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Proteomic profiling in acute pulmonary embolism and potential for metabolic modulation with GLP-1 agonist: a prospective controlled study

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Background: Molecular mechanisms affecting thrombus resolution and right ventricular (RV) functional recovery in acute pulmonary embolism (PE) remain poorly understood, but multiple inflammatory and immune factors have been implicated. Reduction in vascular inflammation, oxidative stress and vasoconstriction have been demonstrated across multiple vascular beds in response to GLP-1 agonists, supporting a potentially beneficial role in PE. This study aimed to characterise the proteomic profile in PE and potential for metabolic modulation.

Methods: A total of 22 patients with acute intermediate and high-risk PE (median age 66 years, IQR 55.5–72.5) were prospectively recruited, and blood samples collected at diagnosis. Protein abundances were measured in patients with PE (n=20) and compared to an age and sex-matched Controls (n=21) without thromboembolic disease. Subsequently, in the acute PE cohort, n=8 received semaglutide 0.25mg s/c + standard of care for 4-weeks and n=14 standard of care alone. Baseline and 4-week follow-up proteomic profiles were compared.

Results: Plasma proteomics included measurement of 2,554 circulating proteins. Higher abundance of complement and metabolic stress proteins were observed in patients with acute PE compared to controls (Figure 1A). Semaglutide downregulated forty-four proteins which were significantly enriched for glycoproteins (FDRq < 0.01) (Figure 1B). Downregulated proteins included regulators of metabolic stress and key complement intermediates (C3 - C5) with reduction in complement glycoproteins and plasma MMP-9 validated by ELISA. Glycopeptide analysis demonstrated deglycosylation of highly abundant candidate glycoproteins in response to Semaglutide as the plausible mechanism for glycoprotein downregulation. Exploratory CT markers of RV strain improved between baseline and follow up only in those patients who received Semaglutide.

Conclusion: Increased abundance of complement and metabolic stress glycoproteins were observed at the time of acute PE diagnosis compared to controls without thromboembolic disease. GLP-1 agonists may have a potential role in immunometabolic changes in the plasma proteome during PE recovery.

Figure 1: Plasma proteomics profile in acute PE compared to controls without PE (Panel A) and change in regulators of metabolic stress and key complement intermediates pre and post Semaglutide

