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CENTRE FOR TRAUMA SCIENCES

Venous thromboembolic events after traumatic injury are associated with early changes to the fibrinolytic system

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Introduction

Venous thromboembolic events (VTE) occur in up to 20% of trauma patients and of these, pulmonary embolus is fatal in up to 50%. It is unknown whether fibrinolytic activation and consumption of precursors may subsequently render patients hypercoagulable. We hypothesised that an early hyperfibrinolytic state would lead to a propensity for developing VTE.

Methods

A cohort study of adult trauma patients admitted for >48 hours to a major trauma centre. Blood was obtained within 2 hours of injury and at 24 and 72 hours. Electronic records were reviewed to identify diagnoses of deep vein thrombosis (DVT) and pulmonary embolism (PE). Prothrombin fragments (PF), plasminogen-activator inhibitor-1 (PAI-1), tissue plasminogen-activator (tPA), plasmin-antiplasmin complex (PAP), plasminogen, and D-dimer were measured in patients developing VTE and 103 control patients without VTE.

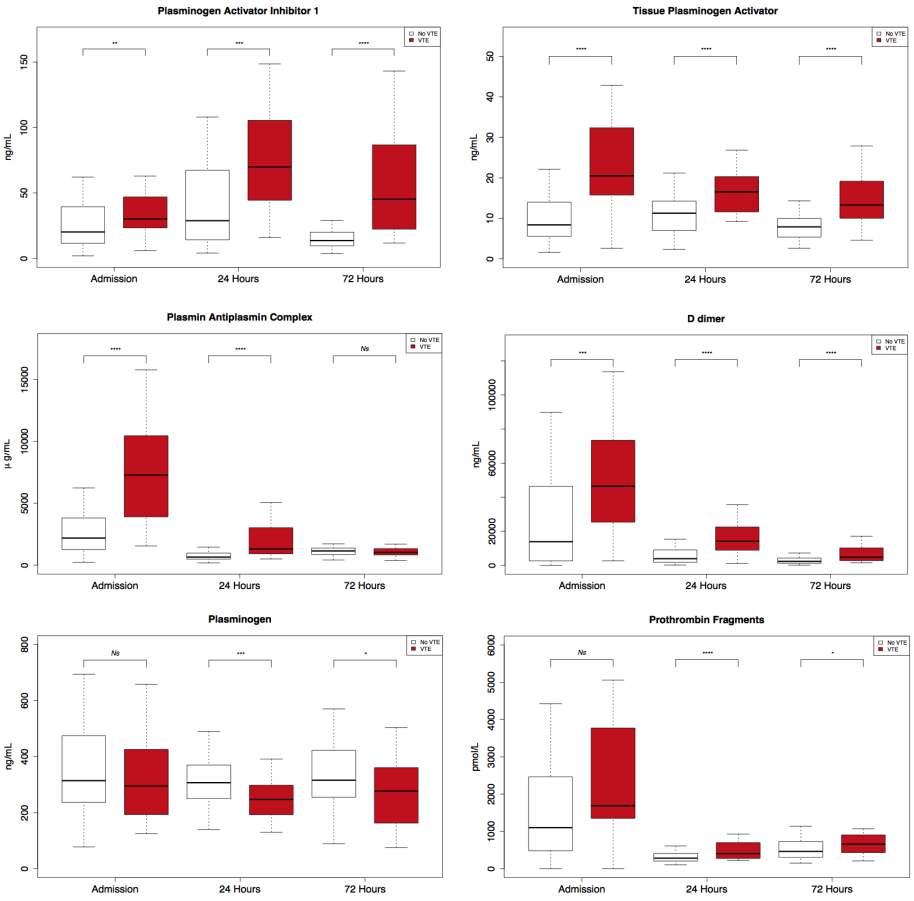
Figure 1: Patient characteristics and outcomes

	No VTE	VTE	*p* value
Number (%)	758 (96.2)	30 (3.8)	
Age	36 (25 – 52)	47 (36 – 57)	**
% Male	81	87	*Ns*
Injuries			
ISS	16 (9 – 29)	27 (17 – 25)	***
AIS Head	0 (0 – 3)	0 (0 – 3)	*Ns*
AIS Chest	2 (0 – 3)	3 (0 – 4)	*
AIS Abdo	0 (0 – 2)	2 (0 – 2)	**
AIS Extremity	2 (0 – 3)	3 (2 – 3)	***
Admission Parameters			
GCS	14 (10 - 15)	14 (6 – 15)	*Ns*
SBP (mmHg)	130 (110 – 149)	127 (97 – 142)	*Ns*
Base Excess (mM)	-1.5 (-4.2 to 0.7)	-2.9 (-7.0 to -1.4)	**
Prothrombin Time (s)	11.1 (10.7 – 11.7)	11.4 (10.9 – 12.4)	*
Transfusion (24 hour)			
PRBC	0 (0 – 2)	2 (0 – 7)	**
FFP	0 (0 – 0)	0 (0 – 4)	**
Platelets	0 (0 – 0)	1 (0 – 1)	***
Cryoprecipitate	0 (0 – 0)	0 (0 – 2)	***
Outcomes			
28-day mortality (%)	0.08	0.07	*Ns*
28-day ventilator free days	28 (26 – 28)	23 (8 – 28)	***
Hospital stay (survivors)	12 (5 – 26)	39 (28 – 54)	***

ISS, Injury Severity Score; AIS, Abbreviated Injury Score; GCS, Glasgow Coma Scale; SBP, Systolic Blood Pressure; PRBC, Pack Red Blood Cells; FFP, Fresh Frozen Plasma. Continuous data presented as median (interquartile range). *p* values calculated by Mann Whitney Test or Fisher's Exact Test. Significance: *p* ≤ 0.05 *, ≤ 0.01 **, ≤ 0.001 ***, ≤ 0.0001 ****

Results

There were 788 patients eligible for inclusion. Thirty patients (3.8%) developed VTE (10 DVT, 18 PE, 2 DVT+PE). **Figure 1.** On admission, VTE patients had increased levels of PAI-1 (29.8 *vs.* 20.3 ng/mL, p=0.02), tPA (20.5 *vs.* 8.4 ng/mL, p<0.001), PAP (7279 *vs.* 2193 µg/L, p<0.001) and D-dimer (46398 *vs.* 13896 ng/mL, p=0.001) compared to controls. At 24 hours, these increases were maintained (all p≤0.01), PF was elevated (405 *vs.* 283pM, p=0.007) and plasminogen was decreased (307 *vs.* 247 ng/mL, p<0.001). By 72 hours, PAP was comparable between groups (1035 *vs.* 1153 µg/L, p=0.44) while other markers were unchanged.



Conclusion

Patients developing VTE demonstrate early hyperfibrinolysis following injury. Hyperfibrinolysis depletes plasminogen and may induce a procoagulant state increasing susceptibility to VTE. Fibrinolytic profiling may improve risk stratification and enable targeted prophylaxis.