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Magnetic Resonance Elastography: A Novel Technique for the Detection of Hepatic Fibrosis and Hepatocellular Carcinoma After the Fontan Operation

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Abstract

Objective: To evaluate the utility of magnetic resonance elastography (MRE) in screening patients for hepatic fibrosis, cirrhosis, and hepatocellular carcinoma after the Fontan operation.

Patients and Methods: Hepatic MRE was performed in conjunction with cardiac magnetic resonance imaging in patients who had undergone a Fontan operation between 2010 and 2014. Liver stiffness was calculated using previously reported techniques. Comparisons to available clinical, laboratory, imaging, and histopathologic data were made.

Results: Overall, 50 patients at a median age of 25 years (range, 21-33 years) who had undergone a Fontan operation were evaluated. The median interval between Fontan operation and MRE was 22 years (range, 16-26 years). The mean liver stiffness values were increased: 5.5±1.4 kPa relative to normal participants. Liver stiffness directly correlated with liver biopsy-derived total fibrosis score, time since operation, mean Fontan pressure, γ-glutamyltransferase level, Model for End-Stage Liver Disease score, creatinine level, and pulmonary vascular resistance index. Liver stiffness was inversely correlated with cardiac index. All 3 participants with hepatic nodules exhibiting decreased contrast uptake on delayed postcontrast imaging and increased nodule stiffness had biopsy-proven hepatocellular carcinoma.

Conclusion: The association between hepatic stiffness and fibrosis scores, Model for End-Stage Liver Disease scores, and γ-glutamyltransferase level suggests that MRE may be useful in detecting (and possibly quantifying) hepatic cirrhosis in patients after the Fontan operation. The correlation between stiffness and post-Fontan time interval, mean Fontan pressure, pulmonary vascular resistance index, and reduced cardiac index suggests a role for long-term hepatic congestion in creating these hepatic abnormalities. Magnetic resonance elastography was useful in detecting abnormal nodules ultimately diagnosed as hepatocellular carcinoma. The relationship between stiffness with advanced fibrosis and hepatocellular carcinoma provides a strong argument for additional study and broader application of MRE in these patients.

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Functionally single ventricle anatomy represents approximately 8% of all patients with congenital heart disease, with a birth incidence of 4 to 8 per 10,000.[1] The Fontan operation was originally described in 1968 by the French cardiac surgeon Francis Fontan for patients afflicted with this lesion.[1] Nearly all patients with functionally single ventricles are expected to undergo the Fontan operation.[2] This operation represents 4.2% of all congenital heart operations performed in the United States.[2] This palliative operation consists of various surgeries to entirely reroute systemic bicavalvenous return directly into the pulmonary arterial confluence, effectively bypassing the subpulmonary ventricle (Figure 1).[3,4] The resultant

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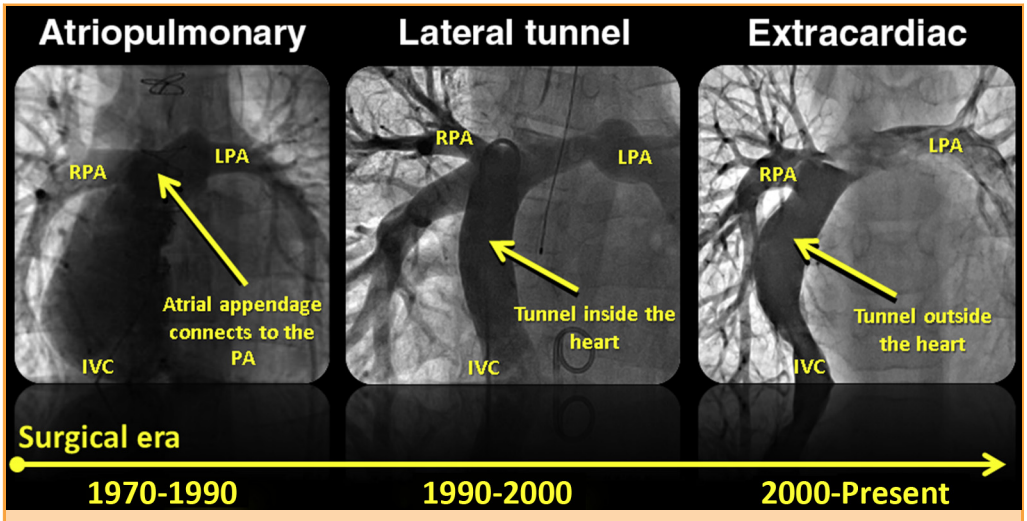

FIGURE 1. Fontan surgical subtypes. The Fontan operation consists of rerouting systemic bicaval venous return directly into the pulmonary arterial confluence, effectively bypassing the subpulmonary ventricle. These angiograms demonstrate the Fontan subtypes in order of the surgical era: atriopulmonary, in which the right atrial appendage is directly sewn to the pulmonary arterial confluence, the superior vena cava is left in continuity with the atrium, and the atrium acts as a functional conduit (left); lateral tunnel, in which the conduit lies within the right atrium, connecting the inferior vena cava (IVC) to the pulmonary artery (PA) and the superior vena cava is sewn directly to the right PA (middle); and the extracardiac type of Fontan connection, in which a conduit lying outside the heart connects the IVC to the inferior portion of the pulmonary arterial confluence and the superior vena cava is sewn directly to the right PA (right).

nonpulsatile passive venous filling of the pulmonary arterial bed results in markedly increased central venous pressure. This elevated central venous pressure can increase the afterload experienced by the liver and, in combination with the inherent low cardiac output state of patients after Fontan operation, lead to congestive hepatopathy (Figure 2).[3,4]

Hepatic dysfunction after the Fontan operation frequently has an indolent subclinical course. Liver fibrosis often precedes laboratory or ultrasonographic imaging abnormalities, and many patients may remain free of clinical signs of cirrhosis until late stages of hepatic dysfunction. Most concerning is the report that some patients have developed hepatocellular carcinoma.[3,4] There is no criterion standard for the diagnosis of cirrhosis after the Fontan operation. Liver biopsy is the criterion standard for the diagnosis of hepatic fibrosis and cirrhosis in routine adult hepatology practices.[5,6] However, liver biopsy is limited by intra- and interobservational variability in interpretation, sampling error due to the nonhomogeneous pattern of hepatic fibrosis, high cost, and need for anesthesia or sedation.[7-10] Consequently,

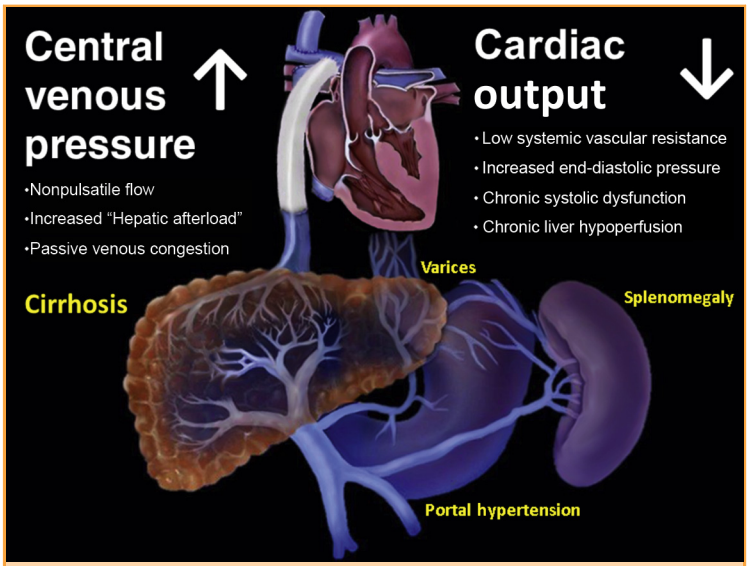

FIGURE 2. Fontan operation and pathophysiology of cirrhosis. In patients after the Fontan operation, systemic venous return is directly connected to the pulmonary arteries with nonpulsatile passive venous filling of the pulmonary arterial bed, resulting in markedly increased central venous pressure. Over time, elevated central venous pressure can increase the afterload experienced by the liver and, in combination with the inherent low cardiac output state and chronic systolic and diastolic dysfunction of patients after the Fontan operation, lead to congestive hepatopathy.