Research Article

Gastroenterology, Hepatology & Digestive Disorders

Hepatocarcinoma in Instituto Guatemalteco de Seguridad Social Functional Three Phase Computed Tomography as Diagnosis Tool

Sandoval G. Luis*[1], Tolaque A. Yolanda[2], Gatica Manuel[3] and Ranero Jorge[4]

[1]*Internal Medicine Attending Physician, Instituto Guatemlateco de Seguridad Social, College of Physicians and Surgeons of Guatemala, Association of Internal Medicine of Guatemala, Guatemala.*

[2]*Internal Medicine Resident, Instituto Guatemlateco de Seguridad Social, College of Physicians and Surgeons of Guatemala, Internal Medicine Residents Association, Guatemala.*

[3]*College of Physicians and Surgeons of Guatemala, Guatemalan Association of Gastroenterology Hepatology and Gastrointestinal Endoscopy, Guatemala.*

[4]*Intesive Care Unit Attending Physician, Instituto Guatemlateco de Seguridad Social, College of Physicians and Surgeons of Guatemala, Critical Care Guatemalan Association, Association of Internal Medicine of Guatemala, Guatemala.*

***Correspondence:**
Luis Fernando Sandoval García, Attending Physician, Internal Medicine, Instituto Guatemalteco de Seguridad Social, Guatemala, Tel: (502) 30342311; E-mail: lufesandoval@ufm.edu.

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ABSTRACT

Background: *Hepatocellular-carcinoma (HCC) diagnosis can be made by imaging, if imaging is not definitely we need to individualized and include additional imaging or biopsy. However is important to determine if there is cirrhotic or non-cirrhotic liver for prognosis and treatment. In this study we aimed to compare the findings obtained for liver masses between three phase computed tomography (CT) with the anatomopathological results and characterized them epidemiologically.*

Methods: *Using an observational, retrospective and analytic study, all the liver masses seen by functional three phase CT were included and compared with the pathology result during 2015 – 2017 at Instituto Guatemalteco de Seguridad Social (IGSS). Categorical variables were presented in frequency and percentages and analyzed by Chi squared of homogeneity. Normality was tested with Kolmogorov-Smirnov. Numerical data was evaluated with t-student of independent samples. At relational level a bivariate study was made, then elevated to multivariate level. To measure sensitivity and specificity we constructed receiver operating characteristics (ROC) curves and calculate area under the curve (AUC). Negative predictive value (NPV) and positive predictive value (PPV) were calculated.*

Results: *Of 76 liver masses evaluated by three phase CT, 53% were confirmed by biopsy; 84% of HCC diagnosis were non-cirrhotic livers. In ROC curves, AUC for three phase CT for all samples was 0.646, then we stratified in cirrhotic and non-cirrhotic, AUC for cirrhotic was 0.65, PPV of 0.54 and NPV of 0.69 for HCC diagnosis. AUC for non-cirrhotic patients was 0.665, PPV of 0.67 and NPV of 0.62.*

Conclusion: *Our findings were the opposite of global epidemiology, most of the liver masses diagnosed as HCC are in non-cirrhotic livers. Three phase CT can diagnose HCC with good sensitivity and specificity and it has better PPV in non-cirrhotic patients, nevertheless biopsy should be done because they are low risk patients.*

Keywords

Cirrhosis, Guatemala, Needle biopsy, Liver neoplasms, Tomography.

Introduction

According to the World Health Organization, hepatocarcinoma is the fifth most common worldwide tumor and the second cause of cancer related dead [1,2]. Is more common in male than female,

in relation 2:1 [1]. The incidence has been raisin in the last years and it will continue to rise until 2030 with the highest increase in Hispanics, African Americans and Caucasians [1]. Cirrhosis remains the most important risk factor, additional risk factors are Hepatitis B and C, alcohol, genetic hemochromatosis, non-alcoholic fatty liver disease, etc [3,4]. Guatemala has the highest incidence and mortality of hepatocellular-carcinoma (HCC) in America. Incidence in Guatemala of HCC in both sexes in 2012 was 11.6%, 13.2% for male and 10.5% for female. Liver cancer is the second cause of cancer mortality in Guatemala with 14.5% and this is the country with the highest incidence and mortality in this type of cancer in America [5].

Early diagnosis is important for curative options and improve outcomes and the detection is based in different guidelines [1]. Correlation with underlying liver disease increase mortality and only about 10% of HCCs develop in non-cirrhotic livers [2,3]. There is strong consensus that the imaging diagnosis of HCC requires multiphasic imaging, commonly used methods are three phase CT and magnetic resonance imaging (MRI) as standard test for HCC diagnosis [1,3]. If imaging is not definitely HCC and no definitely benign we need to individualized and include additional imaging or biopsy [3,4,6].

The incidence of HCC in cirrhotic patients is seventy to ninety percent (70%-90%) according to World Journal of Hepatology [6]. There are no statistical data in Guatemala as a country but previous data at IGSS showed more than expected HCC in non-cirrhotic with 71%. We used three phase CT in our diagnostic protocol and confirm it with biopsy. However three phase CT has not previously been evaluated as diagnostic test for patients with HCC in our center. Therefore we evaluate the dynamic imaging results of liver masses and compared the results against biopsy.

Materials and Methods

We conducted 3 year retrospective, observational and analytic study involving Guatemalan patients with liver masses at Hospital General de Enfermedades (HGE), IGSS. The study was conducted from January 2015 through December 2017, protocol was approved by the local research committee and by Internal Medicine Department of the hospital involved. Authors designed the study and analyzed the data, and all authors had access to the data and made the decision to submit the manuscript for publication.

Patient recruitment

The study included adults (>18 years old) hospitalized with liver mass at HGE, IGSS. Results of the functional three phase CT were obtained from Radiology Department and then compared with pathology reports at IGSS electronic medical records. Only were included adult patients who had both diagnostic studies. Mayor exclusion criteria was no found biopsy or three phase CT and previous diagnosis for HCC.

End-points

The primary study end-point was to compare the findings obtained for liver masses between three phase CT with the anatomopathological results. Our secondary end-points were: obtain the pre-test and post-test probability and characterized epidemiologically the liver masses.

Statistical Analysis

Statistical analysis was performed with PSPP 2007. Categorical variables were presented with frequency and percentages and analyzed by chi squared of homogeneity. Normality was tested with Kolmogorov-Smirnov. Numerical data were evaluated with t-student of independent samples. At relational level a bivariate study was made, then elevated to multivariate level. NPV and PPV was calculated. We also constructed a nonparametric receiver operating characteristic (ROC) curve and area under the curve (AUC) was calculated. The level of statistical significance was p<o.o5.

Results

A total of 76 patients were included, basic demographic and clinical characteristics are shown in Table 1, a total of 60 men and 16 women. The median age was 61.61 (13.95 SD (standard deviation)), liver masses mean diameter was 8.56 cm. From all the three phase CTs 42.1% made diagnosis of HCC and 68.4% of anatomopathological results were negative for cirrhosis (p=0.763). Biopsy in HCC was positive for only 5 patients for cirrhosis and 27 (84.4%) were non-cirrhotic livers (Table 2). Anatomopathological results for liver masses diagnosed 6 different pathologies: 34 for HCCs, 9 Adenocarcinoma, 7 liver metastasis and 1 choriocarcinoma, lymphoma and cholangiocarcinoma (Figure 1, panel A). After the stratification for cirrhotic and non-cirrhotic we observed that 27 of 34 HCC were in non-cirrhotic patients (Figure 1, panel B).

Characteristic		Media	SD	f	%
Age		61.61	13.95		
Mass diameter (cm)		8.56	5.37		
Sex	Female			16	21.1
	Male			60	78.9
HCC by CT	Yes			32	42.1
	No			44	57.9
Satisfactory biopsy	Yes			52	68.4
	No			24	31.6
Cirrhosis	Yes			24	31.6
	No			52	68.4

Table 1: Variables Distribution.
Abbreviations: SD: standard deviation, HCC: hepatocellular carcinoma, CT: computed tomography.

Variables		Cirrhosis		Non Cirrhosis		Total	p
		f	%	f	%	f	
Biopsy	HCC	5	15.6	27	84.4	32	0.013
	No HCC	19	43.2	25	56.8	44	

Table 2: Cirrhosis confirmed by biopsy.
Abbreviations: HCC: hepatocellular carcinoma.

The total of liver masses evaluated by functional three phase CT were analyzed, with 53.85% of HCCs confirmed by biopsy. To measure sensitivity and specificity of our diagnostic tests we constructed ROC curves (Figure 2); taking all the samples, our functional CT has AUC of 0.646 (Figure 2, panel A), PPV of 0.54 and NPV of 0.69 for HCC diagnosis. Then we stratified in cirrhotic and non-chirrotic samples, AUC for cirrhotic was 0.650 shown in Figure 2 (Panel B), a PPV of 0.25 and NPV of 0.83 was found for this group of patients. For non-cirrhotic patients AUC was 0.665, higher than the AUC for cirrhotic (Figure 2, panel C) and we found PPV of 0.67 and NPV of 0.62.

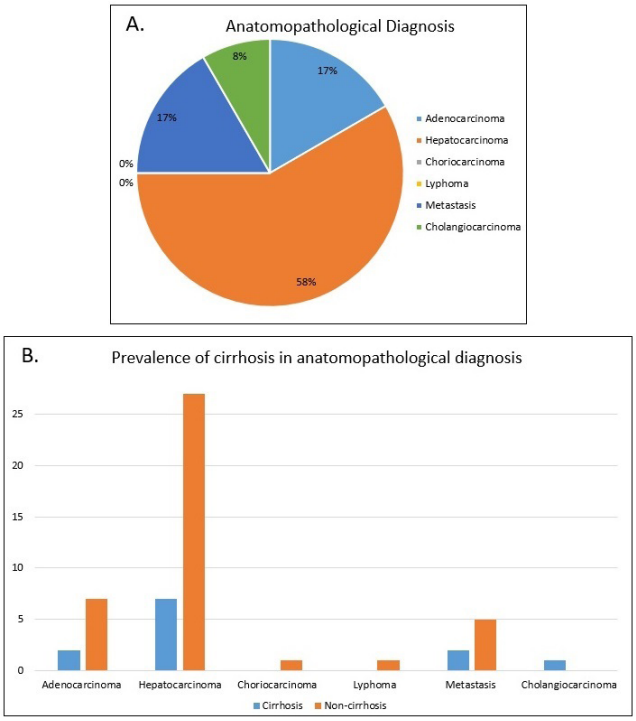

Figure 1: Anatomopathological diagnosis of liver masses, 2015-2017. Panel A shows the diagnosis obtained in anatomopathological samples. Panel B shows the prevalence of cirrhotic and non-cirrhotic liver in different diagnosis.

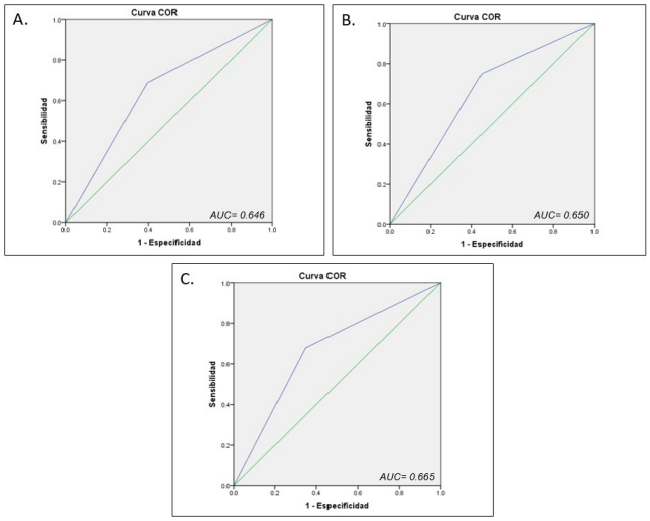

Figure 2: Receiver operating characteristic curves for three phase CT (A) ROC curve for all samples with diagnosis of hepatocarcinoma. (B) ROC curve for cirrhotic livers. (C) ROC curve for non-cirrhotic livers.

Discussion

There are several protocols for screening and diagnosis of hepatocarcinoma. The most recommended imaging is functional tomography or magnetic resonance and if it is not conclusive or generates diagnostic doubts, biopsy is the next step. It is important in addition to the diagnosis of hepatocarcinoma to determine if there is a cirrhotic vs. non-cirrhotic liver, which will help us to establish prognosis and treatment.

This study showed that liver masses in our hospital corresponded mainly to hepatocellular carcinoma, however despite the fact that data such as gender and age correspond to international data, our most important finding is the absence of cirrhosis associated to hepatocarcinoma, which was found only in 31.6%, unlike the 70-80% mentioned in world articles and reviews. It was also shown that the presence of cirrhosis was mainly in men.

Media of liver masses diameter was 8.56 cm. at diagnosis, with this data we can infer that we are doing late diagnosis in advance stages, which may be because there are not standardized screening protocols for healthy liver.

All the liver masses diagnosed by three-phase tomography were taken for biopsy, then compared both studies, tending to biopsy as a Gold standard, the three-phase tomography showed a positive predictive value of 0.54 for all hepatocarcinoma without stratification, however after the stratification the positive predictive value was 0.25 for cirrhotic and considerably higher for non-cirrhotic in 0.67 and a negative predictive value of 0.62, which allows us to establish an adequate pre-test and post-test for non-cirrhotic patients.

Despite advances in tomographies such as quadruple phase CT, CT perfusion, dual-energy CT and double arterial phase, in our study the ROC curves, PPV and NPV showed that three-phase tomography is a good diagnostic test with good sensitivity and specificity mainly in non-cirrhotic patients with AUC of 0.65, and we can infer that it´s because the radiology department is used to observe hepatocarcinoma in non-cirrhotic liver. All of our patients had biopsy because there is no approved protocol for not performing biopsy in non-cirrhotic liver for being low risk patients.

Limitations

The limitations of the study were that it was performed in a single hospital and the number of patients involved was small. The non-satisfactory biopsy percentage was high maybe because biopsy is operator dependent.

Conclusion

Hepatocarcinoma is more frequent in males and in healthy livers (81%). Three phase tomography can diagnose HCC with good sensitivity and specificity in our patients nevertheless biopsy should be done because there is no approved protocol for not performing a biopsy in non-cirrhotic liver. Three phase CT has better positive

predictive value in non-cirrhotic patients than cirrhotic.

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