WHAT THE NEIGHBORS SAY

1 | ADDING TO THE GENETIC PUZZLE OF VENOUS THROMBOGENESIS


Venous thromboembolism (VTE) is a classical complex pathology with an etiology that is well recognized to involve contributions from both the patient genome and the environment. In the past decade, progress has begun to be made in identifying the genetic contributors to this phenotype beyond the previously recognized variants affecting the natural anticoagulant genes, factor V Leiden and the prothrombin gene variant. It is assumed that the many additional genetic variants that are associated with VTE risk contribute small increments in the risk profile, although there may still be rare variants that demonstrate a greater influence. In their Blood report, Lindstrom et al. have now identified 16 new genetic associations for VTE using both genome- and transcriptome-wide evaluations (GWAS and TWAS). They meta-analyzed 18 studies comprising 30,234 cases of VTE and 172,122 controls and evaluated associations with ~13 million variant sites in the genome. The GWAS meta-analysis identified 34 distinct genetic associations of which 11 represented new genetic associations. Analysis of the TWAS data identified a further 5 new associated loci. Some of the identified genetic loci have no obvious connection with the hemostatic system. Studies will now be required to validate these associations using orthogonal methodologies that will undoubtedly lead to new knowledge concerning the process of venous thrombogenesis.

2 | PREVENTION OF PULMONARY EMBOLI: TO FILTER OR NOT?


The development of venous thromboembolism in patients who have experienced severe trauma is a major clinical concern. The complication usually occurs within the first few days following the accident, and more than half the patients who develop proximal vein thrombosis can experience a subsequent pulmonary embolism (PE). In these patients, prophylactic systemic anticoagulation is often contraindicated and thus the placement of a vena cava filter is sometimes deemed appropriate. In the multicenter randomized study performed by Ho et al in four tertiary care Australian hospitals, 240 severely injured patients (median age 39 years) with contraindications to anticoagulation were randomized within 72 h to filter insertion or not. The primary end point was a composite of symptomatic PE or death at 90 days after study enrolment. Early filter placement did not result in a significantly lower incidence of PE or death (13.9% in vena cava filter group and 14.4% in the controls).

3 | PLATELETS COME IN FROM THE COLD

Chen et al. Short-acting anti-VWF (von Willebrand factor) aptamer improves the recovery, survival, and hemostatic functions of refrigerated platelets. ATVB https://www.ahajournals.org/doi/abs/10.1161/ATVBAHA.119.312439

Normally, donor platelets for transfusion must be stored at room temperature and have only a 5 day shelf life. Refrigerated platelets have recently received FDA approval for specific applications, but refrigeration results in apparently pre-activated platelets that are cleared rather rapidly after infusion. During refrigeration, VWF has increased binding to GPIb-α and this appears to be a major player in accelerating platelet clearance. Blocking VWF/GPIb-α interactions can prolong the circulation of refrigerated platelets, but unfortunately this limits the function of the transfused platelets. In this study, Chen et al. employed a short-acting DNA aptamer that potently blocks VWF/GPIb-α interactions but which is cleared from the circulation within about 2 h. In mouse experiments, platelets treated with aptamer during refrigeration exhibited increased posttransfusion recovery and survival than untreated platelets, and the aptamer improved the long-term (>2 h after transfusion) hemostatic function of refrigerated platelets. Furthermore, they showed that including a DNA-based antidote to the aptamer allowed immediate (15 min after transfusion) hemostatic function of the transfused platelets. This study may therefore bring us one step closer to routinely prolonging the storage of platelets by refrigeration.