Digestive and Liver Disease 47 (2015) 1052–1058

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

Liver, Pancreas and Biliary Tract

Circulatory response to volume expansion and transjugular intrahepatic portosystemic shunt in refractory ascites: Relationship with diastolic dysfunction

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ARTICLE INFO

Article history:
Received 10 March 2015
Accepted 27 August 2015
Available online 3 September 2015

Keywords:
Cirrhosis
Echocardiography
Heart failure
Right heart catheterization
Transjugular portosystemic shunt

ABSTRACT

Background: Cirrhotic cardiomyopathy may lead to heart failure in stressful circumstances, such as after transjugular intrahepatic portosystemic shunt (TIPS) placement.
Aim: To examine whether acute volume expansion predicts haemodynamic changes after TIPS and elicits signs of impending heart failure.
Methods: We prospectively evaluated refractory ascites patients (group A) and compensated cirrhotics (group B), who underwent echocardiography, NT-proBNP measurement, and heart catheterization before and after volume load; group A repeated measurements after TIPS.
Results: 15 patients in group A (80% male; 54 ± 12.4 years) and 8 in group B (100% male; 56 ± 6.2 years) were enrolled. Echocardiography disclosed diastolic dysfunction in 30% and 12.5%, respectively. In group A, volume load and TIPS induced a significant increase in right atrial, mean pulmonary, capillary wedge pressure and cardiac index, and a decrease in systemic vascular resistance (respectively, 4.7 ± 2.8 vs. 9.9 ± 3.6 mmHg; 13.3 ± 3.5 vs. 21.9 ± 5.9 mmHg; 8.3 ± 3.4 vs. 15.4 ± 4.7 mmHg; 3.7 ± 0.7 vs. 4.6 ± 1 lt/min/m^2; 961 ± 278 vs. 767 ± 285 dyn s cm^{-5}; and 10.1 ± 3.3 vs. 14.2 ± 3.4 mmHg; 17.5 ± 4 vs. 25.2 ± 4.2 mmHg; 12.3 ± 4 vs. 19.3 ± 3.4 mmHg; 3.4 ± 0.8 vs. 4.5 ± 0.91 lt/min/m^2; 779 ± 62 vs. 596 ± 199 dyn s cm^{-5}, $p < 0.001$ for all pairs). At 24 h, cardiopulmonary pressures returned towards baseline.
Conclusions: Acute volume expansion predicted haemodynamic changes immediately after TIPS. All patients had adequate haemodynamic adaptation to TIPS; none developed signs of heart failure.

1. Introduction

A series of structural and functional cardiac abnormalities, such as left ventricular hypertrophy and cardiomyocyte oedema have been described in patients with cirrhosis with no valvular or ischaemic heart disease [1]. Altered haemodynamic response

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http://dx.doi.org/10.1016/j.dld.2015.08.014
1590-8658/

to physical and pharmacologic stress was later highlighted in alcoholic cirrhosis, despite the fact that a high cardiac output is usually present when the patient is at rest [2,3]. This was initially interpreted as a consequence of direct toxicity of alcohol on the myocardium. However, similar findings were found later in patients with non-alcoholic cirrhosis, suggesting that the cardiac abnormalities were related to cirrhosis rather than to its aetiology [4]. In 1989, the term "cirrhotic cardiomyopathy" [5] was introduced to denote the cardiac dysfunction of patients with cirrhosis, which comprise an impaired chronotropic and inotropic response to stress, altered indexes of ventricular diastolic relaxation on echocardiography (diastolic dysfunction), and electrocardiographic abnormalities (tachycardia and prolonged QT segment), in the absence of a history of cardiac disease [6–12].

The clinical relevance of cirrhotic cardiomyopathy has been hypothesized by some investigators on the basis of the observation, in a small longitudinal study, that development of hepatorenal syndrome was accompanied by a decline in cardiac output. This, in turn, suggested that in patients with cirrhotic cardiomyopathy the inability to maintain a high cardiac output may contribute to a worsening of renal function, and the development of refractory ascites and hepatorenal syndrome [13,14]. Moreover, it has been hypothesized that acute cardiovascular stress, such as transjugular intrahepatic portosystemic shunt (TIPS) placement can precipitate overt heart failure in patients with cirrhotic cardiomyopathy [15–19], which may be suspected through signs of left ventricular diastolic dysfunction, even with a preserved systolic function.

However, the clinical relevance of cardiomyopathy has been questioned, particularly because overt cardiac failure is rare in cirrhotic patients [20]. According to this interpretation, the cardiac abnormalities found in cirrhosis are an expression of circulatory adaptative phenomena in response to the hyperdynamic/hypervolemic state typical of cirrhosis, rather than a specific cardiomyopathy [21,22]. In favour of this interpretation, the reversibility of the echocardiographic and electrocardiographic aspects of diastolic dysfunction was demonstrated after liver transplantation [23–26]. Alternatively, patients with cirrhosis are typically at an age of high incidence of atherosclerosis, and available studies show that over 50% of them have carotid artery plaques and/or endothelial dysfunction, without clinical signs of heart disease [27]. N terminal brain natriuretic peptide (NT-proBNP), a polypeptide released by ventricular myocytes in direct proportion to wall tension, and a sensitive noninvasive marker of heart failure [28,29], has been found to be significantly elevated in patients with cirrhotic cardiomyopathy [24,30].

This study aimed at investigating the cardiac response to haemodynamic stress in cirrhotics with different disease severity.

2. Materials and methods

2.1. Patients and study protocol

Between May, 2008 and October, 2011, 15 patients with decompensated cirrhosis (Child–Pugh B-C class) complicated by refractory ascites [31] requiring TIPS placement, and 8 patients with compensated cirrhosis (Child–Pugh A class) were enrolled in the study (group A and group B, respectively).

Patients with valvular or ischaemic heart disease, total portal vein thrombosis, chronic renal failure with creatinine value >2.5 mg% or on haemodialysis were excluded. Patients who had taken beta-blockers in the previous 5 days, or with alcohol consumption >30 g/day in the last month were also excluded. Before entering into the study, in order to rule out a previously unknown ischaemic or valvular heart disease, all patients underwent a full evaluation protocol, including physical exam, EKG, and echocardiography dobutamine stress test; selective coronary angiography was performed in cases of a positive stress test.

Patients in group A underwent paracentesis through the insertion of an intra-abdominal pigtail catheter followed by intravenously albumin infusion (50 ml of 20% albumin for every litre of ascites removed); diuretic therapy was stopped, and patients went on a sodium-restricted diet. The study protocol included measurement of the NT-proBNP. The NT-proBNP analysis was performed with a commercially available immunoassay (Dimension System, Siemens) according to established methods. Patients also underwent echocardiography and right heart catheterization with measurements of cardiopulmonary pressures and cardiac output in basal condition and immediately after the acute expansion of the plasma volume by means of a rapid infusion of a plasma expander (Voluven®, Missisauga, ON, Canada) 500 ml in 10 min [32]. The following day, the patients underwent TIPS placement, and measurements of NT-proBNP and right heart catheterization were repeated immediately after TIPS and at 24 hours, while echocardiography and NT-proBNP were also repeated 30 days after TIPS (Fig. 1).

Patients in group B underwent the same evaluations before and after acute volume expansion (Fig. 1).

The study was approved by our institute's Ethics Committee, and informed written informed consent was obtained from all patients.

2.2. Study procedures

2.2.1. Echocardiography

A comprehensive transthoracic echocardiographic examination was performed using a commercially available cardiac ultrasound machine (Vivid System Seven, GE/Vingmed, Milwaukee) at 3.5 MHz. Patients were placed in the left lateral decubitus position, and standard parasternal, apical and substernal views were obtained. Pulsed, continuous and colour-flow Doppler techniques were used to investigate transvalvular flows and deceleration times. All images were digitally recorded for off-line analysis. The following measures were reported: left ventricular end diastolic diameter (EDD), left ventricular end diastolic volume (EDV), interventricular septum (IVS), left ventricular ejection fraction (EF), left atrial diameter (LAD), early maximal ventricular filling velocity (E), atrial maximal filling velocity (A), deceleration time (DT), and pulmonary artery systolic pressure (PASP). The coexistence of an E/A ratio $\leq$1 and DT >220 ms was considered an indication of diastolic dysfunction [33–35].

2.2.2. Cardiac catheterization

A Swan–Ganz catheter (7F, Baxter Healthcare, Edwards Critical Care Division, Deerfield, IL) was introduced through the right internal jugular vein or right femoral vein under fluoroscopic guidance using the Seldinger technique. The following variables were measured: mean right atrial pressure (RAP), PASP, mean pulmonary artery pressure (mPAP), pulmonary artery diastolic pressure (PADP), pulmonary capillary wedge pressure (PCWP), transpulmonary pressure gradient (TPG), cardiac output (CO), pulmonary vascular resistance (PVR) and systemic vascular resistance (SVR). CO was determined with the thermodilution method as the mean of three consecutive measurements not varying by >10%. The PVR, expressed in dyn s cm^{-5}, was calculated using the formula $PVR = (mPAP - PCWP)/CO \cdot 80$. Systemic arterial blood pressure was measured with a cuff sphygmomanometer, and heart rate and rhythm were recorded continuously with 3 surface electrocardiographic leads.

2.2.3. TIPS placement

TIPS placement was performed through the right internal jugular vein. A guiding catheter was inserted into the hepatic vein