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ANTICOAGULATION THERAPY

Warfarin dosing—novel SNP identified

A genome-wide association study conducted in the USA has revealed a novel single nucleotide polymorphism (SNP) that affects warfarin dose requirements in African–American individuals. Several genetic variants associated with response to warfarin therapy have been identified in those of European and Asian ancestry. However, little is known about the genetic factors involved in warfarin metabolism in populations of African descent. "Because of cost issues, warfarin will probably remain the mainstay oral anticoagulant ... in the USA and in developing countries—particularly in Africa—for many years," write the investigators. "Identification of a way to achieve therapeutic anticoagulation efficiently with warfarin is a priority."

Perera *et al*. studied African–American patients aged >18 years who were receiving a stable maintenance dose of warfarin. The 'discovery' cohort comprised 533 individuals, and 432 patients were enrolled in the 'replication' cohort.

The investigators identified a significant association between the SNP rs12777823 on chromosome 10 and warfarin dosing in the discovery cohort, which was supported by additional analysis in the replication group (*P* for combined analysis = 4.5×10^{-12}). Carriers of this SNP required 7–9 mg per week less warfarin than did individuals without this genetic variation. In addition, the inclusion of the rs12777823 genotype to a dosing algorithm improved prediction of therapeutic warfarin dose (absolute 5%; relative 21%). The pharmacokinetics of warfarin were also shown to differ between carriers and noncarriers of rs12777823. Trials are underway to assess whether genotype-guided warfarin dosing is clinically beneficial.

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Original article Perera, M. A. *et al*. Genetic variants associated with warfarin dose in African–American individuals: a genome-wide association study. *Lancet* doi:10.1016/S0140-6736(13)60681-9