA ≥65 mm[3-5] defined hypercoagulability
- PLM MA ≥55 mm[6] defined platelet hyperactivity
- VTE incidence was captured if confirmed by imaging (i.e., Doppler ultrasound for DVT; CT PE for PE)
- VTE incidence was a study endpoint

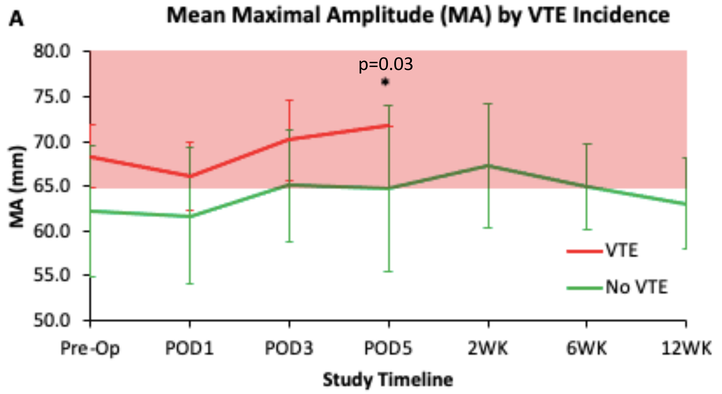
Results

- 19 patients (mean age 68 ± 12 years) were enrolled **(Table 1)**
- Patients who had VTE were more hypercoagulable than those who did not **(Fig. 1A);** VTE risk was highest within 1-week post-operatively **(Fig. 1B)**
- Pre-operatively, platelet activity was increased in ADP (p=0.03) and AA pathways (p=0.04) in patients with VTE **(Fig. 2)**

Table 1. Demographics and Baseline Characteristics (n = 19)

Characteristic	Number (%) of Patients*
Age, mean (SD)	68 (12)
Sex, female	10 (52.6)
Body Mass Index, median (IQR), kg/m^2	26.1 (24.1-31.9)
Primary Cancer	
Haematological (Multiple Myeloma)	2 (10.5)
Breast	4 (21.1)
Colorectal	4 (21.1)
Lung	4 (21.1)
Other Solid Tumour	5 (26.2)

*Except where specified



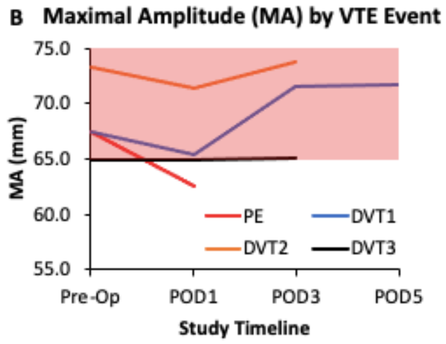


Figure 1A: Patients who had VTE were more hypercoagulable. Patients without VTE remained hypercoagulable at 6-weeks post-operatively.
Figure 1B: VTE rate was 21.1% (PE=1; DVT=3). Mean MA at diagnosis was 68.3 mm (SD ± 5.3).

Results

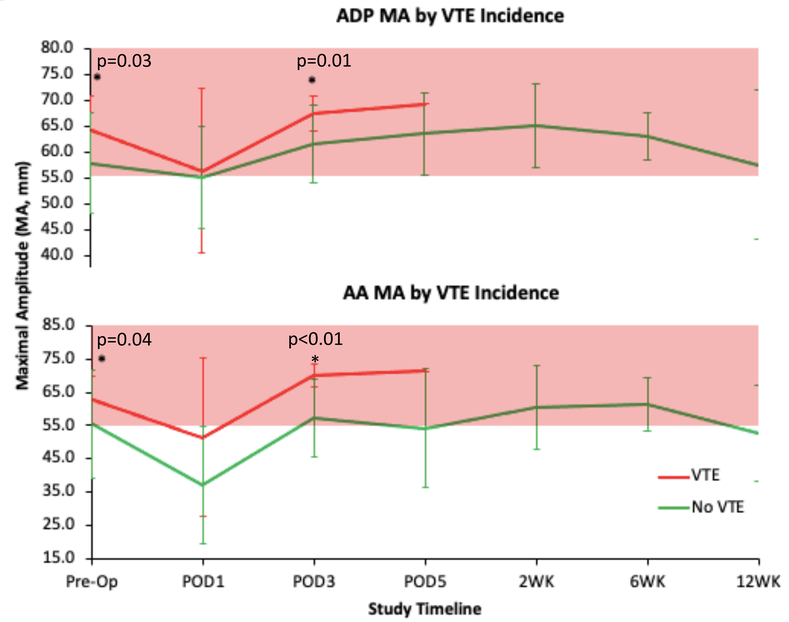


Figure 2: Platelet hyperactivity was observed in patients with VTE (n=4), who had elevated ADP and AA receptor pathway platelet activity compared to those without VTE (n=15).

Clinical Significance

- Serial TEG and PLM analyses identified hypercoagulability and platelet hyperactivity, respectively, in patients with MBD
- Four weeks of post-operative thromboprophylaxis is commonly prescribed, which does not address prolonged hypercoagulability for patients with MBD
- High VTE rates highlight the need for thromboprophylaxis guidelines that address increased cancer-associated VTE risk
- PLM results support further investigation into anti-platelet use in patients with MBD (i.e., clopidogrel to target the ADP pathway; aspirin to target the AA pathway)

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