Respiratory Medicine (2013) 107, 1030–1036

Available online at www.sciencedirect.com

SciVerse ScienceDirect

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

Cirrhotic cardiomyopathy and hepatopulmonary syndrome: Prevalence and prognosis in a series of patients

Irina Enache [a,d], Monique Oswald-Mammosser [a,e], Marie-Lorraine Woehl-Jaegle [b,f], François Habersetzer [c,g], Paola Di Marco [a,h], Anne Charloux [a,i], Stéphane Doutreleau [a,*]

[a] Service de Physiologie et d'Explorations Fonctionnelles, Pôle de Pathologie Thoracique, Hôpitaux Universitaires de Strasbourg, Nouvel Hôpital Civil, B.P. 426, 67091 Strasbourg Cedex, France
[b] Service de Chirurgie et de Transplantations Multiorganes, Pôle des Pathologies Digestives-Hépatiques-Transplantations, Hôpitaux Universitaires de Strasbourg, France
[c] Service d'Hépato-Gastro-Entérologie, Pôle Hépato-digestif de l'Hôpital Civil, Hôpitaux Universitaires de Strasbourg, France

Received 24 November 2012; accepted 11 March 2013
Available online 21 April 2013

KEYWORDS
Carbon monoxide;
Cirrhotic cardiomyopathy;
Diastolic dysfunction;
Liver disease;
Hepatopulmonary syndrome

Summary
Hepatopulmonary syndrome (HPS) is of prognostic value in patients awaiting for orthotopic liver transplantation (OLT), but little is known about the effect of cirrhotic cardiomyopathy (CCM). The aim of the present study was to estimate the prevalence and possible relation between respiratory and cardiac abnormalities in a same series of patients awaiting OLT. Special attention was paid to the prognostic value of CCM in comparison to HPS.

Eighty-three patients were included (19 females, 64 males; 52.1 ± 10.0 yrs). All had lung function testing with arterial blood gases and echocardiographic evaluation at rest with a contrast echocardiography in case of arterial oxygenation defect. To estimate the presence of CCM, patients underwent a complete left and right echocardiography and Doppler

* Corresponding author. Tel.: +33 369551303; fax: +33 369551826.
E-mail addresses: irina.enache@chru-strasbourg.fr (I. Enache), monique.oswald@chru-strasbourg.fr (M. Oswald-Mammosser), marie-lorraine.woehl@chru-strasbourg.fr (M.-L. Woehl-Jaegle), francois.habersetzer@chru-strasbourg.fr (F. Habersetzer), analia.paola.di.marco@chru-strasbourg.fr (P. Di Marco), anne.charloux@chru-strasbourg.fr (A. Charloux), stephane.doutreleau@chru-strasbourg.fr (S. Doutreleau).
[d] Tel.: +33 369550662.
[e] Tel.: +33 369550659.
[f] Tel.: +33 388127280.
[g] Tel.: +33 369551009.
[h] Tel.: +33 369551182.
[i] Tel.: +33 369550878.

0954-6111/$ - see front matter
http://dx.doi.org/10.1016/j.rmed.2013.03.010

examination. Complete echocardiographic assessment could be obtained in 64 of the 83 patients of the study.

HPS was observed in 16.9% (14/83) and CCM in 23.4% (15/64) of patients. There was a tendency of more serious adverse events before and after OLT in patients with HPS in comparison to others but CCM was not of prognostic value.

HPS and CCM were frequent in these patients awaiting OLT but both abnormalities were not found in the same patients. CCM was neither related to death before OLT nor to death or serious adverse events after OLT.

Introduction

Liver diseases are associated with pulmonary complications in a significant number of patients.[1,2] The most common complication is hepatopulmonary syndrome (HPS), which is defined as a defect in arterial oxygenation due to intrapulmonary vascular dilatation in the setting of liver disease,[3,4] and is found in 10—30% of candidates for liver transplantation. Diagnosing this complication is essential, as it has been associated with pre- and post-transplantation mortality.[5—7] Portopulmonary hypertension (PPH) is less common (in 3—5% of cases[1]) and is defined as the combination of pulmonary and portal hypertension.[8,9]

In addition to these pulmonary complications, purely cardiovascular complications, such as cirrhotic cardiomyopathy (CCM), have also been reported. CCM is defined as a cardiac dysfunction characterized by blunted contractile responsiveness to stress and/or diastolic dysfunction at rest and/or electrical conductance abnormalities (prolonged QT interval corrected for heart rate (QTc)) in the absence of other known cardiac disease.[10—13] Orthotopic liver transplantation (OLT) has been reported to reverse some alterations, specifically diastolic dysfunction and the increase in wall thickness, as assessed by echocardiography.[14—18] The prevalence of CCM is not accurately known, and to the best of our knowledge, its prognostic value for mortality and morbidity has not previously been estimated.

The exact mechanisms leading to HPS and CCM are still not completely understood but an overproduction of nitric oxide (NO) and carbon monoxide has been suspected to play a role.[10,11,15,19—21] Thus, it might be helpful to determine whether HPS and CCM occur in the same patients, and if their eventual coexistence may influence the prognosis of patients awaiting OLT.

Therefore, the aims of our study were i) to determine the prevalence and prognostic value of HPS and CCM in patients with liver disease awaiting OLT; and ii) to assess whether CCM is more common in patients presenting with HPS, which could also influence their prognoses.

Materials and methods

Eighty-three consecutive candidates for OLT (19 women and 64 men, aged 51.7 $\pm$ 2.5 and 53.5 $\pm$ 1.2 years, with a body mass index of 25.4 $\pm$ 1 and 27.1 $\pm$ 0.6, respectively) were included in the study. Forty-one patients had alcoholic cirrhosis, 16 had hepatitis C, eight had hepatitis B, four had primary biliary cirrhosis, and two had secondary biliary cirrhosis. Four patients presented with hepatitis B or C or biliary cirrhosis and abusive alcohol consumption. The eight remaining patients presented with less common liver diseases. On the same day, a complete medical history and physical examination were performed, before the assessment and recording of all participants' pulmonary and cardiac parameters.

The severity of liver disease was graded using the model for end-stage liver disease (MELD) score.[22]

Based on coronary angiography or nuclear myocardial perfusion imaging, severe stable ischemic heart disease was observed in nine patients (none of whom were in the HPS group, see below). Sixty-four patients were receiving medical therapy in the form of beta-blockers and/or diuretics, or other antihypertensive treatments.

Informed consent was obtained from each patient. This study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki, and was approved by the Institutional Review Board of the French Learned Society for Respiratory Medicine (Société de Pneumologie de Langue Française; CEPRO 2010-002).

Pulmonary function testing

Lung volume, flow—volume curves, and diffusing capacity for carbon monoxide (DL_{CO}) were determined with a Jaeger device (MasterScreen™ PFT, Jaeger GmbH, Würzburg, Germany). The European Coal and Steel Community reference values were used.[23] Exhaled NO was measured before spirometry with a NIOX® device (Aerocrine AB, Solna, Sweden) at an expiration rate of 50 mL min^{-1} after a deep breath. Arterial blood gases (ABL725, Radiometer, Copenhagen, Denmark) were measured in the sitting position, exhaled gases were analyzed, and $AaPO_2$ was calculated using the simplified alveolar gas equation.[24]

Electrocardiographic and echocardiographic measurements

A conventional electrocardiogram (ECG) was performed at rest on the same day. QT interval duration was automatically determined from the beginning of the QRS complex to the end of the *T* wave. The QTc was calculated using Bazett's formula. A QTc $>$ 440 ms was considered abnormal.[25]

In addition, an echocardiogram was performed using an ATL HDI 5000 (Philips Medical System, Bothell, WA, USA).