

### Prevalence of Fontan associated liver disease using standard investigations

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**Introduction:** Liver fibrosis is increasingly recognized as a potentially serious morbidity associated with Fontan circulation (Fontan associated liver disease, FALD). The purpose of this cross-sectional study was to assess the prevalence of liver abnormalities using standard investigations.

**Methods:** Fontan patients were screened for liver abnormalities by abdominal ultrasound and routine laboratory tests. Patients were divided into three groups based on follow-up since Fontan surgery (<5 years, 5 to 10 years, >10 years). The relation to hemodynamic data from cardiac catheterization and echocardiography was analyzed.

**Results:** 249 Fontan patients who had routine follow-up between January 2014 and November 2017 were included. Median age was 11 (7-16) years, the median follow-up since Fontan surgery 8 (4-13) years. Hepatic ultrasound was performed in 171 (68.7%) patients; laboratory assessment was completed in 247 (99.2%) cases; 211 (84.7%) patients underwent cardiac catheterization, echocardiography studies were available in all cases. Sonographic signs of fibrotic changes included heterogeneous parenchyma, surface nodularity or hyper-echoic lesions in 80 (46.8%) patients. The prevalence of fibrotic changes increased with longer follow-up since Fontan completion (<5 years: 25.6%; 5-10 years: 45.5%; >10 years: 58.4%;  $p=0.004$ ). Elevated gamma-glutamyl-transpeptidase (gGT) levels were observed in 165 (66.8%) patients. Glutamic-oxaloacetic-transaminase (GOT) levels above normal range and thrombocytopenia were more frequently observed in cases with more than 10 years follow-up since Fontan surgery (26/92 vs. 15/150,  $p<0.001$  and 26/94 vs. 5/151,  $p<0.001$ ). Hypoproteinemia and reduced prothrombin activity were found in 5.1% and 27.8%, respectively. The frequency was not different between age groups. Among laboratory parameters, only gGT levels were higher in cases with suspected fibrotic changes ( $70 \pm 48$  U/l vs.  $50 \pm 32$  U/l,  $p=0.003$ ). The number of patients with impaired ventricular function or more than mild atrioventricular valve regurgitation was not different between cases with or without suspected fibrosis. Systemic venous pressures were not different ( $11 \pm 3$  vs.  $11 \pm 2$  mmHg,  $p=0.765$ ).

**Conclusions:** The prevalence of ultrasound and laboratory abnormalities suggestive of FALD increases with time since Fontan surgery. However, ultrasound abnormalities were not necessarily reflected by laboratory abnormalities and vice versa. Further studies are needed to guide surveillance and therapeutic strategies in the management of FALD.