

PULMONARY HYPERTENSION IN PATIENTS WITH HEPATIC CIRRHOSIS AND PORTAL HYPERTENSION. AN ECHOGRAPHIC STUDY

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Abstract

Aim of the study. The aim of the study is to determine the frequency of pulmonary hypertension in patients with hepatic cirrhosis and portal hypertension, to determine the possibility of an accurate ultrasound diagnosis of the characteristics of this complication.

Method. 347 patients with liver cirrhosis consecutively hospitalized at Coltea Clinical Hospital were screened. 61 were excluded because of other possible causes of portal or pulmonary hypertension. All patients were investigated clinically and by abdominal and cardiac ultrasonography.

Results. Of the remaining 286 patients, 116 had portal hypertension, 27 of them (23%) having pulmonary hypertension. In this group we found a higher cardiac index and right atrial volume, higher pressures in the right atrium, suggesting a hyperdynamic state. Porto-pulmonary hypertension was found in only one patient.

Conclusion. Echocardiography permits characterization of patients with cirrhosis and portal hypertension

Keywords: portal hypertension, pulmonary hypertension, echocardiography

Introduction

Pulmonary and cardiac conditions are found in the majority of patients with chronic hepatic disease. Many of them are due to common risk factors (such as alcohol, smoking, etc), some to immunologic suppression secondary to malnutrition. Among them, the hepatopulmonary syndrome (HPS) and porto-pulmonary hypertension (PPH) are especially important because of their therapeutic implications, liver transplantation being the only efficient treatment for the former, if severe, but a formal contraindication in the latter due to nearly 100% mortality. Their diagnosis is made by cardiac catheterization which is an invasive method not devoid of risk in such fragile patients.

Present prevalence data were obtained mainly from patients on waiting lists in hepatic transplantation units and thus do not reflect their frequency among common patients with cirrhosis [1].

Aim of the study

Echocardiography permits the measurement of arterial pulmonary pressure and the hemodynamic characterization of these patients [2,3]. In this study we aimed at evaluating the frequency of pulmonary hypertension in patients with hepatic cirrhosis and its characteristics so as to limit the indications for catheterization.

Material and method

We screened 347 patients with liver cirrhosis consecutively hospitalized in Coltea Clinical Hospital. We excluded 61 because of other conditions which could lead to portal hypertension (hepatic carcinoma, portal vein thrombosis) or pulmonary hypertension (left cardiac disease, pulmonary embolism, atrial fibrillation, obstructive pulmonary disease).

All of the remaining 286 patients were investigated clinically and by laboratory and had abdominal and cardiac echography performed to confirm the diagnosis and evaluate portal hypertension [4]

A group of 53 age and sex matched healthy persons

was investigated as a control group.

The presence of portal hypertension was confirmed by at least 2 of the following criteria: presence of ascites, splenomegaly, collateral portocaval circulation, thickening of the gall bladder walls. The presence of esophageal varices was not a mandatory criterion, but all patients had an upper gastric endoscopy performed [5].

Pulmonary pressure was echographically measured by the peak velocity of the tricuspid regurgitation flow and the acceleration time of the pulmonary systolic flow.

All cardiac cavities were measured in 2 D or TM registrations and cavity volumes calculated according to the current guidelines.

All echographic measurements were repeated three times.

The statistical study comprised the determination of mean values and standard deviation, and comparisons were made by the Mann-Whitney and the Kruskal-Wallis tests. Statistical significance was determined by the exact Fisher test considering as significant a $p < 0.05$.

Results

In the present paper we present only the results concerning pulmonary hypertension in patients with cirrhosis and portal hypertension as compared to those without it.

Out of the 286 patients with hepatic cirrhosis included in the study, 116 (40.56%) had portal hypertension and formed the main study group, and 170 had no portal hypertension. The healthy persons formed the third group necessary for comparing different parameters such as the cardiac index or right atrial volume.

One patient with portal hypertension was excluded from the analysis for lack of usable data concerning pulmonary pressure measurements. Of the remaining 115 patients 27 (23.48%) had pulmonary hypertension.

Pulmonary arterial pressure was determined by the velocity of the regurgitant tricuspid flow and by the acceleration of the flow in the pulmonary artery.

The Child-Pugh functional classification was used to assess the severity of hepatic cirrhosis. In Child-Pugh class A were 30% of the patients with pulmonary hypertension and 36% without, in class B 52% versus 49% and in class C 19% versus 15%. This indicates there is no significant relation between the severity of hepatic cirrhosis as determined by the Child-Pugh classification and the onset of pulmonary hypertension.

The cardiac index was calculated reporting cardiac output to body surface. The cardiac output was measured by calculating the integral of the velocity in the left ventricular outflow tract multiplied by the area of the outflow tract at the same point.

The cardiac index was significantly greater in patients with cirrhosis (1.94 ± 0.77 L/m²/min) than in healthy persons (1.54 ± 0.40 L/m²/min) ($p = 0.002$) and in patients

with pulmonary hypertension (2.24 ± 1.04 L/m²/min) than in patients with cirrhosis without pulmonary hypertension (1.85 ± 0.66) ($p = 0.03$) (Figure 1).

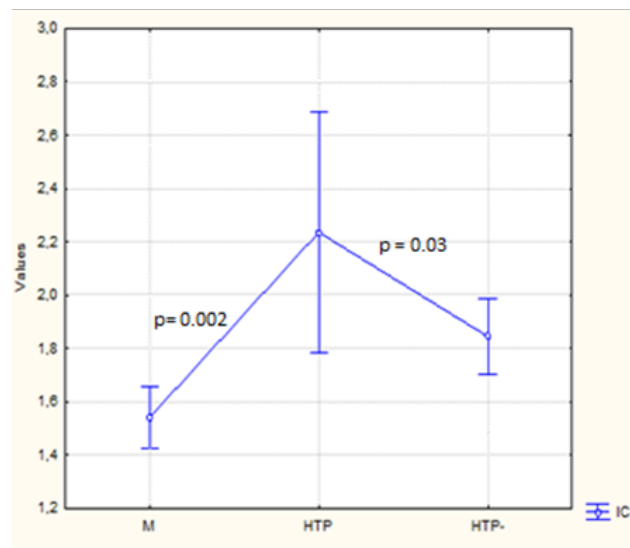


Figure 1. The cardiac index in the control group (M), the group with (HTP) and the group without (HTP-) pulmonary hypertension.

The volume index of the right atrium (volume reported to body surface) was larger in patients with cirrhosis (26.2 ± 8.9 ml/m²) as compared to controls (22.7 ± 10 ml/m²), due to a much larger volume in patients with pulmonary hypertension (30.4 ± 11.3 ml/m² versus 25.0 ± 7.7 ml/m² in those without). The difference was significant between patients with and without pulmonary hypertension ($p = 0.006$), but not significant between patients without pulmonary hypertension and controls (Figure 2).

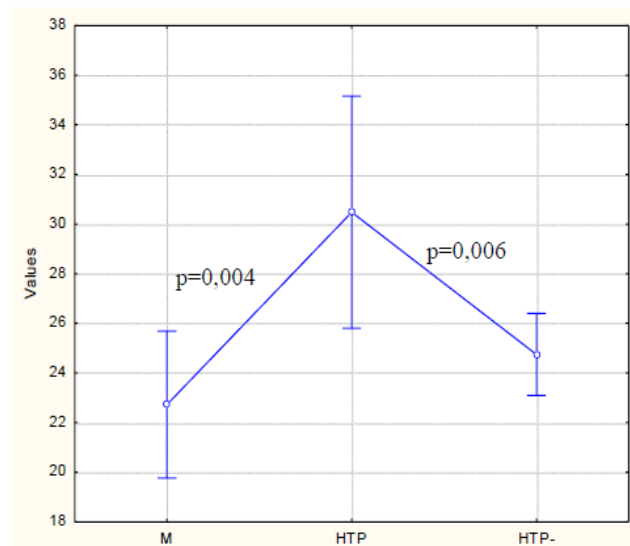


Figure 2. Right atrial volume index in patients with (HTP) and without (HTP-) pulmonary hypertension as compared to controls (M).

The right atrial pressure was appreciated using the Mayo Clinic algorithm based on the diameter and respiratory variation of the inferior vena cava. It can be considered as an indirect measurement of the venous return to the heart. It was significantly greater in patients with cirrhosis (6.5 ± 4.6 mm Hg) and greater in patients with pulmonary hypertension. Out of this group 59% of the patients had an increased right atrial pressure as compared with only 12% in patients with cirrhosis without pulmonary hypertension. The percentage of patients with different pressure values is presented in **figure 3**.

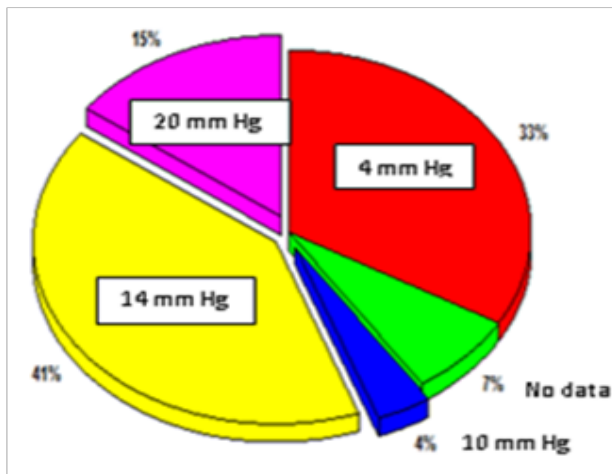


Figure 3. Pressure in the right atrium in patients with pulmonary hypertension.

Considering the left atrial volume an indirect expression of the pulmonary capillary pressure, we found that it was larger in patients with cirrhosis, with no significant difference between those with or without pulmonary hypertension.

Out of the 27 patients with hepatic cirrhosis with portal and pulmonary hypertension we could not characterize the hemodynamic in 5 (18.5%) due to a difficult echographic image. The ratio between the velocity of the tricuspid regurgitation and the time velocity integral in the right ventricular outflow tract (RTvel/VTIRVOT) is considered to be determined by the pulmonary vascular resistance. In only one patient (3.7% of the whole group or 4.5 of the patients with complete evaluation) out of the 27 with pulmonary hypertension was this ratio greater than 2, suggesting an increased pulmonary resistance (i.e. a porto-pulmonary syndrome). In 19 patients (70%) the data suggest a hyperdynamic circulatory status and in 2 (7%) an increased pulmonary capillary pressure as cause of the pulmonary hypertension.

Discussion

Not all patients with hepatic cirrhosis associate pulmonary hypertension. In fact this pulmonary complication

depends on the presence of portal hypertension, but even in this case not all patients will develop this complication [5].

In our study, 20% of the patients with portal hypertension developed pulmonary hypertension. The severity of the hepatic disease could be a determining factor, but in our study in which 64% of the patients were in Child-Pugh B and C classes the odds ratio for them to have pulmonary hypertension as compared to patients in class A was 1.6, which was statistically not significant ($p=0.36$).

The presence of ascites is a marker of the severity of portal hypertension [6]. In our study it was present in 53% of the patients and determined an odds ratio for pulmonary hypertension of 1.32 which was statistically insignificant.

As a consequence we could not relate the severity of the hepatic disease or portal hypertension to the onset of pulmonary hypertension.

In a study performed in the United States published in 2008 [7] a greater incidence of pulmonary hypertension in cirrhotic women was reported. We found no association between gender, age, etiology of the hepatic disease and the appearance of pulmonary hypertension. As a matter of fact other studies showed similar results [8,9].

The mechanism of pulmonary hypertension was in the majority of patients (70%) a hyperdynamic circulation. This state is well-known to appear in hepatic cirrhosis [10]. The best echographic parameter correlated with this state was the pressure in the right atrium as a measurement of the venous return. A second factor was an increase in the vascular volume [11] leading to an increase in the pulmonary capillary pressure independent of any left cardiac disease. In our study this situation was met in approximately 30% of the patients, being the apparently unique cause in 2 patients (7%).

An increase in pulmonary vascular resistance is the marker of the porto-pulmonary syndrome. It was found in only 1 patient in our study. This increased resistance leads to a decreased time-velocity integral in the right ventricular outflow tract - VTIRVOT. Our study suggests that a VTIRVOT over 20 cm is the expression of an increased flow in the pulmonary artery and thus refutes a porto-pulmonary syndrome.

Echography can be used to diagnose the cause of pulmonary hypertension in patients with chronic hepatic disease. We propose the following algorithm: if pulmonary hypertension is confirmed by a systolic pulmonary artery pressure over 35 mm Hg the RTvel/VTIRVOT is determined. If it is over 0.175, porto-pulmonary syndrome is suspected and the patient must have a right cardiac catheterization. If not, the inferior vena cava is evaluated. A diameter over 15 mm of the inferior vena cava, with/ or a respiratory collapse under 50 % characterize a hyper dynamic state. A dilated left atrium suggests an excess of pulmonary blood volume (Figure 4).

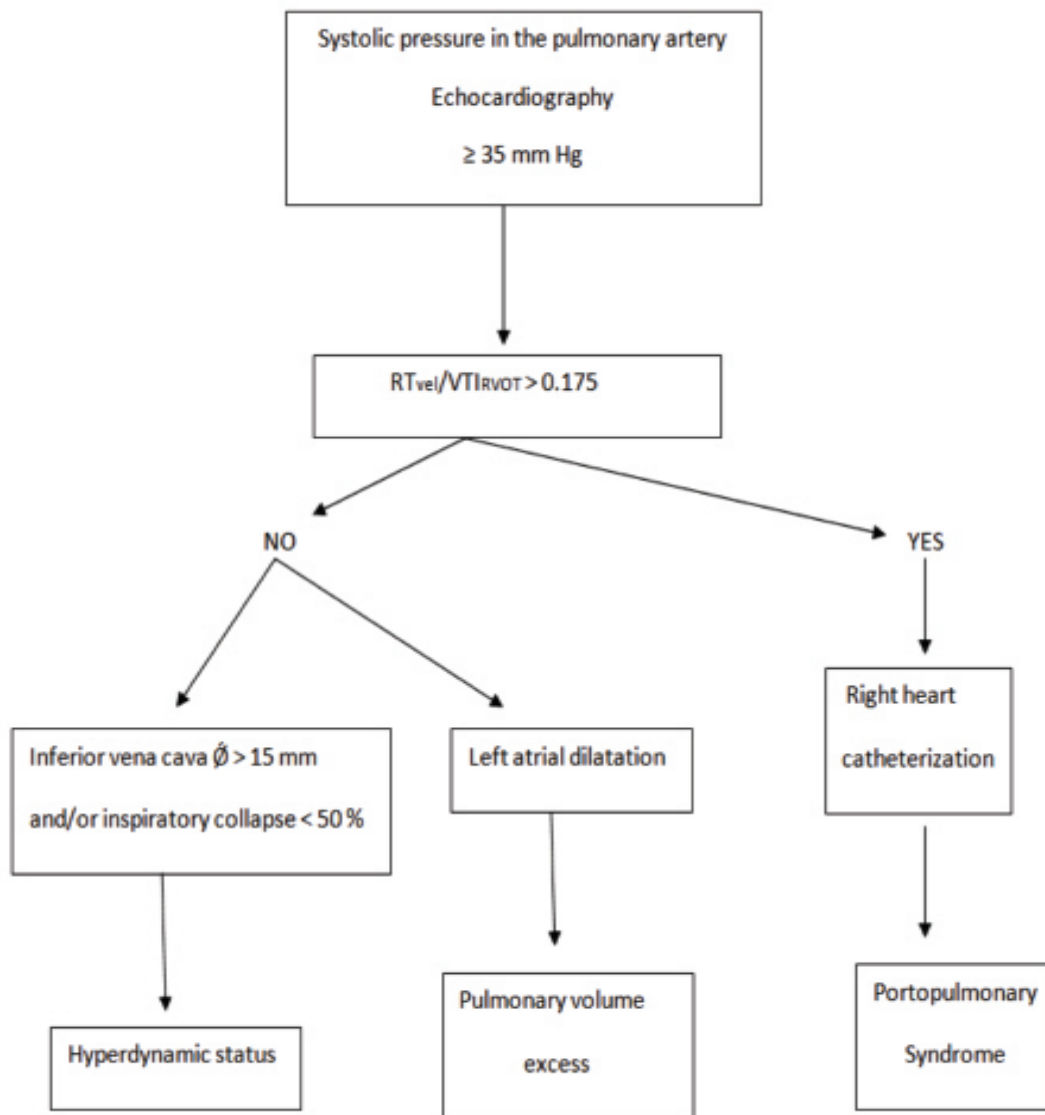


Figure 4. Algorithm for the diagnosis of pulmonary hypertension in patients with cirrhosis.

Conclusions

Echocardiography is a useful and easy method for the evaluation of pulmonary hypertension in patients with portal hypertension.

Pulmonary hypertension is relatively frequent in these patients and not related to the etiology of the hepatic disease.

Pulmonary hypertension is in the majority of cases due to the hyperdynamic circulatory status found in hepatic cirrhosis.

The portopulmonary syndrome is relatively rare and can be suspected by echocardiography.

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