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Hepatic changes in the Fontan circulation: which modalities are useful for follow-up screening?

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Objective
Fontan completion induces liver congestion, a precursor for liver fibrosis, cirrhosis and ultimately hepatocellular carcinoma. Timely detection of liver dysfunction is essential to identify patients at risk. We sought to determine which serum markers and liver imaging modalities could be most useful for follow-up screening.
Methods
In a prospective set-up, 28 Fontan patients, aged 24,2 ± 5,1 years, underwent echocardiography, blood analysis and liver imaging. Median interval since Fontan completion was 19,5 years (IQR 14,6-21,1 y). Serum analysis included trombocyte count (TRC), albumin, liver enzymes, α-foetoprotein, α1-antitrypsin, and proBNP. Fibrosis indices APRI, FIB-4 and Forns-index, validated for liver fibrosis in hepatitis C, were calculated. Liver morphology and Dopplers of hepatic vein, portal vein, hepatic artery and superior mesenteric artery (SMA) were performed, and resistance indices (RI) calculated. Liver stiffness (LS) was measured with elastography. Correlations between the serum markers and imaging results, and relation to time indices (age, Fontan interval) were established.
Results
Lab analysis showed abnormal values for YGT, bilirubin, ALT, and TRC (in 74%, 33%, 33% and 29% of patients). APRI and FIB-4 were unindicative for liver fibrosis. Forns-index indicated moderate fibrosis in 24% of patients, only Forns index correlated significantly with Fontan interval (p=0,05). Ultrasound liver morphology was normal in 61% of patients, in 22% and 17% lobulated contour and nodular hyperplasia was found. Doppler velocities and indices fell within the normal range. Lower AMS RI showed tendency to correlate with longer interval (p=0,09). LS (mean 10,4 ± 3,7 kPa) was abnormally increased in 96% of patients, higher LS was significantly related to longer interval (p=0,02), lower AMS RI (p=0,02), larger spleen (p=0,02), and lower albumin (p=0,01).
Conclusion
Adult Fontan patients show moderate signs of liver dysfunction. The usefulness of post-Fontan screening with classical fibrosis indices remains unclear. The morphologic changes we found sustain the use of ultrasound liver and spleen imaging in regular follow-up of Fontan patients, while liver Doppler indices seem to result largely normal. Liver stiffness, partially due to liver congestion, seems to overestimate the grade of fibrosis, but increases with time and higher mesenteric vascular resistance, and needs validation through sequential measurements.