

**Internationalized normal ratio reflects not only warfarin dose but also liver function in Fontan patients**

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**Background.**

Dosage amount of warfarin (Wf) is adjusted by internationalized normal ratio (INR) of prothrombin time in patients with bi-ventricle. Values of INR reflect not only drop of prothrombin time but also deterioration of other coagulation factors. Fontan patients are easy to suffer liver disturbance, which influences production of coagulation factors. We predicted high INR was influenced by liver disorder as well as warfarin dose in Fontan patients.

**Methods.**

The medical records of 250 Fontan patients were reviewed who were administered Wf. They underwent cardiac catheterization and blood tests between 2010 and 2015. First, we divided 250 patients into two group: 22 patients with INR 2.0 or over (INR2.0-up), and 228 patients without INR2.0-up. We employed clinical data as assay variable, and INR2.0-up as state variable. We examined whether the area under a receiving operating characteristics curve (AUROC) was calculated to determine the best discriminating each assay variable for predicting INR2.0-up. Second, we performed same analysis for INR1.5-up patients.

**Results.**

There were significant differences in cardiac performances and hepatic indexes between Fontan patients with INR2.0-up and without INR2.0-up: end-diastolic ventricular pressure (10.5 vs. 8.0 mmHg), albumin (4.2 vs. 4.5 g/dl), total bilirubin (1.1 vs. 0.9 mg/dl), activated partial thromboplastin time (42 vs. 37 sec), and platelet counts (17.2 vs. 23.5 x10<sup>4</sup>/μl). However, doses of Wf were not different between two groups. We gained significant AUROC for predicting INR2.0-up by platelet counts (0.284, 95% C.I.=0.163-0.405), by albumin (0.339, 95% C.I.=0.219-0.458), and by activated partial thromboplastin time (0.692, 95% C.I.=0.541-0.843). Similarly, we gained significant AUROC for predicting INR1.5-up by doses of Wf (0.598, 95% C.I. 0.525-0.672), by platelet counts (0.411, 95% C.I.0.337-0.485), and by activated partial thromboplastin time (0.714, 95% C.I. 0.620-0.809). Study ages were significantly higher both in INR2.0-up group (17.9 vs. 10.6 yrs) and in INR1.5-up group (14.3 vs. 9.7 yrs).

**Conclusion.**

Dose of Wf was associated with value of INR in Fontan patients with INR1.5-up. In INR2.0-up patients, however, INR value was not related to Wf dose but hepatic disorder or diminished production of coagulation factors. We should carefully interpret high INR values in Fontan patients.