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Original article

A detailed evaluation of cardiac function in cirrhotic patients and its alteration with or without liver transplantation

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ABSTRACT

Background: Cirrhosis has been shown to be associated with left ventricular (LV) myocardial dysfunction, but studies of right ventricular (RV) function in cirrhotic patients compared with controls are scarce. Limited studies have prospectively evaluated the progression of myocardial function in patients with cirrhosis and assessed changes in cardiac function following liver transplantation (LTx). So the aim of the study was to evaluate biventricular myocardial function in cirrhotic patients and its alteration with or without liver transplantation.

Methods: A total of 103 patients with cirrhosis (age 55 ± 7 years, male 75%) were recruited. Conventional and 2-dimensional speckle tracking echocardiography was performed to determine the presence of LV and RV (biventricular) dysfunction. For comparison, 48 matched control subjects were included. Follow-up echocardiography was performed in 41 patients following LTx and in 26 patients who did not undergo LTx.

Results: Patients with cirrhosis had biventricular dilatation, increased LV mass, impaired LV diastolic function, and biventricular systolic strain compared with controls. Following LTx, cirrhotic patients had reduced biventricular dilatation, a smaller LV mass, and improved biventricular systolic strain after a mean duration of 18.2 ± 6.6 months. Patients who did not undergo LTx had a further increase in LV mass but no significant change in biventricular dimensions or systolic strain (mean duration of 20.4 ± 8.3 months).

Conclusions: The present study demonstrates that patients with cirrhosis had biventricular dilatation and impaired biventricular systolic strain compared with controls. Following LTx, biventricular dilatation reduced and biventricular systolic strain improved. In contrast, patients who did not undergo LTx experienced a further increase in LV mass.

Introduction

Patients with cirrhosis have been shown to have myocardial dysfunction: a distinct entity termed cirrhotic cardiomyopathy has been attributed to this phenomenon [1,2]. Previous studies using echocardiography have demonstrated that patients with cirrhosis have impaired left ventricular (LV) diastolic function [3,4]. With the use of advanced 2-dimensional (2D) speckle tracking derived strain analysis that enables detection of subtle myocardial dysfunction, a recent study has further shown that patients with cirrhosis have impaired LV myocardial contractility [5]. Nonetheless these studies have been cross-sectional and the focus was on degree of LV dysfunction in cirrhotic compared with non-cirrhotic subjects.

Recently, right ventricular (RV) function has been shown to be superior to LV function in the prediction of adverse clinical outcome in patients with cirrhosis who undergo liver transplantation (LTx) [6]. Nonetheless studies of RV function in these patients compared with controls are scarce. Further, only limited studies have prospectively evaluated the altered myocardial function in patients with cirrhosis and assessed the changes following LTx

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[7,8]. Therefore the aim of the present study was to compare the LV and RV (biventricular) function in cirrhotic patients with controls and prospectively evaluate the difference in progression of biventricular function in cirrhotic patients with and without LTx.

Patients and methods

Study population

From January 2011 to August 2013, a total of 103 consecutive Chinese patients with cirrhosis, aged over 18 and referred to the Department of Surgery at Queen Mary Hospital (the only center in Hong Kong) for LTx were recruited. Patients with any one of the following were excluded: documented history of cardiovascular disease including coronary artery disease, myocardial infarction, stroke or peripheral vascular disease, acute liver failure, and LTx not related to liver cirrhosis. Patients with clinical and echocardiographic features of hepato-pulmonary syndrome and pulmonary hypertension were also excluded. For comparison, 48 control subjects recruited from a health screening program organized by the Cardiology Division, Department of Medicine, The University of Hong Kong, were matched with patients for age, sex, body mass index (BMI), and cardiovascular risk factors.

The study was approved by the local institutional ethics board and all subjects gave written informed consent.

Study protocols

Data on baseline demographics and clinical characteristics, and blood sampling were obtained prospectively on the same day in all study subjects after overnight fasting. BMI and conventional cardiovascular risk factors such as history of diabetes mellitus (defined as a serum fasting glucose 7.1 mmol/L or prescription of anti-hyperglycemic medication), and hypertension (defined as either resting systolic or diastolic blood pressure $\geq$140/90 mmHg on two occasions or prescription of antihypertensive medication) were documented. The use of medications, including beta blocker, calcium channel blocker, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, and diuretics were recorded in patients. Clinical status was assessed by the Child-Pugh score and the model for end-stage liver disease (MELD) score.

Conventional echocardiography

All patients with cirrhosis and controls were imaged in the left lateral decubitus position using a commercially available echocardiography system (Vingmed Vivid 7, General Electric Vingmed Ultrasound, Milwaukee, WI, USA). A 3.5-MHz transducer was used to obtain images that were digitally stored in cine-loop format (3 cardiac cycles). Offline analysis was performed using EchoPAC version 108.1.5 (General Electric – Vingmed, Horten, Norway). The LV end-diastolic septal and posterior wall thickness, LV dimensions, volumes, and ejection fraction were measured according to the current recommendations [9]. LV mass was calculated using Devereux's Formula [10]. Evaluation of LV diastolic function was based on the pulsed-wave Doppler of mitral valve inflow, measuring peak early diastolic velocity (E), peak late (A) diastolic velocity, and E/A ratio. Using tissue Doppler imaging, the early diastolic velocity (E′) was measured at the level of the LV basal lateral segment. In addition, E/E′ ratio was calculated as an estimation of LV filling pressure [11]. LV diastolic dysfunction was therefore categorized as previously described: normal; mild, defined as LV impaired relaxation without evidence of increased filling pressure; moderate, defined as LV impaired relaxation associated with moderate elevation of filling pressure or pseudonormal filling; and severe, defined as restrictive LV filling [11].

Right ventricular end-diastolic area (RVEDA) and right ventricular end-systolic area (RVESA) were measured by manually tracing the RV endocardial border on the apical 4-chamber view; care was taken to obtain a true non-foreshortened view oriented to obtain the maximum RV dimension. The right ventricular fractional area change (RVFAC) was calculated using the following equation: (RVEDA − RVESA)/RVEDA $\times$ 100% [9], with a lower reference valve for normal RV systolic function of 35%. Tricuspid annular plane systolic excursion (TAPSE) was measured from the apical 4-chamber view: an M-mode cursor was placed through the tricuspid annulus and the displacement of the base of the RV free wall along the cursor from end-diastole and end-systole was measured, with a lower reference value for impaired RV systolic function of 1.6 cm. Finally, right ventricular systolic pressure (RVSP) was determined from peak tricuspid regurgitation velocity by continuous-wave Doppler using simplified Bernoulli equation and combining this value with an estimate of the right atrial pressure (RAP): $RVSP = 4(V)^2 + RAP$. For conventional echocardiography parameters, RV systolic function was quantified with RVFAC and TAPSE.

Two-dimensional speckle tracking strain analysis

Two-dimensional speckle tracking strain analysis is an advanced imaging technique that provides detailed assessment of myocardial deformation by tracking natural acoustic markers (speckles) on a frame-to-frame basis within the cardiac cycle. The speckles are detected on the standard gray-scale 2D images and are distributed evenly within the myocardium.

Myocardial systolic strain of the LV can be assessed in three orthogonal directions: longitudinal strain, circumferential strain, and radial strain. The detailed measurement of LV systolic strain was determined from the 3 apical (2-, 3-, and 4-chamber) views and has been described in detail [12,13]. Global longitudinal and circumferential strains are expressed as negative values, and a lower strain is represented by a less negative value. Global radial strain is expressed as a positive value, and a lower value indicates lower strain.

The measurement of RV global longitudinal systolic strain using 2D speckle tracking analysis has been described previously [14,15]. Briefly, from the apical 4-chamber view, a region of interest (ROI) was manually traced along the endocardial border of the RV free wall and septal wall, and the width was set to match wall thickness. The tracked ROI was visually checked and adjusted if necessary and the RV global longitudinal strain calculated (Fig. 1). RV longitudinal strain is expressed as a negative value: a lower strain is represented by a smaller negative value.

Follow-up echocardiography

During the study period, 41 patients underwent LTx and a repeat echocardiography was performed after a mean duration of 18.2 $\pm$ 6.6 months following LTx. A total of 62 patients remained on the waiting list for LTx; 14 patients refused a follow-up echocardiography evaluation and 22 patients died during the study period. Accordingly, 26 patients who did not receive LTx underwent a follow-up echocardiogram at 20.4 $\pm$ 8.3 months as well as baseline echocardiography.

Statistical analysis

Data are expressed as mean $\pm$ standard deviation for continuous variables and frequencies or proportions for categorical variables. Continuous demographic variables of the two groups were compared using independent sample Student's *t* test. Categorical demographic variables were compared using Pearson Chi-square test or the Fisher's