Can genetic changes in ApoM gene differentiate the patients at high risk of recurrent venous thrombosis?

Venous thrombosis (VT) is a major health problem worldwide and third most common type of cardiovascular disease. It causes more than half a million deaths every year in the European Union. An alarming proportion of VT patients experience recurrent VT and the rate of VT recurrence is ~30%, and it has been difficult to predict who these patients are. However, all the patients diagnosed with the primary VT are treated with anticoagulant drugs that can save the patients from VT recurrence at the cost of “sever bleeding”, leading to death. Thus, there is a need of clinical predictive markers that can help to differentiate those 30% patients at higher risk of VT recurrence from others that are at low risk of recurrent VT (70% patients).

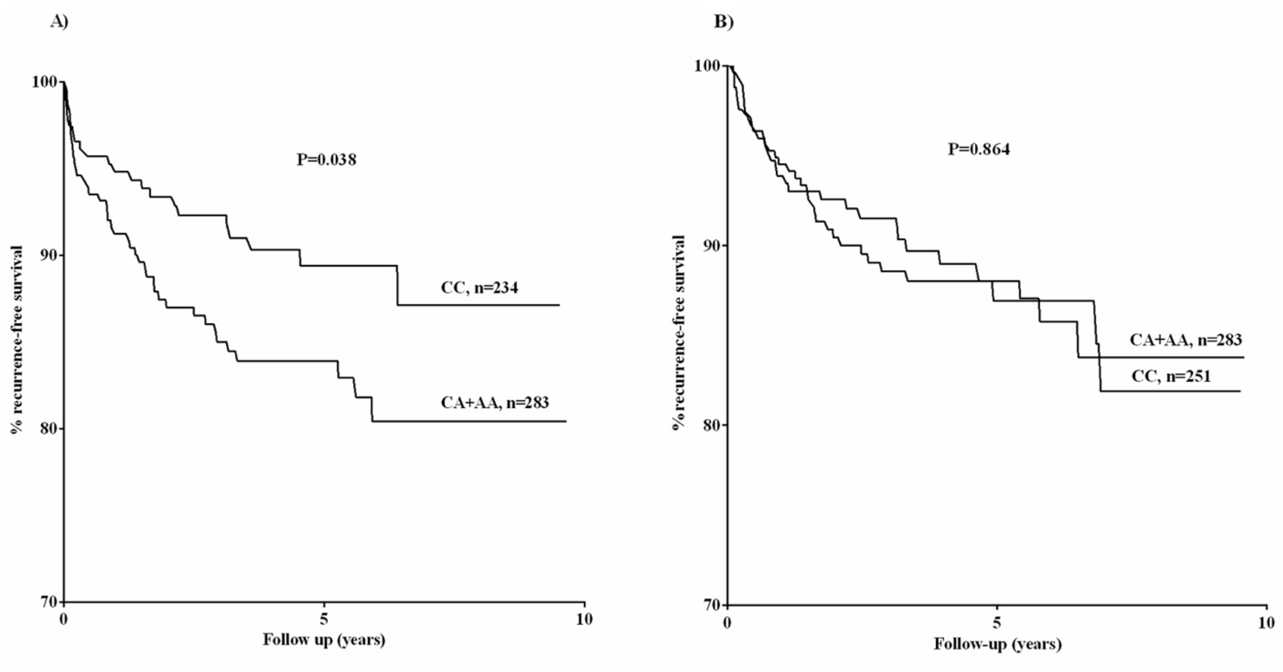

Fig. 1. Survival curves representing the different genotypes in ApoM rs805297 polymorphism and their association with risk of VT recurrence in male (A) and female patients (B). P=log-rank test.

Several factors have been reported to be involved in the development of VT recurrence. Now researchers from all over the world believe that 60% of these factors causing VT are genetic and most of them are still unknown. They have reported that the key may lie in genetic factors. So (this means that), if we can find those genetic factors, it will (also) be possible to find/isolate the patients with a high risk of VT recurrence so that clinicians can tailor therapy according to risk.

In recent years, researchers have been looking for so-called mutations: genetic changes in the cells, as possible predictive markers for complex diseases. Now, they may have found it: Apolipoprotein M (ApoM); a gene that plays an important role in lipid metabolism process. Mutations in ApoM are associated with cardiovascular diseases i.e. Coronary Artery Disease. However, their role in recurrent VT is not explicated yet. We aimed our current study to sequence the whole Apolipoprotein M gene in VT patients to identify the genetic changes and their association with the risk of recurrent VT.

A total of 1465 VT patients were followed for ~10 years after diagnosis with primary VT. During follow up, 156 (10.6 %) had VT recurrence. ApoM whole gene sequencing was performed by Sanger's sequencing and Taqman polymerase chain reaction. We identified a total of 6 genetic variants (polymorphisms) in ApoM gene in VT patients. Cox regression analyses were performed to analyse the risk of VT recurrence. Among the identified polymorphisms, *ApoM* rs805297 polymorphism was significantly associated with higher risk of VT recurrence in male patients (p= 0.038, hazard ratio = 1.72, 95% confidence interval =1.03–2.88). This association was independent of the other known risk factors for VT recurrence.

This study demonstrates that male patients with *ApoM* rs805297 polymorphism have a high risk (72%) of VT recurrence as compared to those without this polymorphism. These results will be validated and may be used for future patients to select them for long term anticoagulant therapy.

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Publication

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