

# FOCUS ON RESEARCH

## A PROSPECTIVE OBSERVATIONAL STUDY TO IDENTIFY CLINICAL & LABORATORY PREDICTORS OF RECURRENT VENOUS THROMBO-EMBOLIC DISEASE

### Researchers

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### Aim

In order to more precisely identify patients with venous thrombo-embolic disease (VTE) who are most likely to suffer recurrent VTE following anticoagulation cessation, and therefore benefit from long term anticoagulation from the outset, we sought to assess the predictive power of coagulation activation markers, thrombophilia blood tests and clinical characteristics (individually or in combination) for recurrent VTE.

### Project Outline/Methodology

This prospective observational study followed 480 patients with acute VTE, mainly deep vein thrombosis (61%) or pulmonary embolism (36%), for a median of 1.9 years (total 950 patient years). Three coagulation activation markers (proteins which indicate heightened activation of the coagulation system in the blood), fibrin D-dimer [Dd], thrombin-antithrombin complex [TAT] and prothrombin F1+2 [F1+2], were serially assessed during anticoagulation and after warfarin cessation (when laboratory thrombophilia tests were also undertaken). The predictive power of these laboratory tests, and of baseline clinical characteristics, were then assessed for subsequent episodes of recurrent VTE during the 1-4 year follow-up period.

### Key Results

The strongest individual risk factor for recurrent VTE was high Dd levels measured 3 weeks after anticoagulant cessation (4-fold increased comparing patients with Dd levels in the top third with those in the bottom third). Other significant risk markers included high levels of TAT & F1+2 (3-fold risk), Factor VIII & IX and initial idiopathic (spontaneous) VTE (all 2-3 fold risk). Importantly Dd prior to anticoagulation cessation, and as early as 6 weeks after initial VTE, was associated with a 2.8-fold risk for subsequent recurrent VTE. This implies that patients at high risk of recurrent VTE may be identifiable before they would normally have stopped anticoagulant therapy.

### Conclusions

Study results are consistent with existing literature and emphasise the potential of coagulation activation as a marker for recurrent VTE. We postulate that a combination of Dd, Factor VIII and clinical details of initial VTE will be most useful in identifying high risk patients who will merit long term anticoagulation.

### What does this study add to the field?

The results from this study corroborate recent data demonstrating the association of elevated Dd or Factor VIII levels and increased risk of recurrent VTE. However we have now shown, for the first time, that other coagulation activation markers (TAT and F1+2) show a similar association and that Dd, as early as 6 weeks after initial VTE can help predict recurrence risk.

### Implications for Practice or Policy

Assessment of D-dimer and selected thrombophilia tests, by simple and widely available laboratory techniques, may assist clinicians in identification of those VTE patients at highest risk of recurrent thrombotic events. Such patients could then be targeted for long term anticoagulation.

### Where to next?

We are currently undertaking further data analysis and modelling to identify the optimal combination of clinical and laboratory variables which together best separate patients at low and high risk of recurrent VTE. This combination would then be tested in a prospective management study.

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