Magnetic Resonance Imaging Identifies Unsuspected Liver Abnormalities in Patients after the Fontan Procedure

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Objective To determine whether abdominal magnetic resonance imaging (MRI) detects hepatic abnormalities before clinical or biochemical perturbations in patients after the Fontan procedure.

Study design Thirty-nine children and adolescents who underwent the Fontan procedure and were referred to a pediatric hepatologist by cardiology services between 2011 and 2012 were reviewed retrospectively. Physical examination findings, routine laboratory tests of liver function, evaluation for chronic liver disease, and abdominal MRI findings were recorded. MRI findings were evaluated relative to time elapsed since surgery by 2 radiologists (blinded).

Results Assessment for coexisting chronic liver disease was negative in all patients. All patients had a normal serum albumin level and International Normalized Ratio. Twenty-six of the 39 patients (67%) underwent abdominal MRI, 4 had MRI-incompatible hardware, and 9 did not undergo MRI because of insurance denial. All MRI scans demonstrated morphologic liver changes with varying degrees of reticular contrast enhancement compatible with fibrosis and congestion. Reticular contrast enhancement was often nonuniform, and 9 patients (35%) had multifocal arterially enhancing lesions.

Conclusion MRI can identify hepatic abnormalities in patients after Fontan surgery that go undetected by standard clinical and laboratory assessments. These abnormalities are not uniformly distributed throughout the liver, and thus assessment by liver biopsy analysis is subject to sampling error. *(J Pediatr 2013;163:201-6)*.

The Fontan procedure, used to treat complex congenital cardiac defects, was first described in 1971 to treat tricuspid atresia.[1] Since then, the indications for this surgery have broadened considerably to include various forms of single-ventricle physiology. The Fontan procedure is now the most common surgery performed for congenital heart disease after age 2 years.[2] With advances in surgical techniques and medical therapies, long-term survival in patients undergoing the Fontan procedure has improved dramatically, with a current 20-year survival rate of 70%-85%.[3]

With prolonged survival, extracardiac complications arising from long-standing supraphysiological right-sided heart pressure and/or flow-related abnormalities are frequently encountered and contribute significantly to morbidity and mortality in these patients. Clinical issues include the development of protein-losing enteropathy, embolic cerebrovascular accidents, and liver disease.[4] Patients who have undergone the Fontan procedure are at increased risk for developing hepatic dysfunction, eventually leading to cirrhosis and its related complications.[5-8] The time frame for the evolution of these hepatic changes is unclear, with the degree of liver dysfunction often underestimated by serum biochemical testing.

Recently, with increased awareness of late complications of the Fontan procedure, many pediatric cardiologists at our center are routinely referring patients for evaluation by a pediatric hepatologist, even in the absence of signs of failing Fontan physiology or overt liver dysfunction. Because of this referral pattern, many Fontan recipients undergo clinically standardized physical examination and laboratory evaluation. Given our center's experience with magnetic resonance imaging (MRI) assessment of liver disease in children in other clinical settings, we postulated that abdominal MRI studies might detect hepatic abnormalities before clinical or biochemical perturbations in patients who have undergone the Fontan procedure. Thus, we used this technique as our preferred clinical imaging modality in the initial evaluation of patients after Fontan surgery.

Methods

This study was approved by the Institutional Review Board at Children's Health Care of Atlanta. The study population comprised all patients who had previously undergone the Fontan procedure and were referred by their primary pediatric cardiologist for evaluation by a pediatric hepatologist at Children's Healthcare

MRI	Magnetic resonance imaging
AST	Aspartate aminotransferase

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of Atlanta between January 2010 and December 2011. At the time of referral, no patients had clinical evidence of a failing Fontan circuit.

Study patients were evaluated by 1 of 3 pediatric hepatologists using a clinical protocol that included history and physical examination, routine biochemical testing, and serologic evaluation for coexistent chronic liver disease. Data extracted from the patient charts included age at the time of the Fontan procedure, age at the time of evaluation by a hepatologist, and time elapsed between the Fontan procedure and hepatology evaluation. Physical examination findings reviewed included documented hepatomegaly, splenomegaly, and/or ascites. Hepatomegaly was defined as a liver span exceeding acceptable age-appropriate norms as determined by the examining pediatric hepatologist. Splenomegaly was defined as the presence of a palpable spleen below the costal margin. Detection of ascites on physical examination was noted. Routine laboratory evaluation data at the hepatology visit that were abstracted included results of a comprehensive metabolic panel, γ-glutamyl transpeptidase, partial thromboplastin time, prothrombin time, international normalized ratio, complete blood count, hepatitis B surface antigen, hepatitis B surface antibody, hepatitis C antibody, ceruloplasmin, α-1 antitrypsin, and α-1 antitrypsin phenotype.

In clinical practice at our center, MRI of the abdomen is frequently performed to evaluate liver disease when possible. In patients in whom MRI was contraindicated owing to incompatible electronic or metallic implants or was otherwise unable to be performed, a duplex abdominal ultrasound was obtained to evaluate for hepatic parenchymal and blood flow abnormalities. This subset of patients is not otherwise included in the analysis of this report. All but 1 patient undergoing MRI were scanned on a 3.0 Tesla system (Magnetom, TrioTrim; Siemens Healthcare, Ehrlangen, Germany) that patient was scanned on a 1.5 Tesla machine (Twinspeed; GE Healthcare, Milwaukee, Wisconsin) with an equivalent protocol, owing to the presence of orthodontic appliances. A standardized departmental protocol with and without intravenous gadolinium 0.1 mL/kg was used. Scan times were <30 minutes for both breath-holding and free-breathing examinations. All patients completed standard screening questions to evaluate the need for sedation based on their perceived ability to remain still for the duration of the examination. Sedation was used for MRI only when a patient could not hold still.

MRI scans were interpreted independently by 1 of 2 pediatric radiologists at our center, who were aware only of each patient's status after the Fontan procedure but were blinded to other clinical information. The independent reading was subsequently reviewed by both study radiologists to reach a consensus interpretation for the study while still blinded to all clinical data. Statistical analysis of interreader reliability was not performed.

MRI scans were evaluated for the presence of fibrosis, congestion, and any other hepatic abnormalities, including focal lesions, hepatomegaly, ascites, and evidence of portal hypertension (Figure 1). Fibrosis was determined based on

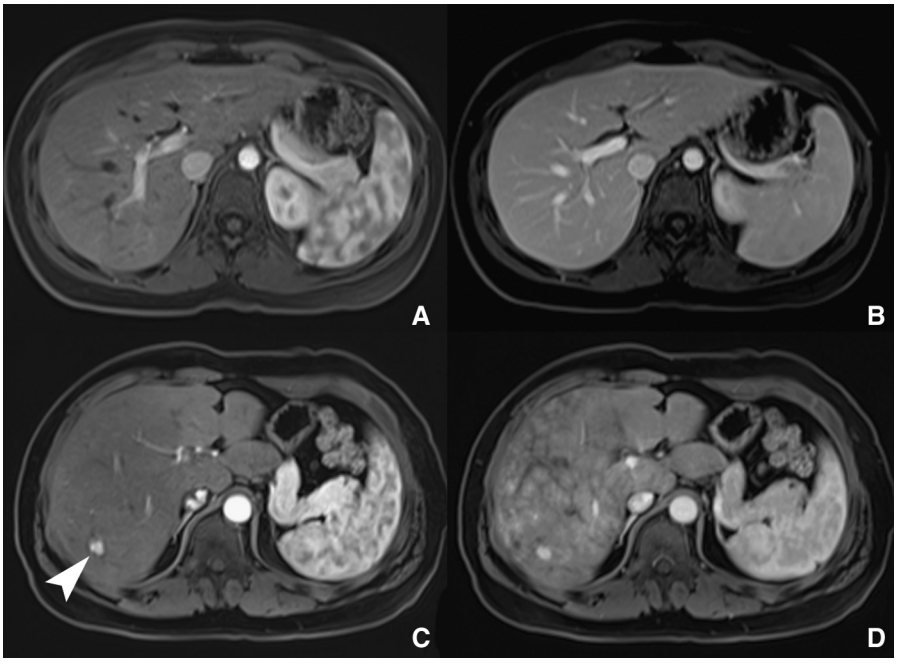

Figure 1. **A,** Axial T1-weighted gradient echo sequence arterial phase postcontrast showing normal hepatic parenchyma with homogeneous enhancement. Note the characteristic zebra pattern within the spleen. **B,** Venous phase, also showing homogeneous enhancement in normal liver. **C,** Arterial phase enhancement in a patient after Fontan surgery with a single arterially enhancing lesion in segment 6. **D,** Venous phase in the same patient showing the characteristic cloud-like enhancement of venous congestion.