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## **ABO blood type and ABO gene with susceptibility to deep vein thrombosis following orthopedic surgery: a case-control study in Chinese Han population**

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The *ABO* gene encodes a glycosyltransferase with three main alleles (A, B, and O). The ABO blood group molecules are expressed in varieties of human tissues. Individuals with type O blood group have about 25% lower plasma FVIII and VWF levels [1]. Increased plasma FVIII and VWF levels are associated with an increased risk for VTE, and non-O blood group type is associated with an increased VTE risk which is independent of FVIII [2]. Yet the risk of ABO blood group type has not been studied in Asian population. In a genome-wide association study and subsequent replication studies, two single-nucleotide polymorphisms (SNPs) in *ABO*, rs657152 and rs505922 were associated with VTE [3]. However, there has been no study regarding the association between ABO gene and acute deep vein thrombosis (DVT) in Chinese population. We hypothesized that ABO blood type and ABO gene associated with acute DVT after orthopedic surgery and carried out a case-control study in patients after orthopedic surgery in Han Chinese population.

The study was approved by the ethics committee of the Medical School of Nanjing University, and written informed consent was obtained from patients and controls before they attended this study. A total 214 acute DVT patients and 636 control subjects with negative venography results were studied. All subjects in this study underwent

joint surgery in our department. Patients' ABO blood type was identified before surgery, and all DVT cases and controls were routinely diagnosed by venography on the third post-operative day. No anti-inflammatory or thrombolytic drugs were prescribed unless DVT was diagnosed.

A tag SNP of ABO gene (rs505922) was selected with Haploview software (<http://www.hapmap.org>). The NucleoSpin Blood QuickPure Kit (Macherey-Nagel GmbH & Co. KG, Düren, Germany) was used to extract DNA from peripheral blood. SNP was genotyped using TaqMan genotyping assays (Applied Bio-systems, Foster City, CA, USA). Unconditional logistic regression analysis was used to compare genotypes of rs505922 and allele distributions. Hardy-Weinberg equilibrium (HWE) was determined by  $\chi^2$ -test. A logistic regression analysis was carried out to identify risk factors in each group.

Significant difference in sex and age distribution (Table 1) was observed between the cases and controls ( $P < 0.001$ ). Non-O blood type was a significant risk factor for DVT ( $P < 0.001$ ). This association between Non-O blood type and DVT still existed after adjusting for allele distribution of rs505922 ( $P < 0.001$ ). The distributions of rs505922 (Table S1 in Supporting Information) was conformed to HWE. Significant difference was observed in the allele frequencies of rs505922 between cases and controls. However, this identified association between DVT and the allele frequen-

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**Table 1** Basic characteristics of the DVT patients and controls<sup>a)</sup>

	DVT, n=214 (%)	CONTROL, n=636	P*
Sex			
Male	61 (28.5)	258 (40.5)	0.004
Female	153 (71.5)	378 (59.5)	
Age (years)	62.7	55.3	<0.001
Blood type			
O	60 (28.0)	286 (45.0)	<0.001
Non-O	154 (72.0)	350 (55.0)	
BMI (kg m <sup>-2</sup> )	24.4	23.9	0.099

a) \*, Significance is evaluated as  $P < 0.05$ .  $P$  value is obtained after adjusting for sex, age, blood type and BMI of the studied population.

cy disappeared after adjusting for age, sex and blood type ( $P > 0.05$ ).

Our current study investigated the association between ABO blood type, ABO gene and the acute DVT after orthopedic surgery in Chinese population. Age and sex distribution were significantly different between case and control subjects. This is coincident with the previous conclusion that age is a major risk factor for DVT [4]. Our study showed an association between rs505922 and DVT after orthopedic surgery in Han Chinese population. However, the association disappeared after adjustment for risk factors, suggesting that it was rendered insignificant considering

dominant non-genetic factors such as age, sex and Non-O blood type. This finding was in consistence with outcome of a previous association study [6]. However, Non-O blood type was associated with DVT and this cannot be explained by rs505922. Our findings indicate that age, sex and Non-O blood type of patients undergoing orthopedic surgery should be considered when deciding post-operational thromboprophylaxis.

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## Supporting Information

**Table S1** Association between rs505922 and DVT

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