Diastolic Dysfunction in Liver Cirrhosis: Prognostic Predictor in Liver Transplantation?

F. Carvalheiro[a,*], C. Rodrigues[b], T. Adrego[c], J. Viana[b], H. Vieira[b,d], C. Seco[b,d], L. Pereira[b,d], F. Pinto[b,d], A. Eufrásio[b,d], C. Bento[b,d], and E. Furtado[d]

[a]Department of Anesthesia, Centro Hospitalar do Algarve, Portimão, Portugal; [b]Department of Anesthesia, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal; [c]Public Health Unit of Baixo Mondego, Coimbra, Portugal; and [d]Adult and Pediatric Liver Transplant Unit, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal

ABSTRACT

Background. Patients with liver cirrhosis may develop cirrhotic cardiomyopathy (CC), characterized by blunted contractile responsiveness to stress, diastolic dysfunction (DD), and electrophysiological abnormalities. It may adversely affect the long-term prognosis of these patients.

Methods. We conducted a retrospective analysis of patients undergoing liver transplantation (LT) for cirrhosis from January 2012 to June 2015. We analyzed demographic characteristics, the etiology of cirrhosis, Child-Pugh and Model for End-Stage Liver Disease (MELD) scores, the corrected QT (QTc) interval in the preoperative period, diastolic and systolic dysfunction, mortality and survival, and duration of mechanical ventilation and vasopressor support in the post-LT period. These variables were compared with diastolic dysfunction and prolongation of QTc, with the use of chi-square, Fisher, and Mann-Whitney *U* tests.

Results. The study included 106 patients, 80.2% male and overall average age 54.83 years. The median MELD score was 16, and Child-Pugh class C in 55.4%. Prolonged QTc interval before LT was present in 19% and DD in 35.8% of patients. QTc before LT or DD did not vary significantly with MELD or Child-Pugh score.

Conclusions. The patients in the pre-LT period presented with a significant incidence of DD, which can predispose them to adverse cardiac events. The presence of DD correlates with mortality after LT in patients with hepatic cirrhosis.

PATIENTS with liver cirrhosis may develop cirrhotic cardiomyopathy (CC), characterized by a blunted contractile responsiveness to stress and/or altered diastolic relaxation with electrophysiologic abnormalities in the absence of known cardiac disease [1].

The hyperdynamic circulation in cirrhosis was described 60 years ago [2] and is characterized by decreased peripheral resistance, increased cardiac output and stroke volume, and low systolic arterial blood pressure. Cardiac dysfunction in cirrhotic patients was first described in patients with alcoholic cirrhosis and was attributed to the direct effect of alcohol. Indeed, alcohol was not correlated with the etiology of cirrhosis [3].

The disease usually remains silent with near normal cardiac function unless the patients are exposed to stress. Systolic function may be maintained at rest, but physical or pharmacologic stress usually unmasks underlying systolic dysfunction in these patients [4].

Left ventricular diastolic dysfunction (DD) seems to be the first manifestation of CC, because it usually appears before the features of systolic dysfunction [5]. The prevalence of DD in cirrhotic patients is ~40% and is not related to the etiology and stage of liver disease, although its severity correlates with the degree of liver failure [5]. Other

*Address correspondence to Filipa Carvalheiro, Department of Anaesthesia, Centro Hospitalar do Algarve, Sítio do Poço Seco, 8500-338 Portimão, Portugal. E-mail: anafcarvalheiro@gmail.com

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studies show that although DD is a frequent event in cirrhosis, it is usually of mild degree and does not correlate with severity of liver disease [6]. DD seems to be a negative prognostic factor for patients undergoing transjugular intrahepatic portosystemic shunt (TIPS) insertion and patients undergoing liver transplantation (LT) [5]. Cardiac failure has emerged as an important cause of mortality after LT and accounts for 7%–21% of deaths in the post–orthotopic LT period [6].

Electrophysiologic abnormalities observed in cirrhosis include prolonged QTc interval, electromechanical dyssynchrony, and chronotropic incompetence [7]. Prolongation of QTc represents the main electrocardiographic (ECG) characteristic of CC. It is detected in 40%–50% of cirrhotic patients and is not related to the etiology of liver disease [5]. It is considered to be one of the earliest signs of CC [1]. It is associated with the severity of the disease. LT has been shown to reverse this anomaly in the majority of patients after 3 months of follow-up [8].

The purpose of the present study was to analyze the incidence of left ventricular DD in patients with cirrhosis and the impact on outcome during the peritransplantation period.

METHODS

We conducted a retrospective analysis of all adult patients undergoing LT for cirrhosis from January 2012 to June 2015 in the Centro Hospitalar e Universitário de Coimbra, Portugal. We excluded pediatric patients, liver retransplantation, and severe heart disease not correlated with cirrhosis (pacemaker or severe valve disorders in pretransplantation echocardiogram).

Analysis included demographic characteristics (age, sex), etiology of cirrhosis, Child-Pugh and Model for End-Stage Liver Disease (MELD) scores, corrected QT (QTc) interval in preoperative ECG, existence of DD and respective type, existence of systolic dysfunction and ejection fraction (EF) in pretransplantation echocardiography, mortality, duration of mechanical ventilation in the postoperative period, number and duration of vasopressor support used in the postoperative period.

We considered long QTc to be present when the value of the QTc interval was >440 ms. The QTc interval was calculated by means of the Fridericia formula. The echocardiographic criteria used for definition of DD were E/A ratio (corrected for age), prolonged deceleration time (>200 ms), prolonged isovolumetric relaxation time (>80 ms), tissue Doppler measurements sampled at the level of the mitral annulus over the septal and lateral wall (annular E′ and E/E′ lateral ratio), and enlarged left atria.

Statistical analysis was performed with the use of SPSS Statistics 20 with percentages for qualitative variables, and mean ± SD or median for quantitative variables, depending on normality. To assess if the variables had a normal distribution, we used the Kolmogorov-Smirnov test. Statistical significance was determined with the chi-square test or Fisher for categoric independent variables; for numeric independent variables (2 groups) we used the Student t test when they had a normal distribution and the Mann-Whitney U test for samples without normal distribution. For numeric independent variables (>2 groups) we used one-way analysis of variance test for samples with normal distribution and the Kruskal-Wallis test for samples without normal distribution. Statistical significance was assumed with $P < .05$.

RESULTS

The study included 106 patients undergoing LT for liver cirrhosis from January 2012 to June 2015; 80.2% (85 patients) were male. The overall average age was 54.83 years (SD 8.52 y), with a minimum age of 30 years and the maximum age of 69 years.

In patients transplanted, the commonest etiology was alcoholic cirrhosis (64.8%), followed by nonalcoholic causes (Table 1). At the time of transplantation, 43.4% of patients had hepatocellular carcinoma.

The median MELD score in our group of patients was 16, with a minimum of 6 and maximum of 45.

Child-Pugh class A was found in 21.6% of patients, class B in 23.0%, and class C in 55.4%.

The presence of a prolonged QTc interval in pretransplantation ECG was found in 19% of patients (20 patients).

In the pretransplantation echocardiography the existence of systolic dysfunction was found in 1.1% of the patients. Median EF was 64%, with a minimum of 50% and maximum of 87%.

DD was present in 35.8% of patients (38 patients), type 1 dysfunction was present in 71.1% of the cases, 26.3% of the cases had type 2 DD, and 2.6% of patients had type 3.

Median mechanical ventilation was 10.0 hours after transplantation, with a minimum of 0 and a maximum of 199 hours.

In 6% of patients there was no use of postoperative vasopressor support, 74% of patients required 2 amines, 5% required 3 amines, and 15% only had 1 amine used in the postoperative period. The median of usage was 2 amines (minimum 0, maximum 3).

Vasopressor support was necessary for a median of 31 hours, with a minimum of 0 and a maximum of 197 hours.

Seventeen patients died during the study period (16%). The hospital mortality rate, at 90 days after transplantation, was 4.72%. The 1-year survival was 86%, the 2-year survival was 81.3%, and the 3-year survival was 78.2%.

The presence of pretransplantation DD did not differ significantly with sex, etiology of cirrhosis, MELD Child-Pugh or score, ventilation time, vasopressor support, or mortality (Table 2). The age and the existence of DD varied

Table 1. Etiology of Nonalcoholic Cirrhosis

Cause	Incidence (%)
Primary biliary cirrhosis	30.0
Hepatitis B	23.33
Hepatitis C	16.67
Autoimmune hepatitis	13.33
Primary sclerosing cholangitis	10.0
Cryptogenic cirrhosis	3.33
Secondary biliary cirrhosis	3.33