

## Effects of diabetes mellitus on fibrin clot structure and mechanics in a model of acute neutrophil extracellular traps (NETs) formation

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**Background** Subjects with diabetes mellitus (DM) have an increased risk of arterial thrombosis, to which changes in clot structure and mechanics may contribute. Another contributing factor might be an increased formation of neutrophil extracellular traps (NETs) in DM. NETs are mainly formed during the acute phase of disease and form a network within the fibrin matrix, thereby influencing clot properties. Our aim was to study how DM affects clot properties in a model resembling an acute phase of disease with NETs formation.

**Methods** Clots were prepared from citrated plasma from subjects with and without DM with the addition of NETs, induced in neutrophils by *S. aureus* bacteria or phorbol myristate acetate (PMA). Structural parameters were measured using scanning electron microscopy, mechanical properties using rheology, and sensitivity to lysis using a fluorescence-based fibrinolysis assay.

**Results** Plasma clots from subjects with DM compared to clots from subjects without DM had significantly thicker fibers ( $195.0 \pm 3.9$  nm vs  $186.6 \pm 3.9$  nm,  $p < 0.01$ ) and fewer pores ( $1616.7 \pm 120.0$  vs  $1907.1 \pm 169.0$ ,  $p < 0.01$ ) and branchpoints ( $2.95 \pm 0.21$  vs  $3.44 \pm 0.29$ ,  $p < 0.01$ ). In addition, fibrinolysis was significantly slower ( $14873 \pm 1321$  AU vs  $15995 \pm 1337$  AU,  $p < 0.05$ ), while mechanical properties were similar between both groups (storage modulus DM  $62.1$  [29.7-188.9] Pa vs no DM  $36.4$  [23.0-80.0] Pa,  $p = 0.24$ ).

**Conclusion** In a model of acute NETs formation, DM plasma shows prothrombotic effects on fibrin clots.