

The relationship of the factor V Leiden mutation or the deletion-deletion polymorphism of the angiotensin converting enzyme to postoperative thromboembolic events following total joint arthroplasty

ABSTRACT

Our results suggest that neither of these potentially hypercoaguable states are associated with an increased risk of symptomatic thromboembolic events following total hip or knee arthroplasty in patients receiving pharmacological thromboprophylaxis.

INTRODUCTION

Background Patients following total hip and knee arthroplasty are at a significant risk for thromboembolic complications. Despite modern prophylaxis against thromboembolism, studies still report a 10 to 40% frequency of deep venous thrombosis and a significant rate of pulmonary embolism following total hip or knee arthroplasty [1]. The high incidence of thrombotic disease despite prophylaxis makes early detection imperative, as treatment with anticoagulation is highly effective. Both DVT and PE manifest few specific clinical signs or symptoms, making the clinical diagnosis neither sensitive nor specific [2]. A high index of suspicion based on risk stratification is necessary for the detection and appropriate implementation of diagnostic studies to identify this complication. The ability preoperatively to identify a subset of patients undergoing adult reconstructive surgery that are at a higher risk of developing thromboembolic complications would aid the clinician in making an accurate diagnosis and make possible further research to determine optimal regimes of postoperative detection and prophylaxis. Until recently, the only known hypercoagulable states were several rare genetic disorders of the coagulation cascade (antithrombin III, protein C, and protein S deficiency), which accounted for only a small percentage of all patients with venous thrombosis. In 1993, Dahlback et al. described a previously unreported hypercoagulable state among members of three families that suffered from recurrent venous thrombosis. Further investigation revealed an autosomal-dominant inherited defect in the anticoagulant function of factor V resulting in resistance to the anticoagulant action of activated protein C (APC). Formal evidence for this association came from a large population-based patient-control study, the Leiden Thrombophilia Study, which followed 474 consecutive patients of less than 70 years of age with a first episode of objectively confirmed DVT. Twenty-eight percent of patients in the study group and 5.7% of controls were found to be APC-resistant. Furthermore, it was estimated that these patients have a sevenfold greater risk of developing a DVT. The abnormal factor V that causes APC resistance was subsequently termed factor V Leiden. Later studies confirmed a seven- to-eightfold increased risk for patients heterozygous for the factor V mutation and an 80-fold increased risk in homozygous individuals. Factor V Leiden is therefore the most common thrombophilic disorder described, 10 times more common than all the other genetic coagulopathies combined, with an estimated prevalence of 5% in the general population. Polymorphisms of the angiotensin converting enzyme have also been associated with a hypercoaguable state. The angiotensin converting enzyme (ACE) digests angiotensin I to angiotensin II (a potent vasoconstrictor) and is thus involved with the regulation of vascular tone. The angiotensin converting enzyme has also been shown to attenuate fibrinolysis and affect both platelet activation and aggregation. The ACE gene has been found to have a polymorphism consisting of an insertion and a deletion of a 287 base pair fragment of intron 16. Patients may thus

be of one of three separate genotypes; insertion/insertion, deletion/deletion or insertion/deletion. Patients with the deletion/deletion genotype have been shown to have mean plasma ACE levels of approximately twice that of patients with the insertion/insertion genotype. Thus patients with the deletion/deletion genotype may be at increased risk for thromboembolic events. Although the majority of patients undergoing total hip and knee arthroplasty are subjected to similar perioperative risk factors that predispose to thromboembolism, only a subset of patients develop this complication. The objective of this study was to determine whether the FVL mutation or the deletion polymorphism of the ACE gene is associated with a higher risk of developing a postoperative thromboembolic complication.

CONCLUSION

Conclusions The objective of this study was to determine whether a specific genetic profile is associated with a higher risk of developing a postoperative thromboembolic complication. Although our results suggest that neither of these potentially hypercoagulable states are associated with an increased risk of symptomatic thromboembolic events following total hip or knee arthroplasty in patients receiving pharmacological thromboprophylaxis, an as yet undescribed genetically determined hypercoagulable state or predisposition may be present in these patients.