IS ATHEROSCLEROSIS A REAL BURDEN IN OLDER PATIENTS WITH LIVER CIRRHOSIS?

Doina Georgescu¹, Mihaela Munteanu¹, Daniela Radu², C. Georgescu¹

SUMMARY: Patients with liver cirrhosis have generally a low risk for cardio-vascular diseases. However association with cigarette smoking, diabetes mellitus, metabolic syndrome could alter the outcome of these patients. Clinical and carotidian ecoDoppler studies many assess the risk for atherosclerosis in a lot of patients with liver cirrhosis. 39 patients with liver cirrhosis with different etiologies and Child scores, were confined to Compartment of Gastroenterology of the City Hospital. They undertook standard biochemical exams including serum glucose and fat profile, CRP. They also did upper digestive endoscopy, abdominal ultrasonography scan, carotidian eco Doppler. We measured MIT (media-intima thickness) at the distal part of the carotid artery, the velocities vmax and vmedium at the bilateral carotid internal and external carotid arteries. The plaque was defined as a focal thickening of the intima >1,2mm with regard to the age and sex of the patients. Results: 8 patients (20,51%), 5 men, 3 women, age between 54-85 years had a significant thickness of the intima, MT>1,2mm, specific for atherosclerosis. Etiology of cirrhosis was C viral infection in 7 patients and alcoholic in 1 patient. The Child classification was: A=3 patients, B=4 patients, and C=1. The taking of history revealed cigarette smoking in 5 male patients, metabolic syndrome with BMI>30 kg/m² in 2 diabetic patients also having mixed dyslipidemia, mild hypertension in 1 patient, positive CRP in 5 patients. 4 patients had multiple cardio-vascular risk factors (10,25%) with calcification at carotidian plaques. Despite the classic view that patients with liver cirrhosis have a low cardio-vascular risk, eco Doppler assessment revealed specific features for atherosclerosis in 20,51% associated to well known risk factors as: life style, age, male gender, women at menopause, cigarette smoking, obesity, VHC infection and diabetes mellitus, dyslipidemia, hypertension. Severity of atherosclerosis decreased with the end stage liver condition: the lowest percentage was observed in patients with Child C score.

Key words: atherosclerosis, MIT (media-intima thickness), liver cirrhosis

ESTE ATEROSCLEROZĂ O ADEVĂRATĂ POVARĂ LA PACIENȚII VÂRSTNICI CU CIROZĂ HEPATICĂ?

Rezumat: Se stie ca in general pacienții cirotici au o prevalență scăzută a bolilor cardio-vasculare. Totuși anumite condiții pot influența riscul cardio-vascular. Studiile clinice și Duplex carotidian pot evalua riscul aterogen la un lot de pacienți cu ciroze hepatice. 39 pacienți cu ciroze hepatice confirmate, internați în Compartimentul de Gastroenterologie al Spitalului Municipal de Urgență Timișoara au fost examinați clinic, și s-au efectuat investigații biochimice incluzând și profilul glicemic, lipidograma, proteine C reactivă și paracroniche: ecografie abdominală și Duplex carotidian, endoscopie digestivă superioară. S-au măsurat grosimea întâlnă-medie (GIM) la nivelul carotidei comune distale, vitezele vmax și vmedium la nivelul carotidei comune, interne și externe bilateral. Placa a fost definită ca o îngrășare focală a intimei >1,2mm, cu corecțiile legate de sex și vârstă. 8 pacienți (20,51%), 5 bărbați (62,5%) și 3 femei (37,5%), cu vârsta între 54-85 ani, prezenteau o îngrășare intimală semnificativă, GIM>1,2mm și parametrii de velocitate caracteristici aterosclerozi. Etiologia cirozelor a fost: infecție cu VHC la 7 pacienți, etanolică la 1 pacient. Clasa Child A=3, B=4, C=1; istoric de fumat la 5 pacienți de sex masculin, sindrom metabolic cu IMC>30kg/m² la 2 pacienți asociat cu diabet zaharat și dislipidemie mixtă, HTA la 1 pacient, proteine C reactivă pozitivă la 5 pacienți. 4 pacienți (10,25%) prezentaau trei sau mai multe factori de risc asociati cu evidența ecografice de plăci carotidiene cu calcificări. Deși ciroza a fost considerată mult timp ca având un potențial redus aterogen, examinarea Doppler a pus în evidență aspecte caracteristice aterosclerozei la un procent de 20,51% asociată factorilor de risc cunoscute: stil de viață, vârstă, sexul masculin, femei la menopauză, fumatul, obezitatea, diabetul zaharat asociat infecției cu VHC, dislipidemii, HTA. S-a remarcat o relație de invers proporționalitate între severitatea aterosclerozei și clasa Child.

Received for publication: 21.01.2009
Revised: 01.02.2009

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INTRODUCTION

Patients with liver cirrhosis have generally a low risk for cardio-vascular diseases. However, association with some conditions could alter the outcome of these patients.

Aim of this study was early identification of patients at high risk of cardiac events and therefore improve preventive and clinical care. Many novel risk factors, markers and innovative techniques including 3-D vascular measurements have been developed to investigate intervening steps in the atherosclerosis progression. B-mode ultrasound measurement of common carotid artery (CCA) intima media thickness (IMT) is a widely available, relatively inexpensive, highly standardized method for evaluating presence and severity of atherosclerosis.

PATIENTS AND METHODS

39 patients with liver cirrhosis with different etiologies and Child scores, age range 54-85 years, 25 men, 14 women, were admitted to the Gastroenterology Department of the City Hospital Timisoara. They undertook standard biochemical exams including serum glucose and fat profile, CRP. They also did upper digestive endoscopy, abdominal ultrasound scan, carotidian eco B mode and Duplex. We measured IMT(intima – media thickness) at the distal part of the common carotid artery, velocity parameters: vmax and medium at the bilateral common, internal and external carotid arteries. The plaque was defined as a focal thickening of the intima >1.2mm with regard to the age and sex of the patients.

The standardized imaging protocol from the Atherosclerosis Risk in Communities study was used to acquire images of the far walls of each carotid artery. We measured the mean combined thickness of the intima and medial layers of the far walls of each carotid artery segment. The common carotid artery segment was defined as the distal 1 cm immediately proximal to the onset of increased spatial separation of the walls of the common carotid artery (before the origin of the bulb). The carotid bifurcation segment was defined as the distal 1 cm of the bulb, the termination of which was characterized by the presence of the flow divider between the internal and external carotid artery. The internal carotid artery segment was defined as the proximal 1 cm of the internal carotid artery, starting immediately beyond the flow divider. Ultrasound images were acquired using an 8.0-MHz linear array transducer in a high-resolution ultrasound system ESAOTE MEGAS CVX/GPX.

B-mode ultrasound is a technique that can visualize non-invasively the lumen and walls of selected arteries. B-mode ultrasound has been validated for measuring intima-media thickness. (IMT) in several independent laboratories, and its reliability has been established in multi- or single-centers studies (figure 1).

RESULTS

8 patients (20,51%), 5 men, 3 women, mean age 65,5±8,9 years had a significant thickness of the intima, IMT >1,2 mm and specific velocity parameters for atherosclerosis. 7 patients had infection with VHC, 1 had history of alcohol drinking. Child-Pugh score of

Figure 1. Measuring intima-media thickness. (IMT) in carotid arteries
patients with features of atherosclerosis was: 12.5% A, 37.5% B and 50% C. During this study 1 of patients (male, age 73 years old) died for cardio-vascular events: CHD and secondary arrhythmias.

Correlation severity of ATS and Child score:
- 5 patients had early features of ATS (thickness of the intima IMT > 1.2 mm), 4 with Child B score and 1 with Child C score.
- 3 patients with severe ATS (plaque with calcifications) had Child A score. They were males, age > 62, smokers, diabetic and HCV infected (figure 2).

The most important risk factors for cardio-vascular events analyzed in this study are listed below (table)

**DISCUSSIONS**

Intima media thickness of the common carotid artery is associated with the risk of stroke and myocardial infarction in asymptomatic older adults (more than 65 years old). The relative risk of stroke and myocardial infarction between the lowest and the highest thickness is 3.87 (Cardiovascular Health Study), within median follow up period of 6,2 years (Fried).

Cholesterol Lowering Atherosclerosis Study cited by Brown et al confirms that measurement of progression of intima-media thickness in the distal common carotid artery is a useful surrogate end point for clinical coronary events: for each 0.03mm increase per year the relative risk for any coronary event is >3 (Brown).

Some studies revealed no difference in atherosclerosis between cirrhotic patients and healthy controls (Kawakami). Vascular sclerosis was decreased with the severity of cirrhosis through hypotension and hyperbilirubinemia. Allocca showed in his studies that hypercholesterolaemia is not consistently associated with subclinical atherosclerosis in PBC, but should be treated if other risk factors for cardiovascular disease are also present.

However the search for factors that may protect patients with hypercholesterolaemic PBC against atherosclerosis should be encouraged.

Otsubo concluded in his study that compared with the general population, chronic liver disease patients have coronary arteries with smaller intimal plaque and less

### Table with cardio-vascular risk factors

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Patients(39)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Gender M/F</td>
<td>5/3</td>
<td>12.82%/7.69%</td>
</tr>
<tr>
<td>2. Age over 50 years</td>
<td>8</td>
<td>20.51%</td>
</tr>
<tr>
<td>3. Cigarettes smoking</td>
<td>5</td>
<td>12.82%</td>
</tr>
<tr>
<td>4. Life style</td>
<td>7</td>
<td>17.94%</td>
</tr>
<tr>
<td>5. Diabetes mellitus</td>
<td>5</td>
<td>12.82%</td>
</tr>
<tr>
<td>6. High titters of CRP</td>
<td>5</td>
<td>12.82%</td>
</tr>
<tr>
<td>7. Multiple risk factors</td>
<td>4</td>
<td>10.25%</td>
</tr>
</tbody>
</table>
vessel inflammation. These findings favor the concept that hepatic disease patients are less prone to develop complicated coronary atherosclerosis.

By contrary Plotkin et al. cited by Karasu reported a higher rate of cardiac morbidity and mortality in cirrhotic patients with angiographic evidence of CAD. Thus, the current rule in many liver transplant centers is to require a cardiac stress test particularly a dobutamine stress test with combined EKG and echocardiographic monitoring prior to transplant listing. Moreover, as a result of this practice, cirrhotics are being subjected to coronary angiography, coronary artery angioplasty or stenting and even cardiac bypass procedures more often than has been the rule in the past.

CONCLUSIONS

- Ultrasound assessment of carotid arteries revealed specific features for atherosclerosis in 20.51%: either early with IMT > 1.2mm or advanced.
- High cardio-vascular risk was associated to well known risk factors: life style, age over 50, male gender, women at menopause, cigarettes smoking, diabetes mellitus, high titer of CRP.
- Severity of atherosclerosis decreased with the end stage liver condition; the lowest percentage was observed in patients with Child C score.
- Infection to VHC had a high prevalence in cirrhotic patients with atherosclerosis possibly related to associated diabetes mellitus.

REFERENCES