

## Screening and diagnosing liver nodes

Adélia Simão\*, Amália Pereira \*\*, Jorge Leitão\*\*\*, Orlando Santos\*\*\*\*, Armando Porto\*\*\*\*\*

### Abstract

Evolution and an ever increasing general use of screening techniques has increased the frequency of liver nodes detection.

For one year, a study of screening and diagnosis of this kind of lesions was made in individuals included in one of the following groups: chronic alcoholic drinkers, with or without liver disease, B virus chronic hepatitis and C virus chronic hepatitis holder, women

taken contraceptives, extra-hepatic solid tumors patients and individuals with nodes detected incidentally in the ultrasound.

The findings confirm the rarity of benign tumors of the liver and the high frequency of secondary malignant tumors. Hepatocellular carcinoma happens among us mainly in men with alcoholic or post-hepatitis B cirrhosis.

### Introduction

The current evolution of image technology and its ever more generalized use, made frequent the identification of liver nodes. To detect such kind of lesions allows in many cases to take timely action, changing the life threatening course of some conditions. In other cases, however, the changes found, do not require any therapeutic intervention, but its detection causes a great deal of concern to the patient and it is often the reason to ask and perform a number of supplementary tests.

There are six types of nodes affecting more commonly the liver, with differences in terms of pathogenesis, macro- and microscopic aspects, clinical manifestations, tending to multiplicity, natural history, usefulness of diagnostic exams, needs and treatment value.<sup>1</sup>

They can be divided in two groups of lesions: those that most often are occasional findings, usually without any consequences (cysts, hemangioma and focal nodular hyperplasia), and those which can be life threatening, but the course can be changed by treatment, mainly if diagnosed in an early stage (adenoma, hepatocarcinoma and metastases).

Several etiologic factors have been pointed as the origin of liver tumors. Therefore, in the case of hepatocarcinoma, cirrhosis, regardless of its etiology,

seems to be the main factor. The risk of developing this kind of tumor is still related with alcoholism, chronic infection by the B virus hepatitis and probably also of C virus hepatitis. Under the light of modern knowledge, individuals at higher risk of developing this kind of tumor are men, over 40 years of age, carrying the B virus or cirrhosis (alcoholic, post-hepatitis or hemochromatosis).<sup>2</sup>

Hepatocellular adenoma is a rare tumor, appearing in women, predominantly between the 3<sup>rd</sup> and 4<sup>th</sup> decade of life. In October 1973, Baum et al, have described seven cases of adenoma in women taking contraceptives. Since then, several other works have been published, relating this kind of tumor with estrogen intake and with pregnancy.<sup>3</sup> Hemangioma is the most frequent benign liver tumor (0.4 to 7.3% in the autopsy series).<sup>4</sup> Its etiology is unknown, although some authors consider to be a birth defect of slow growth, eventually suffering some hormonal influences (oral contraceptives, pregnancy).<sup>2</sup>

The main targets of this work were:

- To screen liver node lesions in the main risk groups;
- To make the etiology diagnostic in the nodes found;
- To know the prevalence of the main types of hepatic tumors in our population.

### Material and methods

This study was made during 1992, in Coimbra University Hospitals and at Leiria District Hospital, has covered individuals who came to this health units belonging to one of the following groups:

- Chronic alcoholic patients (intake above 80 g of ethanol a day, over five years) with or without hepa-

\*Internal Medicine Hospital Assistant to Coimbra University Hospitals(HUC)

\*\*Internal Medicine Resident to Leiria District Hospital

\*\*\*Internal Medicine Resident to HUC

\*\*\*\*General Internship Resident to HUC

\*\*\*\*\*Lecturer at Coimbra Medical School and Head of Medicine III Service at HUC

TABLE I

## Individuals included in the study, by risk and sex groups

Risk Group	Gender		Total
	M	F	
Chronic alcoholic hepatopathy	108	57	165
Alcoholism without hepatopathy	32	9	41
Chronic B Hepatitis	19	4	23
B + C Hepatitis	6	—	6
Chronic C Hepatitis	13	8	21
Women taking oral contraceptives	—	59	59
Extra-liver hepatic diseases	63	47	110
Liver node incidentally detected	6	12	18
<b>Total</b>	<b>247</b>	<b>196</b>	<b>443</b>

topathy. We consider not existing a hepatopathy when the liver function tests were normal;

- B virus chronic carriers;
- C virus chronic carriers;
- Women taking oral contraceptives;
- Patients undergoing staging by extra-liver solid tumors;
- Individuals sent to further study, due to detection of liver nodes in an abdominal ultrasound.

In these patients, after filling a predefined protocol including data as: age, gender, relevant personal background, existing signs and symptoms, it was made an abdominal ultrasound (except in the selected sub-group from the existing node in a previous ultrasound). Being detected the nodes, the subsequent study includes supplementary tests guided by ultrasound and clinical aspects up to the etiologic diagnosis of the lesion concerned.

## Results

443 subjects were included (196 F; 247 M) (Table 1), with an average age of  $54.5 \pm 16.63$  years of age (limit age > 16-89 years), having been detected liver nodes through ultrasound in 65 cases (29 F; 36M), corresponding to 14,7% of the subjects studied. The average age of individuals with  $62.6 \pm 13.35$  years (age limit > 26-89 years old).

In the group of patients with chronic alcoholic hepatopathy (Table 2) made up by 165 individuals (57 F; 108 M), with an average age of  $58.33 \pm 12.26$  years

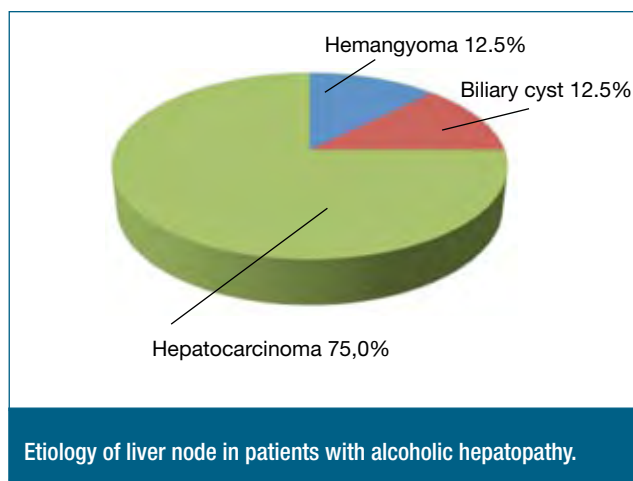


FIG. 1

TABLE II

## Liver histological changes in patients with alcohol hepatopathy

Liver histological changes	Number of patients	Liver nodes
Hepatic cirrhosis	149	8
Steatosis with fibrosis	13	—
Alc. Hepatitis with fibrosis	3	—

(limit age 25-82 years) were detected by ultrasound 8 liver nodes. After a supplementary investigation it was found the existence of hepatocellular carcinoma in six of these patients (3,6%), hemangioma in one case and a simple biliary cyst in the other (Fig. 1).

Five patients in this group (3%) were chronic carriers of B Virus and another five (3%) of C virus, but in the case of hepatocellular carcinoma, the serology was negative for such virus.

The average age of patients with hepatocarcinoma was from  $64 \pm 7.89$  years were all of male gender and had hepatic cirrhosis, histologically documented. Clinically there were stigmas of chronic hepatopathy in all cases, ascites also in all of them, weight loss in 4, jaundice in 2, hepatomegaly in 2 splenomegaly in 2 and abdominal pain complaints in one case.

In the abdominal CAT Scan there were multiple lesions in 3 of the 6 patients and the lesion biopsy by puncture was made through TAC in 3 patients and by ultrasound in the other 3.

TABLE III

## Malignant tumors and hepatic nodular lesions (metastases)

Malignant tumor			Metastasis	
Location	No. Patients	Gender Dist.	Cases No.	%
Prostate	12	12H	3	25%
Rectum	9	3F;6M	6(2F;4M)	66.7%
Colon	17	5F;12M	7(3F;4M)	41.2%
Stomach	18	9F; 9M	8(4F;4M)	44.4%
Kidney	2	2M	1M	50%
Lung	12	6F; 6 M	2(1F;1M)	16.7%
Womb	6	6F	1F	16.7%
Bladder	12	3 F; 9M	2(1F; 1M)	16.7%
Breast	4	4F	2F	50%
Gall bladder	1	1F	1F	—
Pancreas	7	6F; 1M	0	—
Thyroid	2	2F	0	—
Skin (Esp. Cel.)	1	1M	1M	—
Other	7	2F,5M	0	—

41 patients were identified (9F; 32M) with chronic alcoholism, being the average age  $45.59 \pm 14.32$  years (age limits: 21-75 years). A patient was also a B virus carrier and two of the C virus hepatitis. In this group, it was detected only one node by abdominal ultrasound, very suggestive of corresponding to a hemangioma, in a 62 years old woman without symptoms.

23 individuals were included with chronic infection by the B virus (4F; 19 M) being the changes histological: post-hepatitis cirrhosis in 5 cases, active chronic hepatitis in 6 and persistent chronic hepatitis in 7. In 11 a liver biopsy was not carried out.

The average age in this group was  $51 \pm 18.5$  years (age limits: 16-88 years) and liver nodes were detected in 4 individuals (17.4%): 1 cholangiosarcoma and 3 hepatocarcinomas (Fig. 2). These 4 patients were male, three of them referring weight loss and in the clinical exam it was seen jaundice and hepatomegaly in all of them, ascites in 2 and other stigma of chronic hepatopathy in one. Abdominal CAT scan has shown multiple nodes in three of the four cases and the biopsy puncture was guided by TAC in all patients. Liver

histological changes were of cirrhosis.

Among the 21 individuals with chronic infection by the C virus (8 F; 13 M) being the average age  $50 \pm 14.3$  years (age limits: 20-80 years), none presented liver nodes in the abdominal ultrasound.

In 6 patients it co-existed chronic infection by both the B and C virus. They were all of male gender, being the average age  $39.5 \pm 8.2$  years (age limits: 30-53 years) and in neither case there were liver nodes.

59 women taking oral contraceptives were included in this study, for less than 5 years (20 cases), between 5 to 10 years (25 cases) and over 10 years (14 cases) being the average age  $32.3 \pm 7.84$  years (age limits: 18-46 years). The ultrasound made has revealed a liver node in a case – hemangioma, in a 38 years old woman, asymptomatic.

A patients group undergoing staging for a solid malignant tumor, extra-hepatic location, has included 110 individuals (47 F; 63 M) being the average age  $65.5 \pm 13.5$  years (age limits: 28-89 years).

Liver nodes were detected in 34 cases (30.9%), matching all to metastases (Table 3).

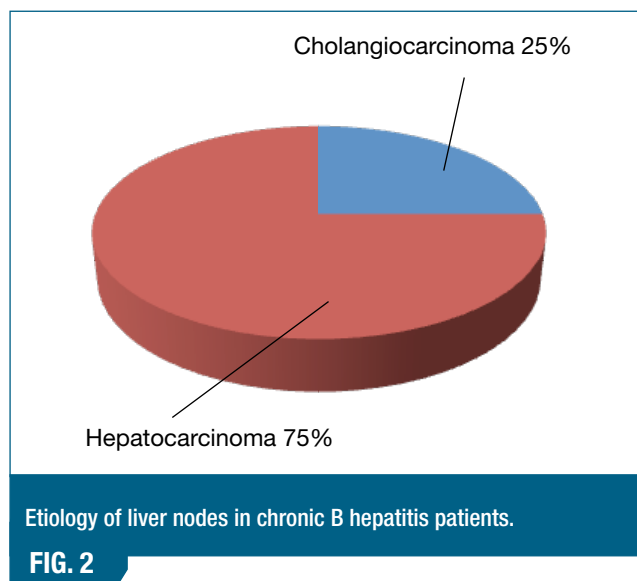
We have also studied 18 individuals (12F; 6M), sent to etiologic clarification of all hepatic node lesions detected in ultrasound, previously made. This group average age  $59.8 \pm 12$  years (age limits: 26-73 years), being the diagnosis: liver metastases (8 cases), hemangiomas (5 cases), hepatocellular carcinoma (2 cases), hepatic cholangiocarcinoma (1 case), simple biliary cyst (1 case), parasite cyst (1 case) (Fig. 3).

Metastases were due to: melanoma (1 case), colon adenocarcinoma (1 case) pancreas carcinoma (1 case), prostate cancer (1 case), gastric carcinoma (1 case); in 2 cases it was not possible to identify the primary tumor.

Hemangiomas were detected in 3 men and 2 women, all asymptomatic and with ages ranging from 43 to 70 years old.

Hepatocellular carcinomas emerged in 2 women aged 68 and 72 years old, with negative markers to B and C virus and without alcoholic drinking habits, both asymptomatic and with multiple nodes in CAT scan. Biopsy was guided by CAT scan.

The hepatic cholangiosarcoma has appeared in a 62 years old woman, asymptomatic with liver and



Etiology of liver nodes in chronic B hepatitis patients.

splenomegaly. TAC has revealed multiple nodes and the biopsy was guided by CAT Scan.

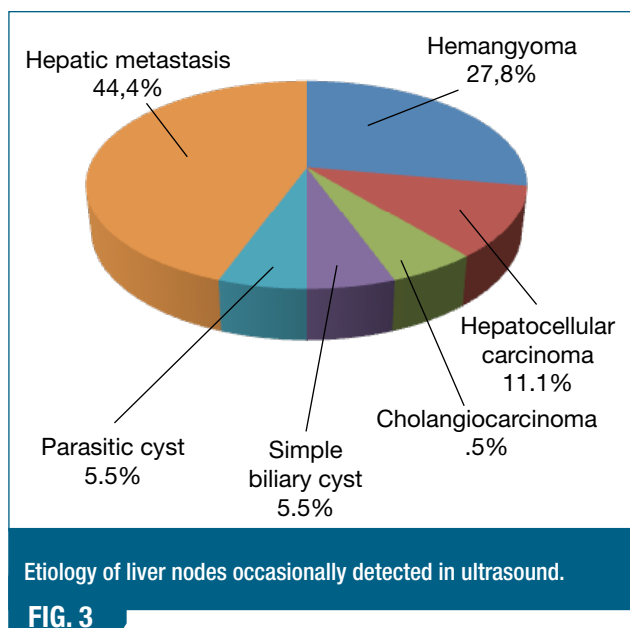
### Discussion and conclusions

Among the 65 cases of hepatic nodes detected by us around half were due to hepatic metastases.

The hepatocellular carcinoma was diagnosed in 11 patients, 6 of them with liver cirrhosis of alcoholic etiology, 3 with post-hepatitis cirrhosis B and 2 apparently without risk factors for this kind of tumor.

The 9 secondary cases to cirrhosis emerged in 9 individuals of male gender and other 2 in the female gender. These findings are in accordance with what is usually described in the literature, being referred a prevalence of cirrhosis in the cases of hepatocellular carcinoma between 60 to 90%<sup>5,6</sup> and a frank preference for the male gender.<sup>7</sup> In our patients with ethylic liver cirrhosis, hepatocellular carcinoma has emerged in 4.02 % of cases, an incidence which is similar to the one found in another study, also made in the Medicine III Service of HUC (5.2%).<sup>8</sup> In a recent prospective study, made in France, the annual incidence of hepatocellular carcinoma in patients with hepatic cirrhosis was 5.8%.<sup>9</sup>

The chronic infection by the B virus hepatitis is closely linked to the development of hepatocellular carcinoma, being responsible for most of these tumors, in certain geographic areas in which the percentage of individuals infected by this virus is very high.<sup>10,11</sup> In our study 3 hepatocellular carcinoma were detected in 23 individuals with a chronic infection



Etiology of liver nodes occasionally detected in ultrasound.

by the B virus.

The risk of hepatocellular carcinoma emerging in C virus carriers seems similar to the B virus, at least evaluating by the most recent work on such matter.<sup>10,11,12,13</sup>

The data obtained in this work suggest to have the B virus a higher rapport with the appearance of a hepatic malignant tumor, than the C virus.

The hepatic hemangioma was the benign tumor more often diagnosed (7 cases). In a group of women, taking contraceptives, it was not detected any case of adenoma, confirming the rarity of this tumor, even in the one which is considered the higher risk group.

The high percentage of cases in which were detected hepatic metastases (30.9%), particularly in gastrointestinal tumors, indicates a high trend to those tumors to be metastised to that organ, but also a later diagnostic of the primary tumor.

The data found confirm the rarity of the hepatic benign tumors and the high frequency of secondary malignant tumors.

The primary malignant tumors exist in a considerable number in our population, particularly in cirrhotic men, whether alcoholic or post-hepatitis B. The prognosis, currently so shady, in this kind of neoplasias, can only be improved through the systematic screening of these individuals which must include an abdominal ultrasound and the serial alpha-fetoprotein dosage every 6 months. ■

## References

1. Adson M.A. Mass lesions of the liver. *Mayo Clinic Proc* 1986; 61:362-368
  2. Dumas O, Barthélémy C, Audigier J C, Faut-il dépister les carcinomes hépatocellulaires sur cirrhose ? *Gastroenterol Clin Biol* 1990 ; 14 : 715-726
  3. Ishak K G, Rabin LK. Benign tumors of the liver. *Med Clin North Am* 1975; 59:995-1013
  4. Bili H, Foll Y, Boyer B, Abgrall J. Le diagnostic d'une image hyper-échogène hépatique en 1990. *Ann Gastroenterol Hepatol* 1990; 26: n° 5:203-208
  5. Johnson PJ, Williams R. Cirrhosis and the aetiology of hepatocellular carcinoma. *J Hepato* 1987; 14: 140-147
  6. Kew M C, Popper H. Relationship between hepatocellular carcinoma and cirrhosis. *Semin Liver Dis* 1984; 2: 136-146
  7. Sherlock S. Hepatic tumours. *Diseases of the liver and biliary system*. Blackwell Scientific Publication 8th Ed. 1989.
  8. Leitão J, Feio M, Sá I et al. Carcinoma hepatocelular e doença hepática celular: incidência, relações, gravidade. *Arq. Hepato-Gastroenterol Port* 2 1993; (2): 51-55
  9. Pateron D, Ganna N, Trinchet J et al. Prospective study of screening for hepatocellular carcinoma in Caucasian patients with cirrhosis. *J Hepatol* 1994; 20: 65-71
  10. Smith S C, Paauw D S, Hepatocellular carcinoma. Identifying and screening population at increased risk. *Postgraduate Medicine* 1993; 94 (8): 71-74
  11. Liang J T, Jeffers L J, Reddy R K et al. Viral pathogenesis of hepatocellular carcinoma in the United States. *Hepatology* 1993; 18: 1326-1333
  12. Kaklamani E, Trichopolous D, Tzonou A et al. Hepatitis B and C viruses and their interaction in the origin of the hepatocellular carcinoma. *JAMA* 1991; 265 (15): 1974-1976.
  13. Simonetti G R, Cammà C, Fiorello F et al, Hepatitis C virus infection as a risk factor for hepatocellular carcinoma in patients with cirrhosis. *Ann Intern Med* 1992; 116: 97-102.
- Work funded by the Comissão de Fomento da Investigação em Cuidados de Saúde do Ministério da Saúde [Health Department Commission to Promote Health Care Research.]