Thrombophilic abnormalities in recurrence of venous thromboembolism (VTE) in patients treated with standardized anticoagulant treatment

Santamaria MG, Agnelli G, Taliani MR, et al; Warfarin Optimal Duration Italian Trial (WODIT) Investigators. Thromb Res 2005;116:301-6

Conclusion: Patients with thrombophilic abnormalities and venous thromboembolism (VTE) have an increased risk of recurrence of VTE.

Summary: The authors studied the recurrence of VTE in patients with and without thrombophilic abnormalities who were treated with a standardized anticoagulation program. The analysis was from a prospective, multicenter, randomized study evaluating clinical benefit of 1 year of oral anticoagulant treatment vs a 3-month period of oral anticoagulant treatment after a first episode of idiopathic proximal deep vein thrombosis. Patients were screened for protein C and protein S deficiencies, antithrombin, hyperhomocysteinemia, antiphospholipid antibodies, mutation 20210GA of the prothrombin gene, and resistance to activated protein C, Factor-5/R506Q mutation, or both. VTE recurrence was documented by objective testing with ultrasound imaging or catheter-based techniques. An independent committee unaware of the results of thrombophilia screening adjudicated all recurrences.

Screening for thrombophilic abnormalities was done in 195 patients. Of 57 patients with detected thrombophilic abnormalities, 20 (35.1%) experienced VTE recurrence compared with 29 (21.0%) of 138 patients without thrombophilia (hazard ratio, 1.78; 95% confidence interval, 1.02 to 3.14; $P = .046$). Differences in VTE recurrence between patients with and without thrombophilia can be accounted for by patients who received only 3 months of oral anticoagulation (hazard ratio, 3.21; 95% confidence interval, 1.349 to 7.616; $P = .008$).

Comment: Like others before it, this study suggests longer durations of treatment for patients with idiopathic VTE. This study has too few patients to allow precise recommendations for duration of therapy on the basis of the thrombophilic abnormality identified. Nevertheless, it is now quite clear that not all VTE is the same. Patients with thrombophilia should be considered at higher risk of recurrence and probably treated with warfarin for at least 1year after their initial VTE event.

The insensate foot following severe lower extremity trauma: An indication for amputation?

Bosse MJ, McCarthy ML, Jones AL, et al, and the Lower Extremity Assessment Project (LEAP) Study Group. J Bone Joint Surg 2005;86A: 2601-8.

Conclusion: Insensation of the plantar surface of the foot after lower extremity trauma is not prognostic of long-term plantar sensory status or functional outcome. More than half of patients who presented with an insensate foot after lower extremity trauma ultimately regained sensation at 2 years. Assessment of plantar sensation should not be a component of the limb salvage decision algorithm.

Summary: Evaluation of plantar sensation is routine in the assessment of the impact of lower extremity trauma. The authors sought to determine long-term outcome after treatment of severe lower extremity trauma in patients who presented with absent plantar sensation. There were 55 subjects with an insensate extremity at the time of presentation, of whom 26 underwent amputation and 29 were treated for limb salvage. Also included was a control group consisting of patients with lower extremity trauma with intact plantar sensation at presentation who underwent limb reconstruction. Injury characteristics and functional and health-related quality-of-life outcomes at 1 and 2years after injury were compared in the three groups.

The insensate salvage group did not have a reported or demonstrated worse outcome at 1 or 2 years compared with the insensate amputation or sensate control groups. Approximately 55% of patients in both the insensate salvage and sensate control groups in whom the limb was salvaged had normal plantar sensation at 2 years after injury. This was regardless of whether plantar sensation had been reported to be intact at the time of presentation after injury. No differences were noted in overall physical or psychosocial scores in the three groups. At 2 years after injury, only one patient in the insensate salvage group had absent plantar sensation.

Comment: The data suggest assessment of plantar sensation after lower extremity trauma is essentially worthless in predicting the ultimate sensory status of the foot. These study findings do not support the widespread belief that absent initial plantar sensation in patients with a leg-threatening injury correlates with poor long-term outcome if the limb were to be salvaged. This study implies that tibial nerve dysfunction at the time of presentation does not necessarily imply transaction of the tibial nerve. It is important to remember that reversible ischemic injuries to nerves as well as neurapraxic injuries of peripheral nerves may mimic permanent loss of peripheral nerve function.

Association between carotid plaque characteristics and subsequent ischemic cerebrovascular events: A prospective assessment with MRI—initial results

Takaya N, Yuan C, Chu B, et al. Stroke 2006;37:818-23.

Conclusion: In patients with 50% to 79% asymptomatic internal carotid artery stenosis, magnetic resonance imaging (MRI) can identify plaque characteristics predictive of future cerebral vascular events.

Summary: Previous studies indicate it is possible to quantify plaque size and composition with MRI. The authors tested the hypothesis that MRI assessment of asymptomatic carotid plaque is predictive of future ipsilateral cerebrovascular events.

The study enrolled 154 consecutive patients with asymptomatic 50% to 79% internal carotid artery stenosis as determined by ultrasound imaging. All patients had ≥12 months of follow-up. All underwent multicontrast-weighted carotid MRIs at baseline. Study subjects were subsequently followed up every 3 months and assessed for occurrence of symptomatic cerebrovascular events. Mean follow-up was 38.2 months. Cerebrovascular events were defined as stroke or transient ischemic attack in the regions supplied by the index carotid artery or the occurrence of ipsilateral amaurosis fugax. Only the events related to the index artery were considered.

There were 12 carotid cerebrovascular events ipsilateral to the index carotid artery. Two patients with events secondary to atrial fibrillation were excluded. Cox regression analysis demonstrated a relationship between subsequent neurologic events and the following plaque characteristics: presence of a ruptured or thin fibrous cap (hazard ratio [HR], 17.0; $P < .001$), intraplaque hemorrhage (HR, 5.2; $P = .005$), increased mean intraplaque hemorrhage area (HR for 10 mm^2 increase, 2.6; $P = .006$), larger maximum percent lipid-rich/necrotic core (HR for each 10% increase, 1.6; $P = .004$), and increased maximum wall thickness (HR for each 1-mm increase, 1.6; $P = .008$).

Comment: Papers such as this represent the second phase of determining which patients with asymptomatic carotid plaques will most likely benefit from prophylactic carotid endarterectomy. Initial studies were all retrospective. Prospective studies such as this are now appearing. The data are extremely interesting and potentially highly clinically significant if in larger multicenter studies validated measurements of plaque characteristic can eventually be used to predict the patient with asymptomatic carotid stenosis who is truly at risk for an ipsilateral neurologic event.

Population-based study of event-rate, incidence, case fatality, and mortality for all acute vascular events in all arterial territories (Oxford Vascular Study)

Rothwell PN, Coull AJ, Silver LE, et al for the Oxford Vascular Study. Lancet 2005;366:1773-83.

Conclusion: Even outside of the coronary circulation, there is a high rate of acute vascular events that increases steeply with age.

Summary: Vascular events involving the coronary, cerebrovascular, and peripheral circulations have common risk factors, pathology, and preventative treatments. These multiple circulatory beds are rarely studied concurrently, however. In this study, the authors compared the incidence of acute vascular events in the coronary, cerebrovascular, and peripheral territories and related these events to aging of the population. This was a prospective study of data collected between 2002 and 2005 assessing 9106 individuals in Oxfordshire, United Kingdom, for an acute vascular event of any type.

There were 2,004 acute vascular events in 1,657 individuals. There were 918 cerebrovascular events (45%), of which 618 were stroke, and 300 were transient ischemic attack. There were 856 coronary events (42%), of which 316 were non-ST elevation myocardial infarction, 159 were ST elevation myocardial infarction, 218 were unstable angina, and 163 were sudden cardiac death. Nine percent of the acute vascular events were peripheral vascular events (n = 188). These included 92 episodes of critical limb ischemia, 53 episodes of visceral or limb ischemia secondary to emboli, and 43 aortic events. There were also 62 unclassifiable deaths.

Compared with coronary events, the relative incidence of cerebrovascular events was 1.19 (95% confidence interval [CI], 1.06 to 1.13). For nonfatal cerebrovascular events, the relative incidence compared with coronary events was 1.40 (95% CI, 1.23 to 1.59). If transient ischemic attacks and unstable angina were excluded, the relative incidence of cerebrovascular events to coronary events was 1.21 (95% CI, 1.04 to 1.41). A steep rise occurred in the incidence of vascular events in all territories with age. Case fatality rates increased with age, and 47% of the 1561 nonfatal events occurred at age ≥75 years.

Comment: There is nothing particularly surprising in this study except that perhaps cerebrovascular events were more common than coronary events. It is also interesting that half of all events occurred in patients ≥75 years. The age distribution of vascular events suggests that trials designed to assess interventions for atherosclerotic vascular disease must include a large proportion of older patients. Limiting studies to patients <80 years, as is frequently done, will exclude that segment of the population with the largest number of events.