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Genotype-guided warfarin dosing

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Background: Observational studies have indicated potential benefits of CYP2C9 and VKORC1 guided dosing of warfarin. However, randomized clinical trials resulted in contradictory findings. One of the reasons for contradiction may be the negligence of possible differences between warfarin indications. The goal of this study was to determine efficacy and safety of genotype- and clinically-guided dosing of warfarin in atrial fibrillation (AF), deep-vein thrombosis (DVT) and pulmonary embolism (PE) within the first five days after the introduction of therapy.

Methods: In this single-center, single-blinded, randomized, controlled trial including patients of both sexes, 18 years of age or older, diagnosed with AF, DVT or PE a total of 205 consecutive patients were allocated into 2 groups: genotype-guided (PHG) warfarin therapy, and 2) warfarin therapy guided by clinical parameters (NPHG). Genotyping of CYP2C9*2*3 and VKORC1 was performed by RealTimePCR method. The primary outcomes were the percentage of time in the therapeutic international normalized ratio (INR 2.0-3.0) range, and the percentage of patients who achieved a stable anticoagulation defined as the INR 2.0-3.0 range in at least two consecutive measurements. Results: In patients with AF percentage of time spent in the therapeutic range of INR was higher in PHG group (mean=26%; SD25.0), than in NPHG group (mean=14%; SD18.6) (delta=12;95%CI 0-23; p=0.040). There was no significant difference in other two evaluated indications for warfarin treatment. Overall, stable dose of warfarin was achieved in statistically higher number of patients in PHG group 14/30 (47%), than in NPHG group 7/32 (22%) (OR=3.13, 95%CI 0.92-10.98;P=0.039). Conclusion: CYP2C9 and VKORC1 genotype guided dosing of warfarin may be beneficial in patients diagnosed with AF. However, we found no evidence to support such conclusion in patients with DVT and PE.