

genotyped with the method of mass spectrometry (Sequenom, USA). The association between genetic polymorphisms and stable warfarin dose were analysed statistically. A multi-stepwise-regression model to predict stable warfarin dose based on clinical and genetic factor was constructed.

Results 312 patients were eligible and reached stable anticoagulation. In clinical factors, age, bodyweight, indications for anticoagulation, history of hepatic cirrhosis and renal dysfunction, combination drugs such as amiodarone, statins were significantly related with stable warfarin dose ($p < 0.05$). Among the genetic factors, five polymorphisms in three genes as CYP2C9 (rs1057910), CYP2C9 (rs4917639), VKORC1 (rs8050894), VKORC1 (rs9923231), CYP4F2 (rs2108622) were significantly related with stable dose of warfarin (the adjusted p value was 0.001, < 0.001 , < 0.001 , < 0.001 and 0.017 respectively). The multiple regression model using the factors of age, bodyweight, indications for anticoagulation, hepatic cirrhosis and polymorphisms of CYP2C9 (rs1057910), VKORC1 (rs9923231) and CYP4F2 (rs2108622) explained 37% of the interindividual variance in stable dose of warfarin.

Conclusion Polymorphisms of CYP2C9 (rs1057910), VKORC1 (rs9923231) and CYP4F2 (rs2108622) are the most important genetic factors that significantly influence stable warfarin dose in Chinese patients receiving low density anticoagulation (target INR 1.8–2.5). It is necessary to genotype these 3 SNPs and predict warfarin dose with pharmacogenomic algorithm in clinical practice and improve warfarin anticoagulation outcomes in Chinese patients.

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ESTABLISHMENT OF PHARMACOGENOMIC ALGORITHM FOR PREDICTING STABLE WARFARIN DOSE IN CHINESE PATIENTS

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Background Genetic variants of cytochrome P450 2C9 (CYP2C9) and vitamin K epoxide reductase (VKORC1) are known to influence warfarin dose, but the effect of other genes has not been fully elucidated. Pharmacogenomic algorithm that incorporating clinical and genetic factors to predict warfarin dose in Chinese patients is lacking but in necessary.

Objectives This study aimed to genotype polymorphisms in candidate genes involved in the action and metabolism of warfarin, and test for association with stable warfarin dose in Chinese patients. A pharmacogenomic algorithm for predicting stable warfarin dose based on the clinical and genetic factors was constructed in Chinese patients.

Methods This study was approved by PLA General Hospital Ethics Committee. 400 consecutive Han Chinese patients who managed to initiate warfarin anticoagulation and signed informed consent were enrolled in this study. The procedures of warfarin anticoagulation were monitored prospectively. With a target INR 1.8–2.5, all patients' stable warfarin dose, time to achieve stable anticoagulation and INR fluctuation were recorded. A total of 38 SNPs in 6 candidate genes that are related to metabolism and anticoagulant action of warfarin were