Distinctive fibrinolysis in contracted versus uncontracted blood clots


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The success of endogenous and therapeutic fibrinolysis is governed in part by the structure of the fibrin clot. An understudied feature that potentially affects fibrinolysis is the degree of platelet-driven shrinkage, i.e. contraction, of blood clots and thrombi. The aim of this work was to examine the effect of clot contraction on the rate of naturally occurring internal fibrinolysis and external fibrinolysis to simulate therapeutic thrombolysis. Clot contraction, which was initiated with 2mM CaCl\textsubscript{2} and 1U/ml thrombin, was impaired by ~75% by inhibiting platelet non-muscle myosin IIa activity (blebbistatin), actin polymerization (latrunculin A), and platelet-fibrin(ogen) binding (abciximab). Internal fibrinolysis measured using dynamic optical tracking of clot size as a function of time occurred 2X faster in contracted clots compared to uncontracted clots in the presence of 75ng/ml tPA. In direct contrast, the dynamic release of radioactive fibrin degradation products as a measure of external fibrinolysis was 4X faster in uncontracted clots when 75 ng/ml tPA was added to the surface of preformed clots. This difference in the susceptibility of contracted and uncontracted clots to internal versus external lysis suggests that the lysis rate is dominated by the interplay of clot permeability to fibrinolytic enzymes as well as the spatial proximity of the fibrin fibers themselves. These results have implications for understanding clot stability in patients with thrombotic disorders and improving clot lysis by Impairing clot contraction to improve thrombolysis, but enhancing clot contraction to improve natural fibrinolysis.

I would like to be considered for the Outstanding Abstract Award.

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