SELDI-TOF MASS SPECTROMETRY TO IDENTIFY URINARY BIOMARKERS OF DEEP VEIN THROMBOSIS

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Deep vein thrombosis (DVT) is a common clinical problem in both primary and secondary care. As the signs and symptoms of DVT are non-specific, diagnostic algorithms incorporating clinical probability scores and D-Dimer levels are used to stratify patients according to risk. Although this will identify a group of low risk patients who do not require further investigation most patients proceed to imaging investigations, most commonly Doppler ultrasound. While this is non-invasive it is time consuming, expensive and usually can only be performed in hospital. Of those referred for ultrasound scanning only 20-30% will have evidence of DVT. The identification of more sensitive markers of DVT would reduce the requirement for ultrasound scanning and perhaps allow prompt diagnosis and initiation of anticoagulation in primary care.

Surface-enhanced laser desorption/ionisation time of flight mass spectrometry (SELDI-TOF MS) enables the screening of complex biological samples for novel biomarkers of disease through a combination of “on-Chip” retentate chromatography followed by mass spectrometry. We report the results of a biomarker scouting study analysing urine samples from 20 patients with DVT and 20 patients with no evidence of DVT on Doppler USS. All samples were stored at -80^0C prior to analysis and samples were normalised to urine creatinine excretion.

We found consistent differences in the urine proteomic profiles from patients with Doppler USS proven DVT compared to those with moderate or high risk of DVT but in whom imaging studies were negative. Three ProteinChip chemistries were particularly informative: CM10 (cation exchange), IMAC-Copper and IMAC-Manganese (bind proteins with an affinity for copper/manganese such as metalloproteinases). Informative biomarkers were m/z 16,791 (CM10); 4,347, 4,536 6,164, 6189 (IMAC Copper) and 48,242(IMAC-Manganese).

Biomarker validation studies are now underway to confirm these findings in a larger cohort of patients and correlate biomarker excretion with serum D-Dimer levels and clinical probability scores.

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