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Review article

Fontan-associated Liver Disease

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ABSTRACT

Fontan-associated liver disease refers to the disturbance in the liver secondary to hemodynamic changes and systemic venous congestion following Fontan surgery. Although the natural history of this disease has not yet been established, patients with more advanced liver injury develop the complications of portal hypertension, such as ascites, variceal haemorrhage, or encephalopathy. Moreover, patients with Fontan surgery may have an increased risk of hepatocellular carcinoma. Periodic liver monitoring is essential to prevent this disease and provide early treatment of liver complications.

Enfermedad hepática crónica asociada con cirugía de Fontan

Palabras clave:
Cirugía de Fontan
Enfermedad hepática
Hepatocarcinoma
Fracaso del Fontan

RESUMEN

La enfermedad hepática relacionada con la cirugía de Fontan hace referencia a los cambios hepáticos secundarios a las alteraciones hemodinámicas y la congestión venosa sistémica que se producen tras ese procedimiento. Aunque su historia natural aún no está establecida, los pacientes con daño hepático más avanzado pueden presentar complicaciones de la hipertensión portal, como la ascitis, la hemorragia por rotura de varices o encefalopatía. En los últimos años se ha demostrado que el riesgo de hepatocarcinoma está incrementado. El seguimiento hepático periódico es fundamental para prevenir y tratar precozmente las complicaciones hepáticas.

Abbreviations

FALD: Fontan-associated liver disease
FS: Fontan surgery
HVPG: hepatic vein pressure gradient
MELD: Model for End-stage Liver Disease
TIPS: transjugular intrahepatic porto-systemic shunt

INTRODUCTION

Fontan-associated liver disease (FALD) refers to a wide range of structural and functional alterations of the liver caused by hemodynamic changes associated with the Fontan circulation (FC). As in all chronic liver diseases, the individual passes through various stages before reaching the final phase, which is when most of the complications appear, such as hepatocellular carcinoma, variceal bleeding, ascites, and hepatic encephalopathy. Although hepatic impairment eventually develops in all patients with FC, its adequate characterization is essential to allow us to determine the degree of liver damage and thereby establish screening and follow-up programs to prevent and/or treat at an early stage any liver complications that may arise. This review summarizes the current evidence on the pathophysiology of FALD, as well as the methods available for its diagnosis and management. Finally, we propose a follow-up strategy tailored to the peculiarities of these patients.

FONTAN SURGERY: DEFINITION, TYPES, AND CONSEQUENCES

The FC is used to treat several complex congenital heart diseases with a common characteristic: the presence of a functional single ventricle. The surgical objective is to ensure that the systemic venous return is directed into the pulmonary artery, bypassing the right ventricle. Simply put, the Fontan technique surgically creates an anastomosis between the systemic venous return from both vena cavae and the pulmonary artery that passively carries the blood to the single ventricular chamber. Therefore, the FC is a curative surgery whose main objective is to mitigate the hypoxemia and prolong survival.[1]

There are 2 main variations of the technique: the atriopulmonary (classic) procedure and the total cavopulmonary

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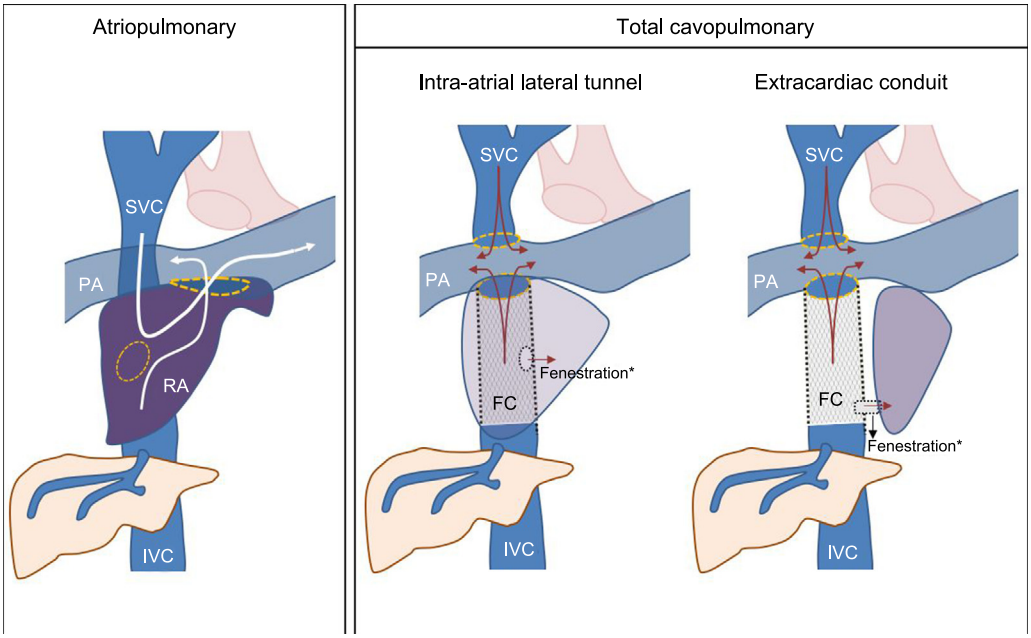

Figure 1. Variants of the Fontan procedure. FC, Fontan circuit; IVC, inferior vena cava; PA, pulmonary artery; RA, right atrium; SVC, superior vena cava. * The creation of a fenestration joining the Fontan circuit and the right atrium is a variant used in only some patients.

(Figure 1). The classic FC involves transformation of the atrium into a channel connecting both vena cavae to the pulmonary artery. For this, an anastomosis is created between the atrium and the pulmonary artery, and the tricuspid valve and atrial septal defect are closed. Although it was initially thought that maintenance of the participation of the atrium in the circuit would facilitate the propulsion of the blood to the lungs, this approach was later found to increase the risk of atrial tachyarrhythmias and thromboses.[2,3] The total cavopulmonary variant, the technique of choice in recent years, is carried out in 2 stages: in the first, the venous return of the superior vena cava is connected to the pulmonary arterial circulation (Glenn procedure), with completion of the procedure at the same time or later with an anastomosis from the inferior vena cava to the pulmonary artery using an artificial conduit (Fontan conduit).

Although the technique was first described in 1968, its use was quite limited until the 1980s.[4] Accordingly, its long-term results are unknown. Nonetheless, the FC represents one of the greatest advances in pediatric cardiology, ensuring survival rates of about 80% at 20 years, which must be considered a huge success given the severity of the cardiac anatomic defects addressed.[5,6] However, the long-term hemodynamic changes caused by the surgery are now associated with a considerable number of complications that can affect virtually all organs.[7,8]

The concept of "Fontan failure" refers to the syndromic set of systemic conditions that develop in the long term in most patients who undergo the procedure. Whatever the cause, the result is always the same: increased systemic venous pressure. Fontan failure can be precipitated by different events, such as heart arrhythmia, stenosis, or obstruction of the Fontan conduit, or, in its

Table 1
Systemic Implications of "Failure" of the Fontan Circulation

Organ/system	Complication	Mechanism	Clinical manifestation
Lungs	Atrial/venovenous shunts	Passive gradient-dependent circulation	Cyanosis, dyspnea, hypoxia, exercise intolerance
	Plastic bronchitis	↓ lymphatic return	
	Chylothorax	↓ lymphatic return	
	Thromboembolism	Hypercoagulability	
	Pulmonary hypertension	Vascular hyperreactivity	
Kidneys	Proteinuria	Hyperfiltration via venous hyperpressure	Edema, ascites
	Renal failure (acute/chronic)	Ischemia due to ↓ CO	Dyspnea, oliguria
Intestine	Protein-losing enteropathy	↓ lymphatic return Splanchnic venous congestion Systemic inflammation Hormonal activation	Malnutrition, edema, ascites, diarrhea
Liver	Chronic liver disease	Hepatic congestion Ischemia due to ↓ CO	Ascites, varices, encephalopathy, hepatocellular carcinoma
Brain	Cerebrovascular disease	Cardioembolic ischemia due to ↓ CO	Diminished executive functions
Heart	Bradyarrhythmias and tachyarrhythmias	Atrial and ventricular remodeling	Hemodynamic instability
	Ventricular dysfunction	Activation of neurohormonal systems	Dyspnea, exercise intolerance
Vascular system	Varices	Venous hyperpressure ↓ venous return	Edema, varicose veins in the extremities

CO, cardiac output.

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