

**Von Willebrand factor reflects Fontan pathophysiology and strongly predicts the all-cause mortality**

*Ohuchi H., Negishi J., Iwasa T., Sakaguchi H., Shiraishi I., Kurosaki K.  
National Cerebral and Cardiovascular Center, Suite, Japan*

**Introduction and Objectives:** Von Willebrand factor (vWF) has prognostic value not only in patients with heart failure but also in those with liver cirrhosis. Liver fibrosis as well as heart failure are major late complications that predict poor prognosis in patients late after Fontan operation. □The purpose of the present study was to clarify clinical significance of measuring plasma levels of vWF antigen (vWF:Ag), including the prognostic value in Fontan patients.

**Methods:** We measured vWF:Ag (%) in consecutive 278 Fontan patients and compared the results with the clinical profiles, including hemodynamics and prognosis.

□**Results:** Plasma vWF:Ag was  $144 \pm 48$  (normal range: 55-190%) and 37 patients (13%) showed high levels of vWF:Ag ( $\geq 190$ ). Male gender, late Fontan operation, greater New York Heart Association (NYHA) class, elevated plasma neurohormons (norepinephrine, brain natriuretic peptide: BNP, renin activity, and aldosterone: PAC), protein losing enteropathy, elevated central venous pressure, low systemic pressure, hypoxia, use of diuretics and anti-arrhythmias and low liver synthetic function (low plasma levels of low albumin and cholinesterase) were associated with high vWF:Ag ( $p < 0.05-0.0001$ ). Of these, low albumin, greater NYHA class and high PAC were independently associated with a high vWF:Ag ( $p < 0.05-0.01$ ). During the follow-up, 51 clinical events, including 9 deaths, occurred. High vWF:Ag predicted the clinical events ( $p < 0.01$ ), especially the all-cause mortality (hazard ratio: 1.3 per 10,  $p < 0.0001$ ), with being independent of significant prognostic value of BNP ( $p < 0.0001$ ). Patients with high vWF:Ag ( $\geq 218$ ) and BNP ( $\geq 65$  pg/ml) had a marked high hazard of 166 for all-cause mortality ( $p < 0.0001$ ). □**Conclusions:** Low albumin and high PAC were associated with a high vWF:Ag which strongly predicted all-cause mortality independent of hemodynamics, including BNP, in Fontan patients. Thus, vWF is a novel clinically useful biomarker of Fontan pathophysiology.