

## MARKEDLY IMPAIRED ENDOGENOUS THROMBOLYTIC STATUS IN ESRF MAY EXPLAIN THE INCREASED THROMBOTIC EVENTS IN THIS GROUP

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**INTRODUCTION:** End stage renal failure (ESRF) patients despite being on renal replacement therapy (RRT) remain at increased risk of acute thrombotic events. The reason for this is unclear, but likely to be related to either increased platelet reactivity, impaired thrombolysis or both.

**AIM:** We hypothesised that impaired endogenous thrombolytic status may be responsible for the increased risk of thromboembolic events in patients with ESRF. It was our aim to assess spontaneous thrombolytic status in ESRF patients and compare them to normal volunteers and to patients with coronary artery disease.

**METHODS:** Peripheral venous blood was tested using the Global Thrombosis test (GTT), a novel near-patient test that allows the measurement of both thrombotic and thrombolytic status from a 3 ml non-anticoagulated blood sample. We tested ESRF patients on RRT (ESRF, n=48), patients with stable coronary artery disease (CAD, n=41) and normal healthy volunteers (Normals, n=49). All ESRF patients had been on established haemodialysis for at least 1 month. For each patient, a 3 ml blood sample was obtained from peripheral veins, (prior to the start of dialysis for those on RRT), and tested immediately after withdrawal. Routine FBC was also performed.

The GTT (Montrose Diagnostics Ltd, UK) is a physiological test of platelet reactivity, which uses non-anticoagulated, native blood, without added external agonists. An occlusive thrombus is formed using high shear stress, analogous to that in a stenosed coronary artery. The first phase of the test measures the time taken to form an occlusive platelet thrombus (occlusion time, OT) as marker of platelet reactivity, the more reactive the platelets the shorter the occlusion time. The second phase of the test measures the endogenous thrombolytic status, which is the time taken to spontaneously lyse the occlusive thrombus formed in phase 1. This is termed lysis time (LT).

**RESULTS:** All CAD patients were on dual antiplatelet therapy with aspirin and clopidogrel. The Normal group were on no medications. Of the ESRF patients, 46% were on no antiplatelet or anticoagulant medication, 6% were on warfarin (1 on warfarin alone and 2 on both aspirin and warfarin), and 50% were on antiplatelet medication (18 on aspirin, 1 on clopidogrel, and 5 on both).

LT was significantly longer in ESRF on RRT ( $3636 \pm 2366$  sec) than that observed in CAD patients ( $1227 \pm 580$  sec,  $p < 0.0001$ ) or Normals ( $1151 \pm 448$  sec,  $p < 0.0001$ ). There was no difference between LT in CAD patients and Normals ( $p = \text{NS}$ ). This shows that ESRF patients have markedly impaired spontaneous thrombolysis, compared to CAD patients and normal volunteers.

**CONCLUSION:** Our results demonstrate that ESRF patients on RRT are have markedly impaired endogenous thrombolysis. This may be a novel explanation for the increased risk of thrombotic cardiovascular events that has been observed in this group.

**RELEVANCE:** Our data provides important insight into the pathomechanism of the increased thrombotic risk in ESRF patients. This may be a novel test to identify those ESRF patients at highest risk of thrombotic events. Future studies are required to correlate these results with clinical outcome and to examine the effect of medications on LT in this group.