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(Research Article)

Contribution of medical imaging in the diagnosis of hepatocellular carcinoma at the CNHU-HKM in Cotonou

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Abstract

Introduction: The World Health Organization (WHO) and the Global Cancer Observatory rank hepatocellular carcinoma (HCC) as the sixth most common cancer in the world and the fourth leading cause of cancer death. According to GLOBOCAN 2022, sub-Saharan Africa is a very highly endemic area. In Benin, despite the high frequency of cirrhosis and viral liver disease, local data remain limited. This study aimed to evaluate the contribution and compare the performance of medical imaging techniques (ultrasound and CT) in the diagnosis of HCC at the CNHU-HKM in Cotonou.

Methods: This was a retrospective, descriptive and analytical study conducted over a one-year period (from 23 May 2023 to 23 May 2024) using the Cotonou Cancer Registry. The study comprehensively included 118 patients suspected of HCC.

Results: The mean age of the patients was 47.46 years with a clear male predominance (sex ratio: 3.72). The main etiologies identified were viral hepatitis B (61.02%) and chronic alcoholism (37.28%). On ultrasound, hypervascular nodules on cirrhotic liver were hypervascularized on cirrhotic liver. On multiphase CT scan, HCC was characterized by arterial wash-in (94.91%) followed by portal wash-out (90.67%). CT had a higher sensitivity (98.1%) than ultrasound (85.2%), while ultrasound maintained perfect specificity (100%).

Conclusion: The complementarity of ultrasound and CT remains essential to optimize the non-invasive diagnostic management of HCC in our health context.

Keywords: Hepatocellular carcinoma; Medical Imaging; Diagnosis

1 Introduction

According to the WHO, sub-Saharan Africa and Asia are very endemic geographical areas: it is estimated that 80% of HCC cases occur there (5). With more than 38,000 new cases in 2020, primary liver cancer (PFC) is a major public health problem in sub-Saharan Africa (1). In northern countries, HCC is usually discovered early in the context of cirrhosis follow-up and mainly affects elderly subjects. On the other hand, in sub-Saharan Africa, HCC is still a late-discovery

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condition at the stage of massive tumor development with distant metastases (6). Medical imaging is a first-line diagnostic tool, including ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI).

In Benin, although the management of HCC is part of hospital practice, few specific data on this condition exist (6). In addition, his prognosis in Cotonou is poor with a median survival of two months (6). This is why we felt it was necessary to carry out a study on the contribution of medical imaging in the diagnosis of HCC at the Hubert K. Maga National Hospital and University Center in Cotonou.

2 Methodology

2.1 Material

Patients diagnosed with HCC between May 23, 2023 and May 23, 2024 in the University Clinics of Hepato-Gastroenterology (CUHGE), Internal Medicine and Palliative Care (CUMI) of the National University Hospital Center Cotonou, Benin.

2.2 Inclusion criteria

All patients diagnosed with liver cancer were included:

- Presence of hepatic nodule on liver, cirrhosis on ultrasound;
- High feto-protein alpha greater than 200 mg/ml;
- And/or hepatic nodule with wash in and wash out on ct;
- And/or hypervascularized hepatic nodule with t1 hyposignal and t2 hypersignal on mri.

2.2.1 Criteria for non-inclusion

All other types of liver cancer, including secondary liver tumors, were not included.

2.2.2 Exclusion Criteria

- Patients with HCC for whom clinical, biological and imaging data are not available;
- Patients who waived their consent during the course of the study.

2.3 Sampling

We made an exhaustive selection of all HCC cases during our study period. The sample size was 118 patients.

2.3.1 Collection techniques

Initially, patient selection was carried out from cancer registries and cases not included according to our criteria were eliminated. The first data are collected from the reports and information available in the registers and the rest by telephone calls.

2.4 Data analysis and processing

The Kobocollect application had been used for data collection using a form published on https://ee.kobotoolbox.org/x/JuDpB04N, pre-tested and validated. After entering the data collected in the Kobocollect software, we checked for any input errors and the consistency of the codified data. Then, MS Excel 2019 software was used for data cleaning and organization.

Finally, we used the R software (R-4.4.2) for data processing and analysis. The significance threshold had been set at \alpha = 0.05.

2.5 Descriptive analysis

Before performing the statistical tests, we had carried out a descriptive analysis of the variables. For quantitative variables, we calculated the mean, standard deviation, median, and quartiles. These position and dispersion parameters provide insight into the distribution of the data and identify any asymmetries. For qualitative variables, we established absolute and relative frequencies in order to analyze their distribution in the sample.

2.6 Statistical tests

2.6.1 Test de Shapiro-Wilk

The Shapiro-Wilk test was used to assess the normality of quantitative variables. This test tests the hypothesis that a sample follows a normal distribution.

The assumptions are as follows:

- H0: The data follow a normal distribution.
- H1: The data does not follow a normal distribution.

The test statistic is denoted W, and a p-value of less than 0.05 indicates a rejection of the normality hypothesis.

2.6.2 Test de Mann-Whitney

When the condition of normality was not met for the comparison of two independent groups, we used the Mann-Whitney (or Wilcoxon-Mann-Whitney) test, which is a nonparametric test to compare the distributions of two independent samples. It was used as an alternative to Student's t-test when assumptions of normality are not satisfied.

The assumptions of the test are:

- H0: the two groups have the same distribution.
- H1: The distributions of the two groups are different.

The test is based on the calculation of the U statistic, and if the p-value obtained is less than 0.05, the assumption of equality of distributions is rejected, indicating a significant difference between the groups.

2.6.3 Fisher's Exact Test

Finally, to analyze the association between two qualitative variables, we used the Fisher exact test, which is particularly suitable for 2x2 contingency tables when the numbers are small (< 5). This test is based on the following assumption:

- H0: There is no association between the two variables.
- H1: An association exists between the two variables.

If the p-value is less than 0.05, the hypothesis of independence is rejected, indicating a significant relationship between the variables studied.

2.7 Evaluation of the diagnostic performance of CT ultrasound in the diagnosis of HCC

The evaluation of the performance of a diagnostic test is based on the comparison with the gold standard, in this case anatomical pathology. For each examination, the results are classified in a 2×2 contingency table, distinguishing between true positives (VPs), true negatives (VNs), false positives (FPs) and false negatives (FNs). From these values, several indicators are calculated: sensitivity, which measures the ability of the test to detect sick patients; specificity, which measures the ability to correctly identify non-sick patients; positive and negative predictive values; likelihood ratios; and correctly classified proportion, which corresponds to the fraction of correctly identified patients among the entire population. 95% confidence intervals (CI95%) were calculated using the exact Clopper–Pearson method, suitable for small sample sizes and extreme proportions. The direct comparison of the performance of the two examinations on the same patients was carried out using the McNemar test, which considers only cases that are discordant between the two tests.

2.8 Ethical and regulatory aspects

The authorization of the Director of the hospital was requested and obtained. The heads of department concerned had been notified before any inclusion of cases in accordance with the memo N°1755/MS/CNHU-HKM/PCME/SSMR of August 29, 2024 authorizing data collection. The study was conducted in strict compliance with professional secrecy and the data collection was done anonymously by the identification numbers.

3 Results

3.1 Anthropopometric parameters

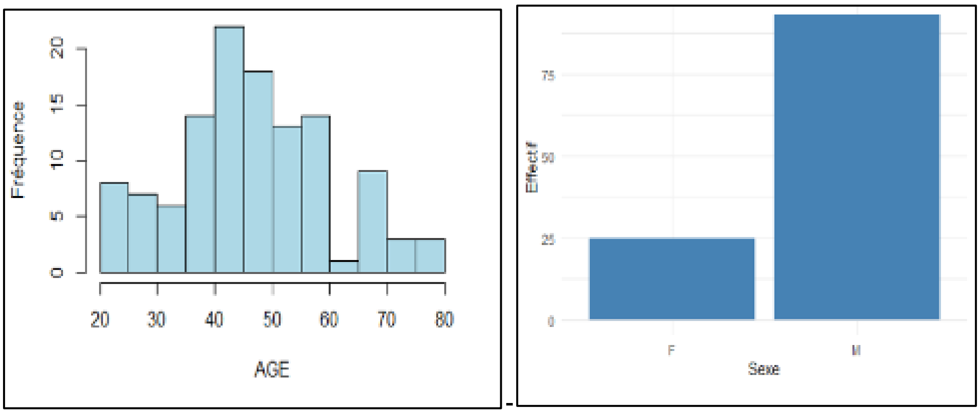

Figure 1 Distribution of HCC by age and sex

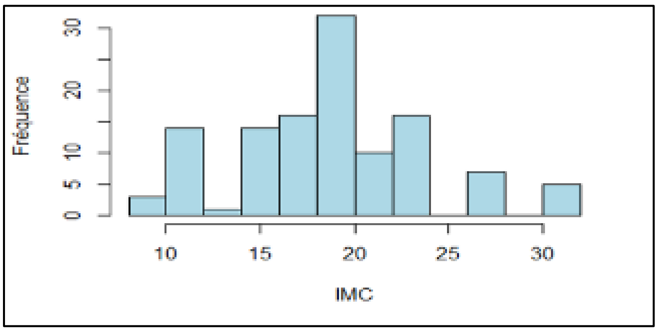

Figure 2 Distribution of HCC by BMI

The graphs in Figure 1 illustrate the age and sex distribution of HCC. From the analysis of its graphs, it appears that the average age of the study population was 47.46 years ± 13.40 years with extremes from 23 to 76 years. Age seems to be normally distributed in the population (median of 47.50 is almost equal to the average), so the majority of the population could have an age that is around 48 years old. In our study population, there was a male predominance with 78.81% and a sex ratio of 3.7. In addition, Figure 2 shows the distribution of HCC according to BMI. It appears that the mean BMI was 18.69 ± 4.98 with extremes ranging from 9.14 to 31.22 and a median of 18.93; suggesting that BMI appeared to be normally distributed.

3.2 Socio-demographic parameters

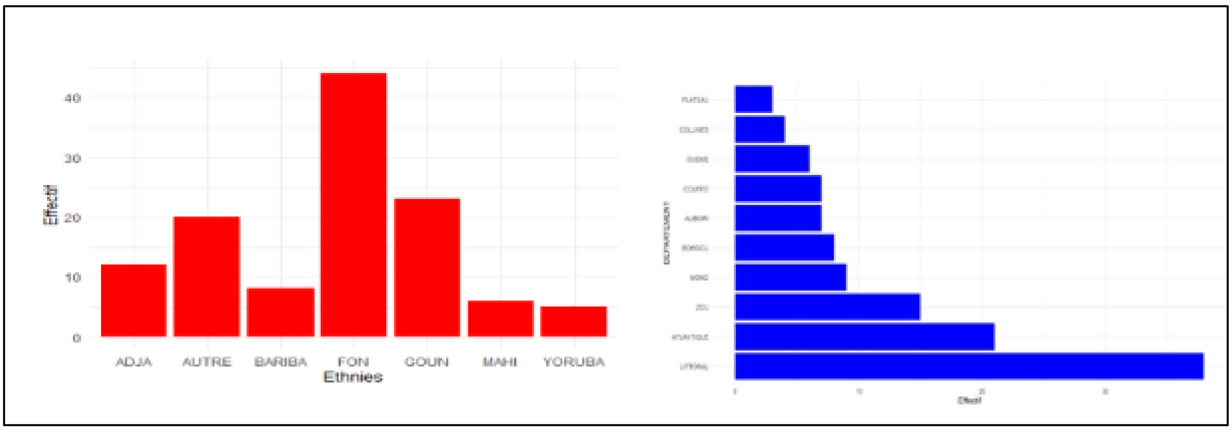

Figure 3 Distribution of HCC by ethnicity and department of origin

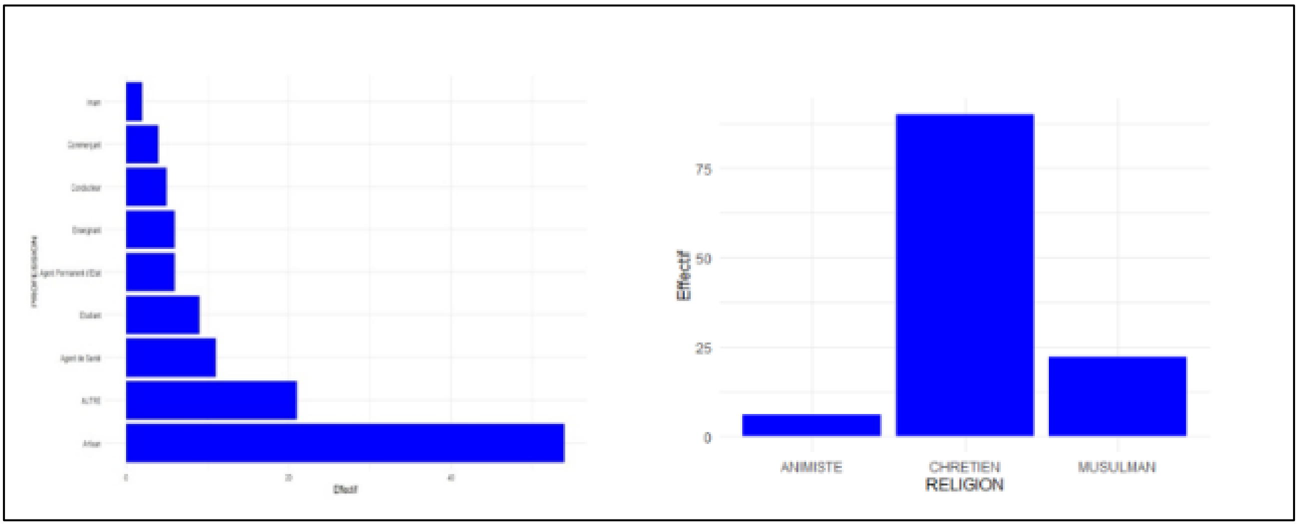

Figure 4 Distribution of HCC by occupation and religion

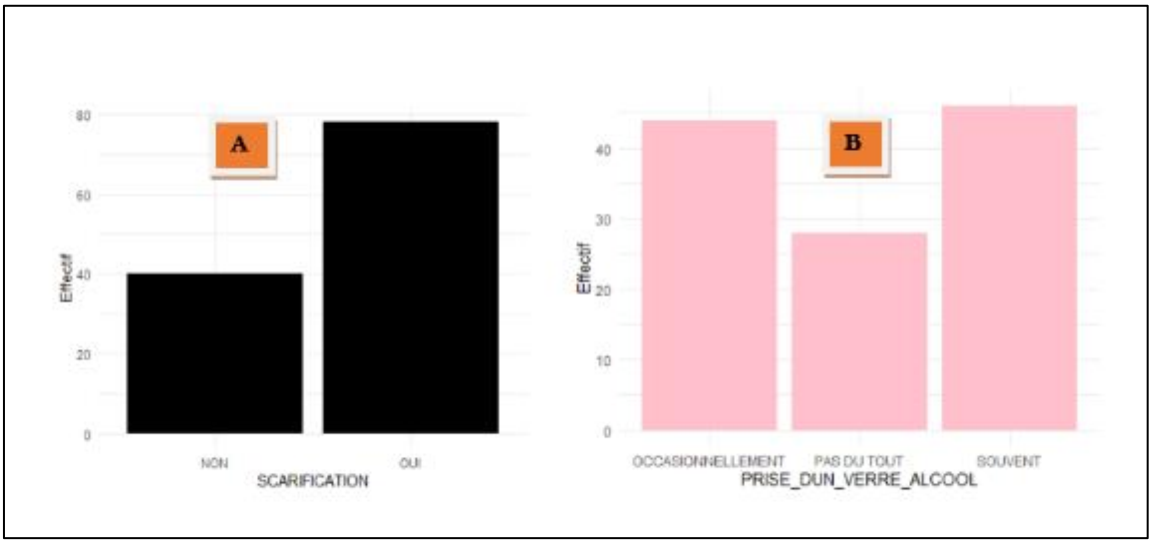

Figure 5 Distribution of HCC by presence or absence of scarification (A) and alcohol intake (B)

On the socio-demographic level, hepatocellular carcinoma (HCC) was evaluated according to ethnicity, department of origin, profession, religion, presence or absence of scarification (A) and alcohol consumption (B). The distributions of HCC are shown in the graphs in Figures 3 to 5. Thus, the majority ethnic group in our study population was the FON (37.29%) followed by the GOUN (26.17%) (Figure 3). Of the ten departments, the coastal region was the most represented in our study population with 32.20% of cases (Figure 3). The Christian religion was the most important (76.27%) (Figure 4). Regarding habits and lifestyles, 38.98% of this population often consumes alcoholic beverages, and this is done occasionally in 37.28% of cases (Figure 5). As a risk factor for viral contamination, the notion of scarification was the main factor found in the majority of cases (66.10%). In terms of occupation, craftsmen and farmers were mainly represented in 55% (Figure 4).

3.3 Clinical parameters

The clinical picture of HCC carriers in our study was dominated by ascites (83.05%), hepatomegaly (72.88%), PH (71.18%), weight loss (58.47%), asthenia (64.40%), anorexia (44.06%) and hepatic colic (39.83%).

Table 1 Distribution of HCC according to clinical parameters

Clinical aspects	**Number of cases**	**%**
Reason for consultation		
Right hypochondrial pain	38	32,20
Oedemato-ascitic syndrome	35	29,66
*Alteration of general condition	13	11,01
Digestive bleeding	11	9,32
Functional signs		
Fever	17	14,40
Melena	8	6,77
Hematemesis	9	7,62
Weight loss	69	58,47
Asthenia	76	64,40
Anorexia	52	44,06
Hepatic colic	47	39,83
Physical Signs		
Ascites	98	83,05
Hepatomegaly	86	72,88
http	84	71,18
Jaundice	22	18,64
Hepatic encephalopathy	15	12,71

3.4 Biological parameters

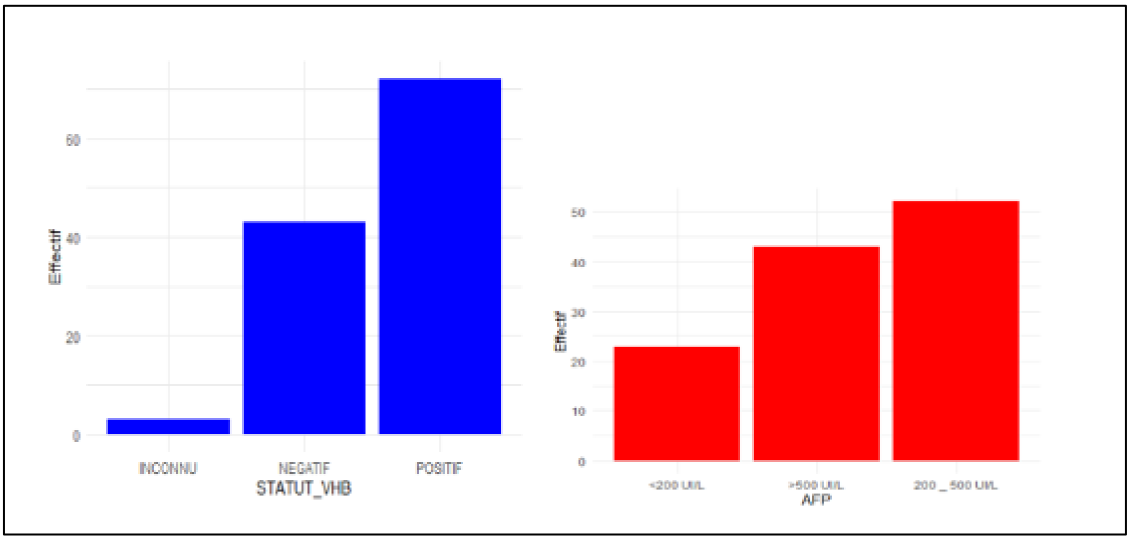

Figure 6 Distribution of HCC by hepatitis B (HBV) seropositivity and alpha-fetoprotein level

The majority of patients were HBV positive (61.02%). The biological marker of hepatocellular carcinoma, AFP, was frequently between 200 and 500 IU/L.

3.5 Diagnostic profile suggestive of hcc in medical imaging

Table 2 Different hepatic aspects observed on ultrasound

Hepatic parameters		**AQHI**	**%**
Size	Normal	8	6.77
	Hepatomegaly	110	93.22
Contours	Regular	6	5.08
	Irregular	112	94.91
Parenchyma	Homogeneous	11	9.32
	Heterogeneous	107	90.67
Number of Tumors	Unique	35	29.66
	Multiple	69	58.47
	Diffuse	14	11.86
Size of the tumor	Small	55	46.61
	Large	63	53.38
Echogenecity of the Tumor	Heterogeneous	71	60.16
	Hypoechoic	11	9,32
	Hyperechoic	36	30,50

Table 3 Different extra-tumoral abnormalities observed

Extra-tumor abnormalities		**AQHI**	**%**
Ascites		97	82.20
Trombose	Portale	49	41.52
	IVC	3	2.54
Lymphadenopathy		103	87.28
Splenomegaly		13	11.01
Vesicular lithiasis		6	5.08
Blister sledding		16	13.55
Bile duct dilation		5	4.23
Mass syndrome		82	69.49

Table 4 Different aspects of HCC on CT

CT ASPECTS		**AQHI**	**%**
Tumor density	Hyperdense	21	17.79
	Heterogeneous	52	44.06
	Hypodense	9	7.62
	Mixed	36	30.50
Vascular kinetics	Wash-in	112	94.91
	Wash-out	107	90.67

The abdominal ultrasounds performed revealed a high rate of hepatomegaly (93.22%), heterogeneous (90.67%) and irregular contours (94.91%) in our study population (Table I). The majority of HCC nodules were heterogeneous (60.16%) (Table I). The extra-tumoral signs observed were mainly ascites (82.20%), portal thrombosis (41.52%), lymphadenopathy (87.28%) and mass syndromes (67.39%) (Table II). As far as CT is concerned, vascular kinetics during the different phases of injection of the contrast medium, namely wash-in (94.91%) and whash-out (90.67%) seem to be pathognomonic of HCC (Table IV).

3.6 Comparative study of the performance of ct ultrasound in the diagnosis of hcc

The cohort included 118 patients, including 108 confirmed HCCs and 10 healthy patients according to pathology. The raw results show that the ultrasound detected 92 positives, while the CT scan detected 112 positives.

3.6.1 Ultrasound

Table 5 shows the contingency for ultrasound.

Table 5 Ultrasound Contingency Table

Ultrasound	CHC+	CHC –	Total
Positive test	92	0	92
Negative test	16	10	26
Total	108	10	118

Ultrasound had a sensitivity of 85.2% (95% CI: 77.0–91.4%) and a specificity of 100% (95% CI: 69.2–100%). The positive predictive value is perfect (100%), while the negative predictive value is lower (38.4%), reflecting the 16 HCCs missed by this review. The proportion of correctly classified patients is 86.4%. The low negative predictive value emphasizes that ultrasound may miss some HCCs, although it has perfect specificity, making it reliable to avoid unnecessary biopsies.

3.6.2 Scanner

The contingency table for the CT scan is shown below

Table 6 CT Contingency Table

Multiphase Scanner	CHC+	CHC –	Total
Positive test	106	6	112
Negative test	2	4	6
Total	108	10	118

The CT scan has a very high sensitivity of 98.1% (95% CI: 93.4–99.8%) and a lower specificity of 40% (95% CI: 12.2–73.8%). The positive predictive value is 94.6% and the negative predictive value is 66.7%. The correctly classified proportion is 93.2%, reflecting that the CT scan correctly identifies the majority of patients, at the cost of a few false positives. The CT scan is an ideal tool for diagnostic confirmation.

3.7 Direct comparison and mismatch table

To compare the two examinations on the same patients, we constructed the following discordance table:

Table 7 Direct comparison and mismatch table

	Scanner +	Scanner –	Total
Ultrasound +	92	0	92
Ultrasound –	20	6	26
Total	112	6	118

The results show that the CT scan outperforms ultrasound in terms of sensitivity, detecting almost all HCCs. Ultrasound, although less sensitive, retains a perfect specificity. The two examinations are therefore complementary.

4 Discussion

Our study consisted in evaluating the contribution of Medical Imaging techniques in the diagnosis and monitoring of HCC at the CNHU-HKM in Cotonou, Benin. A similar study on the contribution of imaging in the positive diagnosis of hepatocellular carcinoma was carried out in 2023 in Algeria by Hichem et al (24). Similarly, in 2015, in China, Haoran et al conducted a study that focused on a specific aspect of the topic, the concept of liver imaging reports, data systems, consensus, and the controversy of key practice guidelines. Like the latter, we carried out a descriptive and analytical study with retrospective data collection that allowed us to achieve our objectives. The limitations of this work were the retrospective nature of the study, which gave access to some incomplete and unusable records (the low socio-economic level of the patients was a factor limiting the performance of certain explorations, in particular MRI). Despite these difficulties, this study has the merit of showing the reality of hospital management of HCC in our country.

The sampling method consisted of an exhaustive selection of all patients meeting the inclusion criteria. During our collection, a total of 31 unusable and incomplete records (HCC patients for whom clinical, biological, and imaging data are not available, and escaped or deceased patients) were excluded. Despite all these limitations, we believe that our study provides sufficient answers to improve diagnosis and patient management.

During the period of our study, which is 12 months, we studied a total of 118 cases of patients hospitalized for HCC, 10 of which were finally disproved. This number is significantly higher than the 54 found by Sehonou et al (6) over a relatively longer period in their study on the epidemiological and diagnostic profile of hepatocellular carcinoma in the internal medicine department of the CNHU-HKM in Cotonou. This major difference denotes the centralization of data in a single medical record regardless of the various services of the patient's stay. On the other hand, in France in 2020, Aubé et al (20) reported 256 cases over the same period. This difference in the number of cases is probably due to the accessibility of a state-of-the-art technical platform. In our study, ultrasound and CT are requested in 98.89% of cases, which is close to the results of Sehonou et al (97.12%) (6).

In our series, the hospital frequency of HCC was 2.6% comparable to data from Sehonou et al in Benin (2.5%) (6) and Nikiéma et al in Burkina Faso (2.4%) (26). Our result was higher than that of Ayuso et al (1.23%) (27) in Senegal.

On the other hand, this frequency is lower than the 6.1% reported by Trinchet Jean Claude in France (28) and the 6.5% described by Diarra M. et al in Mali (29). These objectified differences in frequency could be related to the variability of the methodology.

The mean age was 47.46 years ± 13.40 years with extremes from 23 years to 76 years. Similar results were reported by Nikièma et al in Burkina Faso (45.6 ± 12.5 years) (26) and Sehonou et al in Benin (50.2 years) (6). A male predominance with 78.81% and a sex ratio of 3.72 was noted in our series. Similarly, the mean BMI was 18.69 ± 4.98 with extremes ranging from 9.14 to 31.22 and a median of 18.93 characteristics of weight loss. Our results were consistent with Kanté's results (3), Sehonou et al in Benin (6) and Nikièma et al in Burkina Faso (26) all of whom reported a male predominance with 76.7%, 85.2% and 75.7% respectively and a high proportion of weight loss noted of more than 50% for the most part.

Weight loss (58.47%), lasthenia (64,40%), anorexia (44,06%) and hepatic colic (39,83) were the main clinical signs noted while hepatocellular insufficiency (42.37%) with an AFP level between 200 and 500 IU/L was the main biological parameter characterizing HCC in our series. Our results were similar to those of Sehonou et al in Benin who reported a 61.1% weight loss rate; 59.9% asthenia; 18.5% liver failure with elevated AFP levels in 70% of cases (6). In 2008 in Mali, Salimou Kanté had also reported similar clinical-biological data in his study on the ultrasound aspects of HCC, as well as Hichem et al in Algeria (24). According to them, HCC is most often discovered in a field of chronic liver failure with a high level of alpha-feto-protein.

In a context of suspected HCC, we can say that the search for clinical-biological signs such as weight loss, asthenia and liver failure associated with the elevation of alpha-feto-protein (AFP) levels makes it possible to strengthen the diagnosis.

Positive testing for hepatitis B virus (HBV) as a risk factor was predominant (61.02%). This strong association of HCC with the hepatitis B virus was also reported by Hichem et al in Algeria (75.5%) (24). These results confirm the strong relationship between viral hepatitis B and HCC. Effective preventive measures are needed to decrease the prevalence of these infections and therefore HCC.

Ultrasound exploration allowed a diagnostic approach to the different evolutionary stages of HCC. Indeed, our study found multiple involvement (58,47%) and mostly large (53,38%). These results are in line with the 54% reported by Sehonou et al in Benin (6). In our series, as in that of Sehonou et al in Benin (6) and Hichem et al in Algeria (24), the majority of nodules had a heterogeneous appearance. On the other hand, Nikièma et al in Burkina Faso (26) noted a hyperechoic predominance of nodules.

Ascites (82.20%), portal thrombosis (41.52%) and lymphadenopathy (87,28%) are extrahepatic lesions that reinforce the diagnosis of HCC. These results were consistent with those of Sehonou et al in Benin (6) (81.5% ascites and 50% portal hypertension) and Nikiéma et al in Burkina Faso (26) (51.4% ascites and 48.7% portal hypertension). On the other hand, our result was lower than those of Hichem et al in Algeria (24) which reported 42.3% ascites, 11.9% portal thrombosis and 12.1% lymphadenopathy.

The unique vascular kinetics, namely the wah-in (94.91%) and the wash-out (90.67%) on the CT scan was very suggestive of HCC in our series. These results were in line with those reported by Diop Ba in Côte d'Ivoire (98.7%) (21), as well as Aubé et al in France (96.69%) (20).

According to Rode Agnès, in the context of cirrhosis, the discovery of a nodular lesion of more than 20 mm in diameter, hypervascular in nature during the arterial phase of the exploration after injection of contrast medium, regardless of the imaging mode (ultrasound with contrast, CT scan or MRI), and presenting a "wash out" or "washout" during the acquisitions carried out in the portal or late phase (three, or even five minutes) has a positive predictive value of being a hepatocellular carcinoma greater than 95%.

According to the 2010 Bruix recommendations, Barcelona criteria, such a presentation in the context of liver disease authorizes, even with a single examination modality, to make the diagnosis of HCC without recourse to biopsy.

Also, our study clearly highlights the superiority of CT scan over ultrasound in the diagnosis of HCC. The high sensitivity of the CT scan (98.1%) observed in our series confirms its status as a reference examination, already highlighted by international recommendations (AASLD, OncoBFC, SNFGE), due to its ability to highlight the vascular kinetics typical of HCC. This performance is consistent with data reported by Tasu et al. (4) which recognize the high precision of CT scan, especially for multiple or small nodules.

The use of MRI was required. However, this approach to imaging is very difficult to access in our country.

The concordant boxes include 92 patients who were positive on both examinations and 6 patients who were negative on both examinations. The discrepancies concern 20 patients: no patient was positive on ultrasound and negative on CT, while 20 patients were negative on ultrasound and positive on CT scan.

The McNemar test, based on these discrepancies, showed a value of $\chi^2 = 18.05$ with $p = 2.15 \times 10^{-5}$, confirming that CT detects significantly more cases than ultrasound.

5 Conclusion

Hepatocellular carcinoma (HCC) remains a major public health problem in Benin, due to its high incidence and late diagnosis. This study has made it possible to better characterize the affected population as well as the main risk factors, dominated by hepatitis B and chronic alcoholism. The establishment of the diagnostic profile suggestive of HCC by ultrasound and computed tomography confirmed the usefulness of these two imaging techniques as a first-line tool. Ultrasound, accessible and non-invasive, remains a fundamental examination in the initial detection. However, computed tomography was distinguished by its superior ability and its high sensitivity to characterize lesions, in particular thanks to multiphase analysis which makes it possible to highlight the typical HCC enhancements. The results of this work argue in favor of increased valorization of imaging techniques, intensification of screening programs and improved access to advanced modalities for better management of HCC in Benin.

This study also opens up perspectives, in particular the more systematic integration of standardized protocols, the improvement of the continuous training of operators and the establishment of imaging databases allowing better epidemiological surveillance.

Compliance with ethical standards

Acknowledgments

The authors thank the administrative authorities of the Hubert Koutoukou MAGA National University Hospital Center (CNHUHKM) for authorizing this research. They also express their thanks to the various health workers in these health facilities who facilitated the collection of data.

Disclosure of conflict of interest

The authors declare that there is no conflict of interest in relation to this research and this article.

Statement of ethical approval

The research project has the authorization of the management of the Hubert Koutoukou MAGA National University Hospital Center (CNHUHKM) before the start of the study.

Statement of informed consent

The free and informed consent of patients and their parents, as appropriate, was obtained prior to their inclusion in the study. The anonymity of the data has been respected. All the data collected was analysed and presented anonymously.

Data availability statement

The data is available in the Excel database and is used as part of an end-of-cycle dissertation. These documents are accessible through a link that can be shared upon reasoned request.

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