Proteomics of Arterial Thrombi in Acute Limb Ischemia

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Abstract
Introduction: Acute limb ischemia (ALI) is a medical emergency characterized by a sudden decrease in limb perfusion due to arterial occlusion. Without urgent revascularization, patients are at risk of ischemic damage and amputation. This study employs novel proteomic techniques to investigate the molecular architecture of ALI thrombi, identifying key proteins that may influence coagulation dynamics and fibrinolysis resistance.

Methods: Arterial thromboemboli (n = 12) collected after revascularization procedures were analyzed and compared with *in vitro* clots (n = 10) generated from healthy donor blood via tissue factor–induced coagulation. Proteins were identified and quantified via liquid chromatography–mass spectrometry (LC–MS/MS). A comprehensive literature review of the most abundant proteins was conducted to categorize them according to their functional roles in fibrinolysis, red blood cell (RBC) degradation, complement activation, and platelet activation.

Results: Compared to *in vitro* clots, ALI clots contained 141 proteins with significantly increased abundance and 38 with decreased abundance ($p < 0.05$). These included 17 fibrinolysis regulators, 8 RBC-related proteins, 6 complement proteins, and 36 platelet regulators. The antifibrinolytic protein vitronectin (VTN) was strikingly enriched (1067-fold increase), suggesting a substantial role in fibrinolysis resistance and clot stability. Other highly abundant proteins included scavengers of heme/hemoglobin, thromboinflammatory complement proteins, and platelet activators.

Conclusion: This *proof-of-concept* study introduces novel proteomic methods for arterial thrombus analysis and identifies key proteins involved in ALI pathology. Our findings reveal a delicate balance between antifibrinolytic and profibrinolytic proteins, offering potential therapeutic targets that may enhance thrombolysis and improve ALI management.