COMPARATIVE PERFORMANCE OF GENE-BASED WARFARIN DOSING ALGORITHMS IN CHINESE PATIENTS

Tong Yin, Qiang Xu, Yu Liu, Hongjuan Wang, Jie Yang, Lei Gao, Yuxiao Zhang, Bin Xu, Caiyi Lu, Yusheng Zhao, Tong Yin. *Institute of Geriatric Cardiology, General Hospital of People's Liberation Army, Beijing China*

Objectives Multiple warfarin pharmacogenetic algorithms have been published and been confirmed to predict warfarin dose more accurately than clinical algorithm or fixed-dose approach. However, their performance in Chinese patients has never been evaluated. We sought to compare the performance of published warfarin pharmacogenetic algorithms in a cohort of Chinese patients under warfarin anticoagulation.

Methods The study population consisted of 282 unrelated Han-Chinese patients consecutively admitted to the General Hospital of Chinese People's Liberation Army between January 2008 and

July 2011. The patients had all undergone warfarin anticoagulation for various indications and were stably controlled with a target international normalisation ratio (INR) of 1.6–2.5. Genomic DNA extraction from each patient was followed by genotyping to detect the polymorphisms of CYP2C9*3 (rs1057910), VKORC1 −1639 G/A (rs9923231), and CYP4F2*3 (rs2108622) respectively, using standard techniques. A total of 8 eligible pharmacogenetic algorithms were selected for performance comparison. The performance of each algorithm was evaluated by calculating the percentage of patients whose predicted dose fell within 20% of their actual therapeutic dose (percentage within 20%), and the mean absolute error (MAE) between each predicted dose and actual stable dose.

Results In the entire cohort, the pharmacogenetic algorithms could predict warfarin dose with the average MAE of 0.87 ±0.17 mg/day (0.73–1.17 mg/day), and the average percentage within 20% of 43.8%±8.1% (29.1–52.1%). By pair wise comparison, warfarin dose prediction was significantly more accurate with the algorithms derived from Asian patients (48.6–50.0%) than those from Caucasian patients (29.1–39.7%; OR 1.61–3.36, p≤0.02). Algorithms with additional covariates of INR values or CYP4F2*3 performed better than those without the covariates (adding INR: OR: 1.71 (1.08–2.72), p=0.029; adding CYP4F2*3: OR: 2.67 (1.41–5.05), p=0.004). When the patients were stratified according to the dose range, the algorithms from Caucasian and racially mixed populations tended to perform better in higher dose group (≥4.5 mg/day), and algorithms from Asian populations performed better in intermediate dose group (1.5–4.5 mg/day). None of the algorithms performed well in lower dose group (≤1.5 mg/day).

Conclusions Our study indicated that none of the eligible pharmacogenetic algorithms could perform the best for all dosing ranges in the present cohort of Chinese patients under warfarin anticoagulation. It may be important to consider the ethnic and clinical specific characteristics when choosing the appropriate algorithm for a local service population. A more refinement pharmacogenetic algorithm combining 3 genotypes (CYP2C9, VKORC1 and CYP4F2) and clinical factors with INR response could potentially improve the warfarin dose prediction in Chinese patients.