Risk Factors for Out-of-Range International Normalized Ratio in Patients after Total Cavopulmonary Connection Receiving Warfarin

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Introduction: Warfarin generally prevents thrombosis in patients after total cavopulmonary connection (TCPC); however, out-of-range international normalized ratio (INR) is often occurred. This study sought to identify risk factors for out-of-range INR in patients after TCPC receiving warfarin.

Methods: Patients after TCPC who underwent INR monitoring for dose optimization of warfarin were recruited from 2004 to 2013. INR measurements which were performed <1 week after initiation of warfarin, those from patients who used combined medicines having an interaction with warfarin except aspirin and heparin, and those from patients with liver or renal dysfunction were excluded from the study. No patients experienced pharmacogenomics of warfarin. Age, gender, body weight (BW), warfarin dose, warfarin dose/BW and INR were analysed. INR values were divided into 3 groups; optimal (INR 1.5-3.0), under- (INR <1.5) and over-anticoagulation (INR >3.0).

Results: A total of 602 INR measurements from 19 patients fulfilled the criteria. There were neither thrombotic nor haemorrhagic events during the period. Median age, female gender, median BW, median warfarin dose, median warfarin dose/BW and median INR values were 7.5 years (range 1.6-32.8), 58%, 20.5 kg (range 7.8-59), 2 mg (range 0.3-4.75), 0.081 mg/kg (range 0.026-0.219) and 1.63 (range 1.07-4.48), respectively. Out-of-range INR was observed in 38% of measurements; under- and over-anticoagulation was 35% and 3%, respectively. INR values showed significantly negative correlation with age and BW. The over-anticoagulation group comprised significantly lower age and BW and less female patients compared with the optimal anticoagulation group (median, 4.3 vs. 7.7 years, 12.7 vs. 20.4 kg and 50% vs. 74%, respectively). In addition, the former showed significantly more warfarin dose/BW compared with the latter (median, 0.10 vs. 0.08 mg/kg). Receiver operating characteristic curve analysis determined the sensitivity and specificity for predicting over-anticoagulation to be 58% and 90% for age <6.5 years and 62% and 95% for BW <16.5 kg, respectively.

Conclusions: Out-of-range INR often occurred in patients after TCPC receiving warfarin. Lower age and BW were the risk factors for over-anticoagulation.