THE LIVER CIRRHOSIS - RISK FACTOR FOR BILIARY LITHIASIS

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Keywords: *biliary lithiasis, cirrhosis of the liver*

Cuvinte cheie: *litiaza biliară, ciroza hepatică*

Abstract: *Viral and / or toxic (ethanol) liver cirrhosis is a risk factor for cholesterol and pigment gallstone formation.*

Rezumat: *Ciroza hepatică virală şi/sau toxică (etanolică) reprezintă factor de risc pentru formarea calculilor biliari colesterolici dar şi pigmentari.*

INTRODUCTION

Liver cirrhosis of viral and / or ethanol etiology is a risk factor for cholesterol and pigmented red line gallstone formation when hypersplenism is moderate / severe. Ultrasonography, the main technique of evaluating the gallbladder has a gallstones detection sensitivity of 95% (11). Epidemiological studies have shown a prevalence of ultrasound for 22-26% of gallstones in patients with cirrhosis (1,3,2). It was shown that the frequency of lithiasis in patients with cirrhosis increases with age and severity of liver disease. Frequency of gallstone disease in men with cirrhosis is similar or greater than in women with cirrhosis. Despite conflicting results on gallstone risk factors in patients with cirrhosis, liver disease severity was expressed by Child class as an independent predictor factor most frequently found (12,5,7)

MATERIAL AND METHOD

Retrospective study on 303 patients, 194 men (64%) and 109 women (36%), aged between 25-85 years, mean age was 61 ± 12 years. The presence of cirrhosis was histologically confirmed in 50 patients (16.5%) accepted the criteria (bridging fibrosis, regenerative nodules, hepatic profoundly altered architecture). For 253 remaining patients the diagnosis was made by corroborating clinical data, imaging (ultrasound) direct (point irregular liver surface, caudate lobe ratio / right lobe> 0.65) and indirect (signs of portal hypertension - splenomegaly, increased vein diameter port and / or collateral circulation and / or ascites), endoscopy (presence of esophageal varices) and biochemical (hepatocytolisis and cholestasis syndrome unsteady, hepatodepressive syndrome syndrome, mesenchymal). Alcoholic cirrhosis was found in 127 patients admitted daily consumption of 100g of alcohol in the past 10 years, 145 patients viral etiology of which 47 with viral hepatitis B, 98 C viral aetiology and 31 patients with cirrhosis of unknown etiology. Characteristics of the study are found in Table 1. Ultrasound diagnosis of gallstones was made by the presence of one or more aspects: (a) one or more echogenic structures with posterior shadow cone, possibly moving into the bladder, (b) one or more mobile structures in the bladder without obscurity, (c) shade structures with constant echogenic gallbladder, absence or poor visualization of the gallbladder.

Table no. 1. Sex, age, cause of cirrhosis and the Child class in patients with cirrhosis

Characteristic	**Nr (%)**
Men / Women	194/109 (64%/36%)
Age Group	
<40	15 (5%)
40-49	36 (12%)
50-59	91 (30%)
60-69	100 (33%)
>70	61 (20%)
Cirrhosis	
Alcohol	127 (42%)
Viral	145 (48%)
Cause not specified	31 (10%)
Child Class	
A	145 (48%)
B	109 (36%)
C	49 (16%)

HBsAg, Ac antiHCV - Meia test

Child-Pugh classification takes into account five factors: the presence or absence of ascites and encephalopathy, total bilirubin value, decreased serum albumin concentration, prothrombin time prolonged. There is a score between 1 and 3 for each factor in relation to the disorder degree, with a total score between 5 and 15: a total score <6 corresponds to class A, a score of 7-9 corresponds to class B and a score> 10 corresponds to class C.

The Fischer test was used for the retrospective analysis in order to evaluate the differences in gallstone prevalence compared with the following variables: gender, age group (<40, 40-49, 50-59, 60-69,> 70), Child class (A, B or C) and etiology of cirrhosis. Identify variables with significantly increased risk for gallstone disease was performed by multiple logistic regression.

• Prospective study

There were enrolled 155 patients with cirrhosis and without gallstones who followed 3 years with repeated admissions at varying intervals of time. The group included 101 men and 54 women aged between 35 and 85 years of age (mean 60 ± 9 years).

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The etiology of cirrhosis was: ethanol in 70 patients (45%), viral in 62 patients (40% of while 11 with virus B and C virus 51) and the remaining 15% (23 patients) with unknown etiology. At enrollment, related to Child-Pugh classification, 93 patients were in Child class A (60%), 48 in Child B class (31%) and 14 in Child class C (9%). Duration of observation was 36 months. Characteristics of the study are shown in Table 2.

Table no. 2. Sex, age, cause of cirrhosis and the Child class in patients with cirrhosis

Characteristic	No (%)
Men / women	101/54 (65/35)
Age Group	
<40	9 (6)
40-49	36 (23)
50-59	43 (28)
60-69	48 (31)
>70	19 (12)
Cirrhosis	
Alcohol	70 (45%)
Viral	62 (40%)
Cause not specified	23 (15%)
Child Class	
A	93 (60%)
B	48 (31%)
C	14 (9 %)

The calculation of the cumulative probability of gallstone development was performed using the Kaplan-Meier estimates. Multivariate analysis used a Cox regression model following a review procedure for identifying the best subset of variables with the most important prognostic value for developing gallstones.

We have included the following variables: gender, age group (<40, 40-49, 50-59, 60-69,> 70), Child class (A, B or C) and etiology of cirrhosis. It was considered the interaction between gender and various age groups.

RESULTS

Overall prevalence of gallstone disease was 29% (n = 88). As shown in Table 3, the analysis results shows the prevalence of gallstone disease increased with age from 14% in patients younger than 40 years to 39% without differences by sex or etiology of cirrhosis. Gallstones were significantly more frequent in patients in Child class B (OR1, 63) and C (OR 1.91) than those in Class A (P = 0.001). Multiple logistic regression analysis showed that only severity of liver disease was significantly related to a high risk of gallstone disease (OR 1.54 for Child class C vs class A and class B vs 1.76 for class A, P = 0.001) . Characteristics of the study are found in Table 3.

• Prospective Analysis

During the observation period gallstone occurred in 37 patients (24%) of the 155 enrolled with cirrhosis, 24 (23.7%) males and 13 (24%) women, no significant differences between the sexes. No significant differences were detected in relation to age, etiology of cirrhosis and the relationship between sex and age. The frequency of new cases of gallstone disease in patients in Child classes B and C was significantly higher in patients in Class A [14/48 (29%) and 6 / 14 (40%) vs 17/93 (18%)] . Using multivariate analysis, the only variable identified as an independent predictor for the occurrence of gallstone disease was severe liver damage at baseline, with significantly higher probability for Child class B and class C to A (P = 0.001, C vs. Class A Child , P <0.002, B vs. Child class A).

Table no. 3. The prevalence of the biliry lithiasis in 303 patients with cirrhosis, rapported with the sex, ethiology of the cirrhosis and Child class

Characteristic	Total	Patients with LB No (%)
Sex		
M	194	55 (28,5%)
F	109	35 (32%)
Age Group		
<40	15 (5%)	2 (14%)
40-49	36 (12%)	11 (29%)
50-59	91 (30%)	23 (25%)
60-69	100 (33%)	30 (30%)
>70	61 (20%)	24 (39%)
Cirrhosis		
Ethanolic	127 (42%)	41 (32%)
Viral	145 (48%)	41 (28%)
Cause not specified	31 (10%)	8 (24%)
Child Class		
A	145 (48%)	39 (27%)
B	109 (36%)	33 (30%)
C	49 (16%)	18 (37%)

DISCUSSIONS

The latest data shows that the prevalence of gallstone disease in the general population is increasing, being 7.6% in men and 16.9% in women. The present study confirms that gallstone disease prevalence is higher in women with cirrhosis, although the difference was not statistically significant in men (32% vs 28.5%). Prevalence of gallstone disease in men with liver cirrhosis is higher than the general population. Another factor that has minimal effect on the prevalence of gallstone disease in patients with cirrhosis was the age. In fact, a significand increased prevalence of gallstone disease was observed only for the most advanced age group compared with those aged <40 years. The results also suggests that sex and age, ae closely associated with gallstone disease in the general population are much less important in patients with cirrhosis. In these patients, the main factor affecting the prevalence of gallstone disease was reflected by the severity of liver disease classified as Child. Patients in Child class B and C prevalence for gallstone disease were significantly higher than those in Class A.

Liver cirrhosis increases the risk of gallstones in men with high levels of estrogen leads to supersaturation of bile with cholesterol plus bile acid pool decreased and biliary stasis by affecting gallbladder evacuation similar to that observed in pregnant women (6, 9). Another cause of dismotilității gallbladder in patients with liver cirrhosis is the vesicular wall dysfunction muscle fibrosis. It was shown that there is a significant relationship between levels of connective tissue growth factor (CTGF) and transforming growth factor beta (TGF-beta), with values of 41 and 8 times higher in cirrhosis with gallstone disease and advanced degree of fibrosis the gallbladder wall with significant dysfunction (10). Hypersplenism due to chronic hemolytic status and bilirubin conjugation defects hepatocyte lesions increase the risk of gallstones in cirrhotic patients pigmentosa (8).

CONCLUSION

There is a high positive correlation between gallstone disease and advanced stage of liver cirrhosis and to a lesser extent with additional risk factors such as female sex and older age (4).

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