ELSEVIER

Contents lists available at ScienceDirect

Annals of Hepatology

journal homepage: www.elsevier.es/annalsofhepatology



Original article

Prognosis of hepatocellular carcinoma in the French overseas territories and comparison with a tertiary center in mainland France



Alolia Aboikoni^{a,1,*}, Manon Allaire^{b,c,1}, Dominique Louvel^a, Marthe Alogo A. Nwatsok^a, Paul Ngock Dime^a, Ala Ouni^a, Larissa Tangan^a, Magaly Zappa^{d,e}, Kinan Drak Alsibai^{e,f}, Maylis Douine^{e,g}, Mathieu Nacher^{e,g}, Lucie Catherine^{h,i}, Cecilia Busso^j, Nathalie Ganne^{c,j}, Moana Gelu-Simeon^{h,i}

- ^a Service d'Hépato-Gastroentérologie, CHU de Guyane, site de Cayenne, 97300 Cayenne, French Guiana
- ^b AP-HP Sorbonne Université, Hôpital Universitaire Pitié-Salpêtrière, Service d'Hépato-gastroentérologie, Paris, France
- ^c INSERM UMR 1138, Centre de recherche des Cordeliers, 75006 Paris, France
- ^d Service d'Imagerie médicale, CHU de Guyane, site de Cayenne, 97300 Cayenne, French Guiana
- ^e Université de Guyane, Cayenne, 97300 Cayenne, French Guiana
- ^f Service d'anatomie pathologie, CHU de Guyane, site de Cayenne, 97300 Cayenne, French Guiana
- g CIC INSERM 1424, CHU de Guyane, site de Cayenne, 97300 Cayenne, French Guiana
- h Univ Antilles, Univ Rennes, Insern, EHESP, Irset (Institut de recherche en santé, environnement et travail) UMR_S 1085, F-97110 Pointe-à-Pitre, France
- ⁱ Service d'Hépato-Gastroentérologie, CHU de la Guadeloupe, F-97110 Pointe-à-Pitre, France
- ^j AP-HP Université Sorbonne Paris Nord, Hôpitaux Universitaires Paris Seine Saint-Denis, site Avicenne, Service d'Hépatologie, Bobigny, France

ARTICLE INFO

Article History: Received 17 April 2025 Accepted 5 August 2025 Available online 12 September 2025

Hepatocellular carcinoma Prognosis French overseas territories French guiana Overall survival Outcome

ABSTRACT

Introduction and Objectives: Limited data are available on the prognosis of hepatocellular carcinoma (HCC) in the French overseas territories (FOT). This study aimed to describe the characteristics and outcomes of patients diagnosed with HCC in FOT, comparing them to those from a tertiary center located in Île-de-France (IDF). Materials and Methods: We retrospectively included all patients with HCC diagnosis between 2013 and 2023 in the FOT and IDF. Socio-demographic and medical data were collected, with the first treatment performed and survival data. Overall survival was analyzed using Kaplan-Meier methods and Cox proportional hazards models. Results: A total of 1114 patients were included (FOT 11%, IDF 89%). FOT patients had higher rates of hepatitis B (36% vs. 16%, p<0.001) and worse liver function (defined by higher MELD scores and fewer Child A cases) at HCC diagnosis. In contrast, IDF patients had a higher prevalence of MASLD (29% vs. 16%, p=0.004). HCC was diagnosed at more advanced stages in FOT compared to IDF, with 71% vs. 49% (p<0.001) of cases outside Milan criteria and 29% vs. 5% (p<0.001) in BCLC-D, leading to a significantly lower survival in FOT (median 9 vs. 23 months, p=0.02).

Conclusions: HCC patients in FOT have a poorer prognosis compared to IDF, with diagnoses at more advanced stages, limiting curative treatment options. These findings highlight the need for improved access to care and screening strategies for earlier diagnosis of HCC in FOT.

© 2025 Fundación Clínica Médica Sur, A.C. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

Abbreviations: 95% CI, 95% confidence interval; AFP, Alpha-fetoprotein; ALD, Alcohol-related liver disease; Atezobev, Atezolizumab—bevacizumab; BCLC, Barcelona clinic liver cancer; BMI, Body mass index; CT, Computed tomography; EV, Esophageal varices; FOT, French overseas territories; GPS, General practitioners; HBV, Hepatitis B virus; HCC, Hepatocellular carcinoma; HCV, Hepatitis C virus; HR, Hazard ratio; LT, Liver transplantation; MASLD, Metabolic dysfunction-associated steatotic liver disease; MELD, Model for end-stage liver disease; MRI, Magnetic resonance imaging; OS, Overall survival

 $\label{lem:email_addresses: a.aboikoni@gmail.com} \end{center} \begin{tabular}{ll} Aboikoni), moana.simeon@chuguadeloupe.fr (M. Gelu-Simeon). \end{tabular}$

1. Introduction

Hepatocellular carcinoma (HCC), the most frequent primary form of liver cancer, is a significant global health challenge due to its high morbidity and mortality. It is the sixth most common cancer worldwide by incidence and the third leading cause of cancer-related deaths [1]. Annually, over 800,000 new cases of HCC are diagnosed, and approximately 700,000 deaths are attributed to the disease. Its prevalence varies geographically, with the highest incidence rates observed in Asia and sub-Saharan Africa [2]. In France, cirrhosis and liver cancer account for 15,000 and

^{*} Corresponding author.

¹ Co first author

A. Aboikoni, M. Allaire, D. Louvel et al.

Annals of Hepatology 31 (2026) 102120

10,000 deaths per year, respectively [3,4]. The number of new HCC cases has risen significantly over the decades with around 11,000 new cases in 2023, and HCC became the leading cause of registration on the liver transplant list [5].

Despite advances in medical care, the overall survival (OS) of patients with HCC is relatively poor. The 5-year survival rate varies between 5% and 30% worldwide; in France it is 18% [4]. This is mainly due to late diagnosis, which explains why only 25% of patients are eligible for curative treatment at diagnosis such as resection, ablation or transplantation, worldwide [6]. In France, the rate of patients accessing curative treatment progressively increased, from 23 and 25% [7,8] between 2009 and 2012, to 30% in 2015–2017 and 40% in 2019–2021 [9,10].

The French overseas territories (FOT) have administrative statuses that are similar to mainland France; they share the same universal health system and health insurance. However, they are very different in terms of epidemiology and have specific cultural contexts that may be relevant to HCC. Indeed, the prevalence of hepatitis B, the attitudes towards vaccination, the alcohol consumption, the prevalence of obesity and diabetes are different from mainland France. Furthermore, poverty is more frequent and hampers access to care in a context of low specialized health professional density, notably in French Guiana. All the above raise the question that the epidemiology and prognosis of HCC in the FOT may be quite different from mainland France [11–18]. Yet epidemiological data on HCC in the FOT remains limited [19].

This retrospective study thus aimed to compare OS between HCC patients from two FOT (French Guiana and Guadeloupe) and a tertiary French metropolitan center located in Île-de- France (IDF), focusing on HCC characteristics, staging at diagnosis, treatment approaches by Barcelona Clinic Liver Cancer (BCLC stage), and OS across different BCLC stages in these regions.

2. Patients and Methods

2.1. Study population

This retrospective study included all patients with a diagnosis of HCC discussed in multidisciplinary tumor board meetings at three care centers: Avicenne in mainland France (IDF), Guadeloupe and French Guiana between 2013 and 2023. FOT referred to the combination of Guadeloupe and French Guiana.

The study was approved by the local ethics committee of Guade-loupe (A147_12/11/2024), and data were collected with the consent of patients who were informed individually orally. For patients in mainland France (IDF), clinical data were collected with the consent of patients who were informed individually both orally and by an information notice within the framework of the authorization to establish the AP-HP Data Warehouse filed in July 2016 with the National Commission for Information Technology and Civil Liberties (no. 1980120).

Eligibility criteria were as follows: (1) newly diagnosed HCC, confirmed either histologically or through non-invasive imaging criteria using contrast-enhanced CT or MRI, according to EASL guidelines [20]; (2) cases discussed in the multidisciplinary tumor board meetings of Guadeloupe, French Guiana, and IDF between 2013 and 2023.

Exclusion criteria included: (1) absence of follow-up data, (2) unavailable BCLC classification; (3) previous diagnosis of HCC.

2.2. Study protocol and endpoints

Demographic data, medical history, current treatments, cirrhosis etiology, liver function (Child-Pugh score, MELD score), and tumor characteristics (number/size of lesions, vascular invasion, extrahepatic spread, and AFP levels) were collected at the time of initial HCC

diagnosis. Patients were classified according to BCLC stage, Milan criteria and AFP score as already described. The presence of clinically significant portal hypertension was defined by the presence of esophageal varices (EV) detected on upper endoscopy. Varices were classified into four grades: no varices, grade 1 (small, straight varices), grade 2 (moderately enlarged, beady varices), and grade 3 (large, nodular, or tumor-like varices). Grades 2 and 3 were considered large varices. The selection of HCC treatment during multidisciplinary tumor board meetings was guided by the available treatment options and the expertise of each center. The diagnosis of HCC was made on liver biopsy, or on typical cross-sectional imaging (CT or MRI). The diagnosis of metabolic dysfunction-associated steatotic liver disease (MASLD) was made in the presence of compatible histology or, in the absence of histology, in the presence of a metabolic context (type 2 diabetes, obesity, arterial hypertension and/or dyslipidemia). For the purpose of this study, the first treatment performed after the multidisciplinary tumor board meeting was recorded. Curative treatment was defined as the initial treatment consisting of either ablation, liver resection, or liver transplantation. Patients who benefited from liver transplantation during follow-up were recorded. Follow-up ended in December 2024.

The primary endpoint of the study was to compare the overall survival—defined as the time from HCC diagnosis to death from any cause—between FOT and IDF.

The secondary endpoints were to (i) describe the characteristics of the populations of FOT and IDF, with a particular focus on HCC features and staging at diagnosis, (ii) compare the treatments proposed by each center according to BCLC stage, and (iii) compare the overall survival across different BCLC stages between the centers.

2.3. Statistical analysis

Patient characteristics were summarized as medians with interquartile ranges (IQR) for continuous variables, and as counts (percentages) for categorical variables. To compare continuous and categorical data between groups, the Mann-Whitney U test and Fisher's exact test were employed, respectively. Event times were calculated from the diagnosis of HCC, with event incidence estimated using the Kaplan-Meier method. Group comparisons were made using the log-rank test. Associations between variables and clinical events were evaluated using univariate Cox proportional hazards models. Variables with a P-value < 0.05 were included in a multivariate Cox regression model, with a backward stepwise elimination method employed to identify independent predictors. The hazard ratios (HR) and corresponding 95% confidence intervals (CIs) were calculated for each factor. The proportional hazards assumption was verified graphically and using the Schoenfeld and scaled Schoenfeld residuals method.

3. Results

3.1. Baseline characteristics of the patients

Between 2013 and 2023, 1114 patients with a new diagnosis of HCC met the inclusion criteria (FOT 11%, n=116; IDF 89%, n=998). Among these patients, 7% were diagnosed through a surveillance programs, 46% due to the presence of symptoms, and 47% were identified on imaging in the absence of symptoms—such as in the context of abnormal liver function tests. Patients in FOT had a higher prevalence of Hepatitis B virus (HBV) (36%) compared to IDF (16%) (p<0.001). MASLD was primarily more frequent in IDF (29%) compared to FOT (16%) (p=0.004). There was no significant difference in the etiology of alcohol (p=0.40). The MELD score at diagnosis was higher in FOT, with a median of 12 (10–19), compared to 9 (8–11) in IDF (p<0.001) (Table 1), and

only 43% of patients in FOT were classified as Child-Pugh A, compared to 70% in IDF (p<0.001).

3.2. More advanced HCC in FOT associated with higher mortality

HCC patients in FOT were diagnosed in 71% of cases outside Milan criteria, compared to 49% in IDF (p<0.001). Additionally, 29% of patients in FOT were classified as BCLC-D at diagnosis, compared to 5% in IDF (p<0.001) (Table 1). Only 22% of patients in FOT were able to receive curative treatment compared to 51% in IDF (p<0.001), and 44% of patients received best supportive care as first treatment in FOT compared to 17% in IDF (p<0.001) (Table 2).

Median OS in the whole cohort was 21.2 months, with 60%, 37% and 27% at 12, 36 and 60 months. Median OS was significantly higher in IDF compared to FOT (23 vs. 9 months, p=0.02) (Fig. 1A). In multivariate analysis, MELD score (HR=1.04, 95% CI [1.02–1.07]), BCLC-C stage (HR=1.85, 95% CI [1.44–2.36]), BCLC-D stage (HR=6.38, 95% CI [4.02–10.12]), and AFP serum level (HR=1.01, 95% CI [1.01–1.10]) were associated with higher mortality, while access to curative treatment (HR=0.30, 95% CI [0.24–0.38]) was linked to OS in the whole cohort (Table 3).

There was no significant difference in overall survival between the 2 regions according to whether or not curative treatment was performed (Fig. 2A, 2B). In IDF, older age (HR=1.02, 95 % CI [1.01–1.02], p<0.001), MELD score (HR=1.04, 95 % CI [1.02– 1.07], p=0.005), BCLC-C (HR=1.80, 95 % CI [1.41–2.31], p<0.001) and BCLC-D (HR=5.72, 95 % CI [3.40–9.06], p<0.001) were independently associated with higher mortality, while access to curative treatment (HR=0.30, 95 % CI [0.23–0.37], p<0.001) was associated with lower mortality (Supplementary Table 1). In FOT, BCLC-D (HR=6.20, 95 % CI [1.98–19.40], p=0.002) was associated

with higher mortality while access to curative treatment (HR=0.24, 95% CI [0.08-0.71], p=0.009) was an independent prognostic factor (Supplementary Table 2).

Finally, during a median follow-up of 15.2 months (4-104) of the whole cohort, 43 patients received liver transplantation (4%) including 36 patients in IDF (4%) and 7 patients in FOT (6%). Among them, 24 patients were classified BCLC-0/A, 9 BCLC-B, 8 BCLC-C and 2 BCLC-D respectively. Of these 43 patients, 8 received a liver transplant as their first treatment after diagnosis.

3.3. Similar outcomes in BCLC-0/A across the centers

Among 441 BCLC-0/A patients, MASLD was the most frequent etiology of underlying chronic liver disease in IDF (35% vs. 7%, p=0.001) while it was HBV infection in FOT (42% vs. 15%, p<0.001). Liver function, portal hypertension surrogate markers and HCC characteristics were not statistically different across IDF and FOT (Supplementary Table 3). In 92% of cases, HCC were classified in Milan criteria in IDF compared to 73 % in FOT (p=0.004). Surgery was performed more frequently in FOT (39%) compared to IDF (7%, p<0.001), especially liver transplantation in first line (13% vs. 0.5%, p=0.001), IDF where 80% of the patients were treated by ablation (Table 2). The median survival for BCLC-0/A patients was not statistically different across regions (45 months in IDF vs. 77 in FOT, p=0.18) (Fig. 1B). In multivariate analysis, older age (HR=1.03, 95% CI [1.01–1.05], p=0.004), higher BMI (HR=1.05, 95% CI [1.01-1.09], p=0.02) and higher MELD score (HR=1.10, 95 % CI [1.05–1.15], p<0.001) were independently associated with mortality, while the access to curative treatment was associated with increased survival (HR=0.47, 95 % CI [0.29-0.77], p=0.002) (Table 4).

Table 1Baseline characteristics at first diagnosis of HCC.

Baseline characteristics		Available Data	Whole cohort N=1114	Available data for IDF	IDF N=998	Available data for FOT	FOT N=116	P \$
Gender (male)*		1114	927 (83)	998	829 (83)	116	98 (84)	0.70
Age (years)°		1114	67 (59-74)	998	67 (59-4)	116	63 (56-70)	0.005
Body mass index (Kg/m2)°		950	26 (24-29)	840	27 (24-30)	110	24 (22-27)	< 0.001
Obesity*		950	218 (23)	840	198 (24)	110	20 (19)	0.30
Type 2 Diabetes*		1078	439 (41)	963	403 (42)	115	36 (31)	0.03
Cirrhosis*		1114	955 (86)	998	848 (85)	116	107 (92)	0.03
HCC diagnosed during surveillance pr	ograms*	431	30(7)	315	13 (4)	116	17 (15)	< 0.001
Etiologies of liver disease	ALD*	1114	550 (49)	998	497 (50)	116	53 (46)	0.40
	MASLD*	1114	307 (28)	998	288 (29)	116	19 (16)	0.004
	Hepatitis B*	1114	203 (18)	998	161 (16)	116	42 (36)	< 0.001
	Hepatitis C*	1114	270 (24)	998	250 (25)	116	20 (17)	0.07
	Mixed etiologies with at least viral infection*	1114	158 (14)	998	139 (14)	116	19 (16)	0.50
	Mixed etiologies with at least alcohol consumption*	1114	258 (23)	998	238 (24)	116	20 (17)	0.11
Liver function And Portal Hypertension	•		650 (67)		610 (70)		40 (43)	
features	Child-Pugh B*	964	240 (25)	870	205 (24)	94	35 (37)	< 0.001
	Child-Pugh C*		74(8)		55 (6)		19 (20)	
	MELD°	877	9 (8-12)	796	9 (8-11)	81	12 (10-19)	< 0.001
	No EV*		496 (58)		461 (59)		35 (48)	0.06
	EV (regardless the size)*	849	353 (42)	776	315 (41)	73	38 (52)	
	Large size EV*		211 (25)		180 (34)		31 (41)	0.20
HCC features	In Milan HCC*	1090	529 (48)	981	497 (51)	112	32 (29)	< 0.001
	AFP score ≤ 2*	1003	601 (60)	908	566 (62)	95	35 (37)	< 0.001
	BCLC-0/A*		441 (39)		410 (41)		31 (23)	
	BCLC-B*	1114	203 (18)	998	185 (19)	116	18 (16)	< 0.001
	BCLC-C*		384 (34)		351 (35)		33 (28)	
	BCLC-D*		86 (8)		52 (5)		34 (29)	
	More than 3 HCC lesions*	1089	227 (21)	981	194 (20)	108	33 (31)	0.009
	Size of the largest lesion (mm)°	1035	38 (23–70)	934	36 (22–70)	101	60 (30–100)	< 0.001
	Tumor size > 5cm*	1035	360 (35)	934	307 (33)	101	53 (52)	< 0.001
	Vascular invasion*	1104	278 (25)	989	232 (23)	115	46 (40)	< 0.001
	Extrahepatic lesions*	1052	117 (11)	937	84(9)	115	33 (29)	< 0.001
	Serum AFP (ng/ml)°	1070	14 (5–316)	966	13 (5–220)	104	209 (5–6800)	< 0.001

^{*}Number (percentage); "median [range]; \$Pearson's Chi-squared test; Fisher's exact test; Wilcoxon rank sum test, comparison between FOT and IDF.

ALD: alcoholic liver related disease; AFP: alpha-fetoprotein; BCLC: Barcelona Clinic Liver Cancer; EV: esophageal varices; FOT: French overseas territories; HCC: hepatocellular carcinoma; IDF: Ile de France; MASLD: Metabolic dysfunction-associated steatotic Liver disease; MELD score: Model for End-Stage Liver Disease.

Table 2 First HCC treatments received after HCC diagnosis.

Baseline characteristics	Whole cohort N=1114	IDF N=998	FOT N=116	P ^{\$}
Whole cohort				
Liver transplantation*	8 (0.8)	2 (0.2)	6(4)	< 0.001
Liver resection*	62 (6)	49 (5)	13 (11)	
Ablation*	454 (41)	451 (45)	3(3)	
TACE*	143 (13)	133 (13)	10(9)	
TARE*	13(1)	12 (0.8)	1(1)	
External radiotherapy*	2 (0.2)	0(0)	2(2)	
Systemic therapy*	216 (19)	186 (19)	30 (26)	
Best supportive care*	216 (19)	165 (17)	51 (44)	
BCLC-0/A	. ,	, ,	` ,	
Liver transplantation*	6 (1.5)	2 (0.5)	4(13)	< 0.001
Liver resection*	41 (9)	28 (7)	12 (39)	
Ablation*	331 (75)	328 (80)	3 (10)	
TACE*	30 (7)	26 (6)	4(13)	
TARE*	6 (1.5)	5 (1.5)	1(3)	
External radiotherapy*	1 (0.1)	0(0)	1(3)	
Systemic therapy*	4 (0.9)	4(1)	1(3)	
Best supportive care*	20(5)	17 (4)	5 (16)	
BCLC-B	. ,	. ,	` ,	
Liver transplantation*	1 (0.5)	0(0)	1(5)	< 0.001
Liver resection*	16 (8)	16 (9)	0(0)	
Ablation*	52 (26)	52 (28)	0(0)	
TACE*	73 (36)	71 (38)	2(11)	
TARE*	1 (0.5)	1 (0.5)	0(0)	
External radiotherapy*	0(0)	0(0)	0(0)	
Systemic therapy*	33 (16)	21 (11)	12 (63)	
Best supportive care*	27 (13)	24 (13)	3(11)	
BCLC-C	. ,	` ,	` ,	
Liver transplantation*	1 (0.2)	0(0)	1(3)	< 0.001
Liver resection*,°	6(2)	5 (1.4)	1(3)	
Ablation*,°°	71 (18)	71 (20)	0(0)	
TACE*	40 (10)	36 (10)	4(12)	
TARE*	6 (1.6)	6 (1.6)	0(0)	
External radiotherapy*	1 (0.2)	0(0)	1(3)	
Systemic therapy*	178 (46)	161 (46)	17 (52)	
Best supportive care*	81 (21)	72 (21)	9 (27)	

BCLC: Barcelona Clinic Liver Cancer; FOT: French overseas territories; HCC: hepatocellular carcinoma; IDF: Ile de France; TACE: trans arterial chemoembolization; TARE: trans arterial radioembolization.

- * Number (percentage).
- \$ Pearson's Chi-squared test, comparison between FOT and IDF.
- ° For BCLC-C patients, 4 patients with vascular invasion and 2 with extrahepatic lesion underwent resection as first treatment.

3.4. Less access to curative treatments for BCLC-B in FOT

Except for a higher rate of HBV infection in FOT compared IDF (33% vs. 14%, p=0.04), as well as a higher AFP level (674 vs. 11 ng/ml, p=0.02) and a lower number of patients within AFP score \leq 2 (21% vs. 49%, p=0.05), the characteristics of the population were comparable between the 2 groups, especially regarding liver function (Supplementary Table 4). In IDF, more BCLC-B patients had access to ablation and surgical treatment (37% vs 1%, p=0.007), whereas systemic therapy was more frequently prescribed in FOT for this population of patients (63% vs. 11%, p<0.001) (Table 2). Median OS was 19.2 months in IDF compared to 8.7 months in FOT (p=0.36) (Fig. 1C). AFP score \leq 2 (HR=0.50, 95% CI [0.35–0.72], p<0.001) and curative treatment (HR=0.48, 95% CI [0.33–0.69], p<0.001) were independently associated with lower mortality (Table 5).

3.5. Better survival when curative approaches in BCLC-C patients

Median OS was not statistically different between IDF and FOT (7.8 months vs. 8.52 months) (Fig. 1D). In FOT compared to IDF, patients presented with significant higher MELD (12 vs. 9, p=0.009),

extrahepatic lesions (45% vs. 25%, p=0.01) and HBV infection (45% vs. 21%, p=0.001) (Supplementary Table 5). Curative treatment proportion was not statistically different across regions (6% (3% liver transplantation, 3% liver resection) in FOT vs. 21.4% (20% ablation, 1.4% liver resection) in IDF, p=0.13) (Table 2) and was an independent prognostic factor (HR=0.32, 95% CI [0.21–0.58], p<0.001), as well as an AFP score \leq 2 (HR=0.65, 95% CI [0.44–0.95], p=0.02) (Table 6).

3.6. Poorer prognosis in French Guiana

Patients from French Guiana exhibited worse clinical characteristics compared to those from other centers. Liver function was significantly more impaired, with 81% of patients presenting a Child-Pugh score of B or C, compared to 44% in Guadeloupe and 30% in IDF (p<0.001). The median MELD score was 16 for French Guiana, compared to 10 for Guadeloupe and 9 for IDF (p<0.001). Patients from French Guiana were more frequently classified as BCLC stages D (49% vs. 17% in Guadeloupe and 5% in IDF, p<0.001). They also had larger HCC (median size of the largest lesion: 100 mm vs. 37 mm and 36 mm, p<0.001), more vascular invasion (60% vs. 27% in Guadeloupe and 23 % in IDF, p<0.001), higher rates of extrahepatic metastases (42% vs. 20% and 9%, p<0.001), and significantly elevated AFP levels (median: 530 ng/mL vs. 32 ng/mL and 13 ng/mL, p<0.001) (Supplementary Table 6). Moreover, patients in French Guiana were less likely to receive curative treatment, with 64% receiving exclusively best supportive care, compared to 31% in Guadeloupe and 17% in IDF (p<0.001, Supplementary Table 7). Median OS was 2.2 months in French Guiana compared to 34.5 months in Guadeloupe and 22.8 months in IDF (p=0.02) (Fig. 1F).

4. Discussion

This study is the first to provide a detailed analysis of the prognosis, tumor characteristics, and liver function profiles of HCC patients in FOT. It revealed that HCC was diagnosed at more advanced stages and in patients with more impaired liver function in FOT compared to a tertiary center (IDF), significantly limiting curative treatment options. Additionally, mortality was significantly higher in FOT than in mainland France.

In the whole cohort, the median OS was significantly lower in FOT compared to IDF. However, no significant difference in OS was observed between IDF and FOT when stratified by BCLC classification. The higher proportion of BCLC-D cases in FOT, which are associated with shorter OS, likely explains the poorer outcomes in the global cohort. This finding was further supported by the multivariate analysis, which identified the BCLC-D stage as an independent predictor of increased mortality. These disparities were particularly marked in French Guiana, where 49% of patients were classified as BCLC-D, compared to 17% in Guadeloupe and 5% in IDF. The outcomes observed in French Guiana differed significantly from those in Guadeloupe and IDF, with less favorable results characterized by more advanced disease stages, greater liver function impairment, and a higher frequency of best supportive care being administered. The situation of French Guiana closely mirrors that observed in Mayotte, highlighting regional disparities in disease progression and less access to curative treatments due to lack of specialists in these regions and sometimes, the need to cross the ocean to find them [21]. French Guiana and Guadeloupe differ significantly from the IDF region, particularly the Val-de-Marne locality where the tertiary center in this study is based. Socioeconomic conditions are more precarious in the FOT, with average household incomes of €10,990 in French Guiana, €15,770 in Guadeloupe, and €24,270 in IDF, and poverty rates of 50%, 34%, and 17.2%, respectively [22-24]. Educational levels are also lower: 49.5% of the population in French Guiana and $37.8\,\%$ in Guadeloupe have no qualifications, compared to $18.7\,\%$ in IDF, while only 34.1% and 41.3% hold baccalauréat degree or higher,

^{°°} For BCLC-C patients, among the 71 patients who underwent ablation, 15 presented vascular invasion and 56 were classified BCLC-C due to their performance status score.

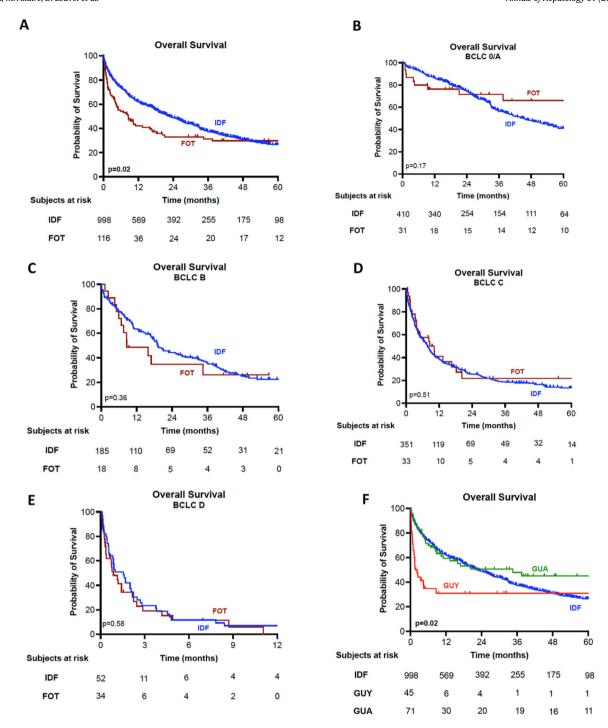


Fig. 1. Overall survival in patients with a first diagnosis of HCC.

- A. OS according to FOT and IDF in the whole cohort.
- B. OS according to FOT and IDF in BCLC 0/A patients.
- C. OS according to FOT and IDF in BCLC B patients.
- D. OS according to FOT and IDF in BCLC C patients.
- $\operatorname{E.}$ OS according to FOT and IDF in BCLC D patients.
- F. OS according to GUA, GUY and IDF.

BCLC: Barcelona Clinic Liver Cancer; FOT: French overseas territories; GUA: Guadeloupe; GUY: French Guiana; HCC: Hepatocellular carcinoma; IDF: Île de France. Results represented using the Kaplan-Meier Method with the log-rank test. The numbers of patients at risk are figured under the x-axis.

versus 60.9% in IDF [22–24]. Medical resources are scarcer in the FOT. In 2023, French Guiana has per 100,000 inhabitants 121 general practitioners (GPs) and 120 specialists, including 3 hepatogastroenterologists. In comparison, per 100,000 inhabitants, Guadeloupe has 145 GPs, 163 specialists (4 hepatogastroenterologists), and IDF has 1115 GPs, 2086 specialists, including 60 hepatogastroenterologists

[25]. Access to care is further hindered by economic barriers, long wait times, and transport issues, with 28–30% of residents in Guade-loupe and French Guiana forgoing medical care [26,27]. Public transport use is limited (2.8% in French Guiana, 5.4% in Guadeloupe vs. 48.5% in IDF), and reliance on cars—often unaffordable for vulnerable populations—can further restrict access to healthcare, such as

Table 3Baseline predictive factors of mortality for the whole cohort (Cox proportional hazard regression models).

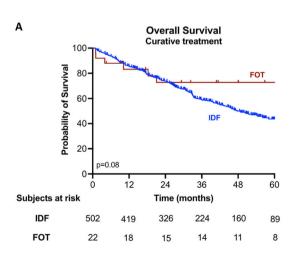
	Available data (n=1114) 1114 1114 950 950 1078 1114 1114 1114 1114 1114 1114 1114 11	Alive (n=386)	Death (n=728)	Į	Jnivariate analy	rsis	N	Aultivariate ana	alysis
	(n=1114)			HR	95 % CI	p value	HR	95 % CI	p value
Gender (male)*	1114	299 (77)	628 (86)	0.77	0.62, 0.95	0.02	0.99	0.75, 1.31	0.96
Age (years)°	1114	67 (57-73)	67 (59-75)	1.01	1.00, 1.01	0.04	1.01	1.01, 1.02	< 0.001
Body mass index (Kg/m2)°	950	27 (24-29)	26 (23-29)	0.99	0.97, 1.00	0.13			
Obesity*	950	83 (24)	135 (23)	0.97	0.80, 1.17	0.72			
Type 2 Diabetes*	1078	142 (38)	297 (42)	1.02	0.88, 1.19	0.75			
Cirrhosis*	1114	324 (84)	631 (87)	1.15	0.93, 1.42	0.21			
ALD*	1114	153 (40)	397 (55)	1.24	1.07, 1.44	0.003	1.21	0.99, 1.47	0.07
MASLD*	1114	108 (28)	199 (27)	0.89	0.75, 1.04	0.15			
Hepatitis B*	1114	84 (22)	119 (16)	0.88	0.72, 1.07	0.20			
Hepatitis C*	1114	108 (28)	162 (22)	0.80	0.67, 0.95	0.01	0.93	0.74, 1.17	0.54
Child-Pugh A*+	964	275 (80)	375 (60)	-	_	-			
Child-Pugh B*+		53 (25)	187 (30)	2.14	1.53, 2.99	< 0.001			
Child-Pugh C*+		14 (4)	60 (10)	6.51	3.57, 11.9	< 0.001			
MELD°	877	9 (7-11)	10 (8-13)	1.07	1.06, 1.09	< 0.001	1.04	1.02, 1.07	0.002
EV (regardless the size)*	849	108 (36)	245 (44)	1.32	1.11, 1.56	0.001	1.18	0.97, 1.44	0.11
Large size EV*+	849	65 (29)	146 (38)	1.35	1.10, 1.66	0.005			
In Milan HCC*+	1090	252 (66)	277 (39)	0.35	0.30, 0.41	< 0.001			
AFP score $\leq 2^*$ +	1003	277 (75)	324 (51)	0.36	0.30, 0.42	< 0.001			
BCLC-0/A*	1114	217 (56)	221 (30)	- 0.66	- 1.57, 2.40	-	_	_	_
BCLC-B*	1114	60 (16)	143 (20)	1.19	2.76, 3.94	< 0.001	1.13	0.85, 1.51	0.40
BCLC-C*	1114	93 (24)	287 (39)	2.43	8.58, 14.97	< 0.001	1.85	1.44, 2.36	< 0.001
BCLC-D*	1114	16 (4)	77 (11)			< 0.001	6.38	4.02, 10.12	< 0.001
More than 3 HCC lesions*+	1089	40 (10)	187 (26)	2.78	2.34, 3.29	< 0.001			
Size of the largest lesion (mm)°+	1035	30 (20-50)	54 (25-80)	1.01	1.01, 1.01	< 0.001			
Tumor size > 5cm*+	1035	84 (22)	276 (42)	2.62	2.24, 3.07	< 0.001			
Vascular invasion*+	1104	50 (13)	228 (32)	3.56	3.02, 4.19	< 0.001			
Extrahepatic lesions*+	1052	18 (5)	99 (15)	4.06	3.25, 5.06	< 0.001			
Serum AFP (ng/ml)°	1070	8 (4–67)	25 (5-531)	1.01	1.00, 1.01	< 0.001	1.01	1.01, 1.10	0.005
Curative treatment*	1114	259 (67)	271 (37)	0.22	0.19, 0.26	< 0.001	0.30	0.24, 0.38	< 0.001
FOT*	1114	43 (11)	73 (10)	1.34	1.05, 1.71	0.02	0.97	0.64, 1.46	0.88

*Number (percentage); °median [range].

ALD: alcoholic liver related disease; AFP: alpha-fetoprotein; BCLC: Barcelona Clinic Liver Cancer; EV: esophageal varices; FOTI: French overseas territories; HCC: hepatocellular carcinoma; MASLD: Metabolic dysfunction-associated steatotic Liver disease; MELD score: Model for End-Stage Liver Disease.

surveillance programs (22–24). Despite these observations, median OS in the entire cohort was comparable between Guadeloupe and IDF, possibly due to a higher rate of curative surgical treatments in Guadeloupe compared to French Guiana. In 2014, Guadeloupe began standardizing its multidisciplinary tumor board meetings with

French metropolitan centers to evaluate patients' eligibility for liver transplantation. This initiative likely contributed to the increased access to surgical treatments observed in the current series, with 17% and 8%, of patients eligible for resection and liver transplantation, respectively, compared to only 12% and 4% respectively, in a



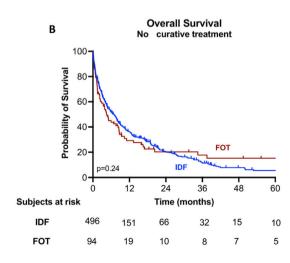


Fig. 2. Overall survival in patients with a first diagnosis of HCC.

A. OS according to FOT and IDF in curative treatment.

 $\ensuremath{\mathsf{B}}.$ OS according to FOT and IDF in no curative treatment.

BCLC: Barcelona Clinic Liver Cancer; FOT: French overseas territories; GUA: Guadeloupe; GUY: French Guiana; HCC: Hepatocellular carcinoma; IDF: Île de France. Results represented using the Kaplan-Meier Method with the log-rank test. The numbers of patients at risk are figured under the x-axis.

⁺ In Milan HCC, AFP score ≤ 2, More than 3 HCC lesions, Size of the largest lesion (mm), Tumor size > 5 cm, Vascular invasion, extrahepatic lesions were not entered in the multivariate analysis in order to avoid collinearity with BCLC classification, as well as Child-Pugh score to avoid collinearity with MELD, and as well as large size EV to avoid collinearity with EV (regardless the size.

Table 4Baseline predictive factors of mortality for BCLC-0/A patients (Cox proportional hazard regression models).

	Available data (n=441)	Alive (n=219)	Death (n=222)	Į	Jnivariate analy	/sis	Multivariate analysis		
				HR	95 % CI	p value	HR	95 % CI	p value
Gender (male)*	441	173 (79)	186 (84)	0.80	0.56, 1.15	0.23			
Age (years)°	441	67 (58-72)	69 (62-76)	1.03	1.01, 1.04	< 0.001	1.03	1.01, 1.05	0.004
Body mass index (Kg/m2)°	404	27 (24-29)	27 (25-30)	1.04	1.01, 1.07	0.006	1.05	1.01, 1.09	0.02
Obesity*	404	46 (22)	55 (28)	1.31	0.96, 1.79	0.09			
Type 2 Diabetes*	382	91 (42)	116 (53)	1.33	1.02, 1.74	0.03	1.02	0.73, 1.43	0.91
Cirrhosis*	441	182 (83)	196 (88)	1.15	0.77, 1.73	0.49			
ALD*	441	94 (43)	121 (55)	1.30	1.00, 1.69	0.06			
MASLD*	441	68 (31)	76 (34)	1.18	0.89, 1.56	0.25			
Hepatitis B*	441	48 (22)	27 (12)	0.60	0.40, 0.90	0.01	0.92	0.54, 1.52	0.72
Hepatitis C*	441	62 (28)	54 (24)	0.88	0.65, 1.20	0.42			
Child-Pugh A*	400	182 (90)	151 (76)	- 2.36	- 1.38, 4.03	-			
Child-Pugh B*+		20(10)	47 (24)			0.001			
MELD°	409	8 (7-9)	10 (8-12)	1.10	1.06, 1.14	< 0.001	1.10	1.05, 1.15	< 0.001
EV (regardless the size)*	381	60 (31)	78 (42)	1.34	1.00, 1.80	0.048	1.35	0.97, 1.88	0.07
Large size EV*	381	34 (22)	48 (34)	1.27	0.89, 1.80	0.19			
In Milan HCC*	440	197 (90)	202 (91)	0.99	0.61, 1.58	0.95			
AFP score $\leq 2^*$	431	190 (88)	186 (86)	0.68	0.46, 1.00	0.06			
Size of the largest lesion (mm)°	338	24 (18-31)	25 (20-35)	1.01	1.00, 1.01	0.02	1.01	0.99, 1.01	0.50
Tumor size > 5cm*	338	20 (9)	18 (8)	1.16	0.72, 1.88	0.55			
Serum AFP (ng/ml)°	434	5 (3-18)	8 (4–37)	1.00	1.00, 1.00	< 0.001	1.00	0.99, 1.01	0.25
Curative treatment*	441	194 (89)	179 (81)	0.42	0.30, 0.59	< 0.001	0.47	0.29, 0.77	0.002
FOT*	441	20 (9)	11 (5)	0.63	0.33, 1.19	0.15			

^{*}Number (percentage); °median [range].

ALD: alcoholic liver related disease; AFP: alpha-fetoprotein; BCLC: Barcelona Clinic Liver Cancer; EV: esophageal varices; FOT: French overseas territories; HCC: hepato-cellular carcinoma; MASLD: Metabolic dysfunction-associated steatotic Liver disease; MELD score: Model for End-Stage Liver Disease.

previous study conducted prior to this period [28]. The situation in French Guiana is further complicated by a shortage of specialists in hepatology, radiology, oncology and surgery. Cancer care remains limited, both diagnostically and therapeutically. Until 2023, there were no practicing oncologists in the region, leading to the establishment of a partnership with an oncological center in Lyon (mainland France) as early as 2009. However, access to specialized care—

requiring travel to mainland France—is limited to individuals with social security coverage, excluding a significant portion of the population, particularly those of foreign origin living in precarious conditions [29]. The average density of hepatogastroenterologists during the study period was just 1.6 per 100,000 inhabitants in French Guiana, compared to 4.5 per 100,000 in Guadeloupe [25]. This shortage likely impacted the quality of chronic liver disease management,

Table 5Baseline predictive factors of mortality for BCLC-B patients (Cox proportional hazard regression models).

	Available data	Alive (n=60)	Death (n=143)	1	Univariate analy	sis	M	lultivariate an	alysis
	(n=203)			HR	95 % CI	p value	HR	95 % CI	p value
Gender (male)*	203	49 (82)	133 (93)	0.68	0.36, 1.29	0.23			
Age (years)°	203	67 (57-75)	66 (59-74)	1.01	1.00, 1.03	0.17			
Body mass index (Kg/m2)°	170	27 (24-29)	26 (24-29)	0.98	0.94, 1.02	0.36			
Obesity*	170	10 (19)	25 (21)	1.19	0.76, 1.86	0.44			
Type 2 Diabetes*	191	18 (32)	49 (37)	1.21	0.85, 1.72	0.30			
Cirrhosis*	203	54 (90)	121 (85)	0.89	0.56, 1.42	0.62			
ALD*	203	28 (47)	88 (62)	1.26	0.90, 1.76	0.18			
MASLD*	203	15 (25)	34 (24)	0.89	0.61, 1.31	0.56			
Hepatitis B*	203	10(17)	21 (15)	0.99	0.62, 1.59	0.98			
Hepatitis C*	203	14(23)	31 (22)	0.90	0.60, 1.34	0.59			
Child-Pugh A*	172	41 (80)	89 (73)	- 0.81	- 0.31-2.16	- 0.68			
Child-Pugh B*		10(20)	32 (26)						
MELD°	149	9 (8-12)	9 (8-11)	0.99	0.95, 1.04	0.77			
EV (regardless the size)*	137	12 (34)	37 (36)	1.13	0.75, 1.69	0.57			
Large size EV*	86	6 (25)	18 (29)	0.96	0.55, 1.67	0.88			
In Milan HCC*+	203	9 (15)	9(6)	0.40	0.20, 0.79	0.008			
AFP score $\leq 2^*$	191	38 (64)	51 (39)	0.46	0.32, 0.65	< 0.001	0.50	0.35, 0.72	< 0.001
Size of the largest lesion (mm)°+	195	45 (35-66)	54 (40-74)	1.01	1.00, 1.01	0.002			
Tumor size > 5cm*+	195	22 (37)	70 (51)	1.61	1.15, 2.26	0.006			
Serum AFP (ng/ml)°	196	9 (4-62)	25 (5-400)	1.00	1.00, 1.00	0.20			
Curative treatment*	203	27 (45)	45 (31)	0.41	0.28, 0.59	< 0.001	0.48	0.33, 0.69	< 0.001
FOT*	203	6 (10)	12 (8)	1.26	0.70, 2.29	0.44			

^{*}Number (percentage); "median [range].

ALD: alcoholic liver related disease; AFP: alpha-fetoprotein; BCLC: Barcelona Clinic Liver Cancer; EV: esophageal varices; FOT: French overseas territoriesHCC: hepatocellular carcinoma; MASLD: Metabolic dysfunction-associated steatotic Liver disease; MELD score: Model for End-Stage Liver Disease.

⁺ Child-Pugh score was not entered in the multivariate analysis in order to avoid collinearity with MELD.

⁺ In Milan HCC, Size of the largest lesion (mm), Tumor size > 5 cm were not entered in the multivariate analysis in order to avoid collinearity with AFP score ≤ 2 .

Table 6Baseline predictive factors of mortality for BCLC C patients (Cox proportional hazard regression models).

	Available data (n=384)	Alive (n=93)	Death (n=291)	1	Univariate analysis			Multivariate analysis		
				HR	95 % CI	p value	HR	95 % CI	p value	
Gender (male)*	384	68 (73)	247 (85)	0.80	0.58, 1.11	0.18				
Age (years)°	384	65 (56-75)	65 (58-74)	1.00	0.99, 1.01	0.87				
Body mass index (Kg/m2)°	300	25 (23-30)	25 (22-28)	0.96	0.94, 0.99	0.003	0.98	0.94, 1.02	0.27	
Obesity*+	300	22 (29)	41 (18)	0.65	0.46, 0.92	0.015				
Type 2 Diabetes*	367	27 (30)	104 (38)	0.96	0.75, 1.23	0.77				
Cirrhosis*	384	75 (81)	249 (86)	1.35	0.97, 1.87	0.08				
ALD*	384	26 (28)	144 (49)	1.23	0.97, 1.55	0.08				
MASLD*	384	21 (23)	73 (25)	0.84	0.64, 1.10	0.21				
Hepatitis B*	384	25 (27)	62 (21)	0.99	0.75, 1.31	0.94				
Hepatitis C*	384	28 (30)	144 (49)	0.71	0.54, 0.94	0.02	0.76	0.52, 1.22	0.17	
Child-Pugh A*	307	51 (68)	130 (56)	-	_	-				
Child-Pugh B*+		18 (24)	90 (39)	1.74	1.03, 2.95	0.04				
Child-Pugh C*+		6(8)	12 (5)	4.51	1.05, 19.44	0.04				
MELD°	269	9 (8-12)	10 (8-12)	1.04	1.00, 1.08	0.03	1.03	0.98, 1.08	0.24	
EV (regardless the size)*	282	31 (49)	101 (46)	1.03	0.79, 1.35	0.84				
Large size EV*	193	20 (43)	58 (40)	1.14	0.81, 1.59	0.45				
In Milan HCC*+	371	43 (47)	53 (19)	0.31	0.23, 0.42	< 0.001				
AFP score $\leq 2^*$	319	43 (52)	74 (31)	0.44	0.34, 0.59	< 0.001	0.65	0.44, 0.95	0.02	
Size of the largest lesion (mm)°+	335	40 (23-71)	70 (40-100)	1.01	1.00, 1.01	< 0.001				
Tumor size > 5cm*+	335	35 (40)	155 (63)	2.27	1.74, 2.95	< 0.001				
Vascular invasion*	345	46 (49)	183 (64)	1.84	1.43, 2.36	< 0.001	1.36	0.91, 2.02	0.13	
Extrahepatic lesions*	328	16 (19)	72 (30)	2.05	1.54, 2.72	< 0.001	1.24	0.79, 1.91	0.34	
Serum AFP (ng/ml)°+	327	42 (5-1325)	132 (9-2866)	1.00	1.00, 1.00	< 0.001				
Curative treatment*	360	36 (39)	47 (16)	0.21	0.15, 0.30	< 0.001	0.32	0.21, 0.58	< 0.001	
FOT*	384	11 (12)	22 (8)	0.87	0.56, 1.35	0.54				

^{*}Number (percentage); °median [range].

ALD: alcoholic liver related disease; AFP: alpha-fetoprotein; BCLC: Barcelona Clinic Liver Cancer; EV: esophageal varices; HCC: hepatocellular carcinoma; MASLD: Metabolic dysfunction-associated steatotic Liver disease; MELD score: Model for End-Stage Liver Disease.

contributing to higher rates of loss to follow-up, longer treatment delays (which may deter care-seeking), and overall poorer outcomes. A recent study found that nearly half (46.8%) of patients with chronic HBV infection in French Guiana were lost to follow-up [30]. In French Guiana, a recent restructuring of the management of HCC since 2021, shortening the care circuit thanks to joint multidisciplinary tumor board meetings with French metropolitan centers and the arrival of new physicians specialized in interventional radiological procedures, and hepatogastroenterology will probably contribute to improving access to curative care in the future. In our study, the difference in OS across the cohort diminished after four years, likely due to the smaller number of patients in the FOT and the higher rates of liver transplantation and surgical resection in Guadeloupe.

In this series, we observed that, despite similar liver function and portal hypertension profiles between FOT and IDF, treatment approaches according to BCLC stage varied by region. Early- stage patients in FOT had more access to surgical treatments, while ablation was more commonly performed in IDF. These differences likely reflect the facilities and expertise available at each center. Additionally, the higher prevalence of HBV-related HCC in FOT may have influenced treatment strategies. Surgical approaches are often preferred in HBV patients due to fewer complications compared to those with metabolic syndrome, where surgery can be more challenging due to higher comorbidities and increased surgical risks [31].

Another interesting finding from this study is the comparable median OS for BCLC-B patients, despite significant differences in treatment strategies between IDF (where 28% underwent ablation and 28% received TACE) and FOT (where systemic treatment was used in 63% of cases). This suggests that systemic therapies, particularly immunotherapy, could represent a promising alternative for this population, especially in centers where radiological treatments are unavailable. As suggested by BCLC algorithm, systemic therapies may also be better suited for patients with bilobar tumors involving over 50% of the liver, infiltrative or poorly defined nodular tumors, or

those with large vessel vascular invasion-conditions typically associated with reduced efficacy of TACE. These results emphasize the potential role of systemic treatments in broadening therapeutic options for intermediate-stage HCC patients in challenging clinical contexts [32].

Chronic HBV infection stands out as a primary contributor to HCC in the FOT, particularly in comparison to mainland France. Recent studies highlight that HBV-related HCC is not only more prevalent in the FOT (26.6% vs. 9.6%) but also more frequently observed, with a standardized incidence of 0.5 per 100,000 inhabitants in mainland France, 0.57 in Guadeloupe, and nearly double that—1.08—in French Guiana. Moreover, it tends to occur at a younger age, reflecting the endemic nature of HBV in these regions [19]. This pattern is particularly pronounced in areas like Mayotte, where nearly all cases of HCC are attributed to HBV, with the majority being diagnosed at advanced stages [21]. Similarly, French Guiana and Guadeloupe demonstrate a high burden of chronic HBV, classified as a medium-endemicity zone [11–15]. In French Guiana, several studies conducted in specific populations—and one in the general population—have reported a prevalence ranging from 2% to 3% [12,14,33]. In Guadeloupe, one study reported a seroprevalence of 1.5% [11]. In contrast, the prevalence in the general population of mainland France is estimated at 0.3 % [34]. The intense migratory patterns, especially in French Guiana and Mayotte, from neighboring countries with higher HBV prevalence, further amplify this issue [35]. Since its introduction in France in 1980 and its mandatory inclusion for infants in 2018, HBV vaccination has achieved over 90% coverage among individuals under 15 in the FOT [36]. This effort represents a critical step in reducing HBVrelated liver diseases, including HCC. However, addressing the ongoing burden requires more than vaccination alone. Effective strategies for early detection, comprehensive antiviral treatment programs, and public health initiatives tailored to the unique demographic and socioeconomic characteristics of the FOT are essential. Although antiviral treatments have been shown to effectively reduce the risk of

⁺ In Milan HCC, Size of the largest lesion (mm), Tumor size > 5 cm were not entered in the multivariate analysis in order to avoid collinearity with AFP score ≤ 2 , as well as Child-Pugh score to avoid collinearity with.

HCC in patients with HBV infection [37-39], we have previously reported in Guadeloupe that at the time of HCC diagnosis, only a small proportion of patients had been treated for chronic HBV infection [28], with 8% of virosuppressed patients at HCC diagnosis. This is largely because the diagnosis of chronic HBV infection and HCC were concomitant. In French Guiana, a cohort study from 2015 to 2018 showed that antiviral therapy had been initiated in just 17% of patients, with 8% subsequently lost to follow-up [30]. By leveraging vaccination, improving healthcare access, and addressing underlying factors such as migration patterns and healthcare disparities, it is possible to mitigate the long- term impact of HBV and reduce the incidence of HCC in these territories. Interestingly, while the leading causes of HCC in the FOT were HBV and chronic alcohol consumption, a meta-analysis reported HCV as the leading cause in Latin America (48%), followed by alcohol (22%) and HBV (14%) [40]. In a multicenter Latin American study (2005-2011), viral hepatitis was also the main etiology, followed by alcohol. HCC due to metabolic-associated liver disease was observed in only 5.5% of cases, compared with 16% in our cohort. Five-year survival in that study was 65%, notably higher than in our population (40%) [41].

Indeed, metabolic syndrome, encompassing obesity, type 2 diabetes, and related conditions, is an increasingly recognized driver of HCC globally, and the FOT are no exception. Both French Guiana and Guadeloupe face significant public health challenges due to high rates of obesity and diabetes [16]. Recent studies in French Guiana report a type 2 diabetes prevalence of nearly 10% and obesity rates of 19%, with 36% of adults being classified as overweight [42,43]. Despite these statistics, MASLD appears less prevalent as an etiology of HCC in the FOT compared to mainland France. This paradox may be attributed to genetic predispositions or distinct environmental factors that influence disease progression in these populations. Nevertheless, the increasing burden of obesity and diabetes in the FOT warrants monitoring, as these conditions could lead to an increase in MASLD-related HCC in the coming decades. Data suggest lower rates of daily alcohol consumption and heavy binge drinking in these territories [17,18]. However, the interplay between alcohol use and other risk factors such as HBV infection or metabolic syndrome must not be overlooked, as combined etiologies can accelerate liver damage and tumorigenesis, as it is reported in Guadeloupe, where 71 % of patients with HCC had regular alcohol consumption [7]. Addressing these challenges requires a multi-pronged approach. Public health initiatives aimed at constraining obesity and diabetes, combined with educational campaigns to raise awareness about the risks of alcohol misuse, will be crucial in mitigating the impact of these risk factors on liver disease and HCC in the FOT.

Our study has several limitations that should be acknowledged. First, the relatively small sample size from FOT may limit the generalizability of our findings, as not all patients in the region were included in the analysis. Furthermore, many patients from French Guiana choose to leave it for mainland France for treatment after being diagnosed with cancer. Consequently, patients who underwent tests outside the hospital system or left the region are not represented in our cohort. This could lead to an underestimation of HCC cases and treatments, as those who leave are often in better general condition. Second, the retrospective nature of the study introduced missing data, particularly regarding access to antiviral therapy, despite the fact that HBV is a leading cause of HCC in FOT. This limitation restricts our ability to assess the impact of antiviral treatment on disease progression and outcomes. In addition, only one center was selected to represent mainland France. However, when comparing the characteristics of patients from the IDF center with preliminary results from the national multicenter French study—the CHIEF cohort, which aims to provide epidemiological and prognostic data on HCC-characteristics between IDF and CHIEF population were similar [10]. Finally, our study lacked detailed information on surveillance strategies and their implementation within the population.

This gap prevents a comprehensive evaluation of how early detection practices might influence patient outcomes, a critical factor in improving prognosis for HCC patients. Despite these limitations, the present study is the first to provide such comparative data which reveal important areas where efforts are required to improve prognosis.

5. Conclusions

In conclusion, HCC patients in FOT have a poorer prognosis compared to IDF, due to diagnoses at more advanced stages, limiting curative treatment options. These findings highlight the need for improved access to care and screening strategies for earlier diagnosis of HCC in FOT.

Author contributions

Drs. Aboikoni, Allaire, Ganne, and Gelu-Simeon had full access to all data in the study and take responsibility for the integrity of data and the accuracy of data analysis; Study concept and design: Drs. Aboikoni, Allaire, Ganne, and Gelu-Simeon; Acquisition of data: Drs. Aboikoni, Allaire, Busso, Ganne, and Gelu-Simeon, and Mrs Catherine; Analysis and interpretation of data: Drs. Aboikoni, Allaire, Ganne, and Gelu-Simeon; Drafting of the manuscript: Drs. Aboikoni, Allaire, Ganne, and Gelu-Simeon; Critical revision of the manuscript for important intellectual content: Drs. Aboikoni, Allaire, Louvel, Alogo A Nwatsok, Ngock, Ouni, Tangan, Zappa, Nacher, Douine, Drak Alsibai, Busso, Ganne, Gelu-Simeon, and Mrs Catherine; Statistical analysis: Dr. Allaire; Study supervision: Drs. Aboikoni, Allaire, Ganne, and Gelu-Simeon.

Declaration of generative AI and AI-assisted technologies

An Al-assisted English corrector was used to improve grammar and spelling in this manuscript.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of interests

AA: none; MA: received travel and congress fees, and consulting fees or honoraria for lectures and presentations from AstraZeneca, Bayer, Gilead and Roche; DL: none; MAAN: none; PND: none; AO: none; LT: none; MZ: none; KDA: none; MD: none; MN: none; LC: none; CB: none; NG: received travel and congress fees, and consulting fees or honoraria for lectures and presentations from AbbVie, Bayer, Gilead, Intercept and Roche; MGS: received travel and congress fees from AbbVie and Ipsen.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.aohep.2025.102120.

References

- [1] Cancer Today. https://gco.iarc.who.int/today/; 2024.
- [2] Llovet JM, Zucman-Rossi J, Pikarsky E, Sangro B, Schwartz M, Sherman M, et al. Hepatocellular carcinoma. Nat Rev Dis Primers 2016;2:16018. https://doi.org/ 10.1038/nrdp.2016.18.
- [3] Haute Autorité de Santé. 2024. Prise En Charge des Patients Atteints De Cirrhose. https://www.has-sante.fr/jcms/c_614245/fr/prise-en-charge-des-patients-atteints-de-cirrhose [accessed 07 july 2025].
- [4] Santé Publique France. Survie des personnes atteintes de cancer en France métropolitaine 1989-2018 - Foie. https://www.santepubliquefrance.fr/import/ survie-des-personnes-atteintes-de-cancer-en-france-metropolitaine-1989-2018foie [accessed 29 december 2024].

- [5] Decaens Thomas, Hurtova Monika, Duvoux Christophe. Transplantation hépatique pour carcinome hépatocellulaire. Hépato-Gastro & Oncologie Digestive 2008:15(6):425-33
- [6] Bruix J, Reig M, Sherman M. Evidence-based diagnosis, staging, and treatment of patients with hepatocellular carcinoma. Gastroenterology 2016;150:835–53. https://doi.org/10.1053/j.gastro.2015.12.041.
- [7] Rosa I, Denis J, Renard P, Lesgourgues B, Dobrin AS, Becker C, et al. A french multicentric longitudinal descriptive study of hepatocellular carcinoma management (the changh cohort): preliminary results. J Hepatology 2010;52:S231-2.
- [8] Goutté N, Sogni P, Bendersky N, Barbare JC, Falissard B, Farges O. Geographical variations in incidence, management and survival of hepatocellular carcinoma in a Western country. J Hepatol 2017;66:537–44. https://doi.org/10.1016/j. jhep.2016.10.015.
- [9] Mathurin P, De Zelicourt M, Kelkouli N, frederic Blanc J. Risk factors, treatment patterns and survival of patients with incident hepatocellular carcinoma in France: A retrospective data analysis. JCO 2021;39:284-284.
- [10] Nguyen Khac E, Merle P, Ben Khadhra Hajer, Amaddeo G, Decaens T, Uguen T, et al. Epidemiology and characteristics of hepatocellular carcinoma in France: results of the first 2000 patients in real-life situations from the French prospective chief cohort. J Hepatol. 2023;78(S1):92–3 | S1–S99.
- [11] Gelu-Simeon M, Pillas V, Deloumeaux J, Delacroix-Maillard H, Saint-Georges G, Do Amaral L, Borel M, Laurent M, Gordien E, Saillard E. Seroepidemiology of chronic hepatitis B and C in the French Caribbean Island of Guadeloupe. BMC Res Notes 2014;7:55. https://doi.org/10.1186/1756-0500-7-55.
- [12] Melanie G, Brousse P, Guarmit B, Adriouch L, Schaub R, Naldjinan-Kodbaye R, et al. Hépatites virales B Delta et C dans les centres délocalisés de prévention et de soins (CPDS) de guyane française. Bulletin De Veille Sanitaire 2017;2:23-8.
- [13] Douine M, Schaub R, Jardin H, Adenis A, Nacher M, Hureau-Mutricy L, et al. High prevalence of hepatitis B and syphilis in illegal gold miners in French Guiana. Clin Microbiol Infect 2019;25:1051–3. https://doi.org/10.1016/j.cmi.2019.04.023.
- [14] Mahamat A, Louvel D, Vaz T, Demar M, Nacher M, Djossou F. High prevalence of HBsAg during pregnancy in Asian communities at Cayenne Hospital, French Guiana. Am J Trop Med Hyg 2010;83:711–3. https://doi.org/10.4269/ajtmh.2010.09-0727.
- [15] Huber F, Vandentorren S, Merceron A, Chaponnay A, Gadio G, About V, et al. HIV-positive in the darkness of a correctional facility: more vulnerable and less treated. Int J STD AIDS 2019;30:460-6. https://doi.org/10.1177/0956462418816452.
- [16] Hernandez H, Piffaretti C, Gautier A, Cosson E, Fosse-Edorh S. Prévalence du diabète connu dans 4 départements et régions d'outre-mer: Guadeloupe, Martinique, Guyane et La Réunion. Résultats du Baromètre de Santé publique France de 2021. Bull Épidémiol Hebd 2023;(20-21):424–31. http://beh.santepubliquefrance.fr/beh/2023/20-21/2023_20-21_2.html.
- [17] Santé Publique France. Alcool en Guadeloupe. Bilan de la consommation en 2021 et des passages aux urgences en 2023, https://www.santepubliquefrance.fr/regions/antilles/documents/bulletin-regional/2024/alcool-en-guadeloupe.-bilan-de-la-consommation-en-2021-et-des-passages-aux-urgences-en-2023 [accessed 07 july 2025].
- [18] Santé Publique France. Alcool en Guyane. Consommation en 2021 et passages aux urgences en 2023, https://www.santepubliquefrance.fr/regions/guyane/documents/bulletin-regional/2024/alcool-en-guyane.-consommation-en-2021-et-passages-aux-urgences-en-2023 [accessed 07 july 2025].
- [19] Mwamba-Kalambayi P, Etienne A, Chirpaz E, Gelu-Simeon M, Cuissard L, Deloumeaux J, et al. Étude comparative de la fréquence des hépatites B et C chez les personnes nouvellement diagnostiquées pour carcinome hépatocellulaire en France métropolitaine et dans les départements et régions d'outre-mer, 2015-2019. Bull Epidémiol Hebd 2022(3-4):85–94. http://beh.santepubliquefrance.fr/beh/2022/3-4/2022 3-4 7.html.
- [20] European Association For The Study Of The Liver. European Organisation For Research And Treatment Of Cancer. EASL-EORTC clinical practice guidelines: management of hepatocellular carcinoma. J Hepatol 2012;56:908–43. https://doi. org/10.1016/j.jhep.2011.12.001.
- [21] Hoarau X, Jean M, Permal S. Épidémiologie des carcinomes hépatocellulaires de 2007 à 2016 à Mayotte. Médecine et Maladies. Infectieuses 2018;48:S107. https://doi.org/10.1016/j.medmal.2018.04.269.
- [22] Dossier complet. Département de La Guyane (973) Insee, https://www.insee.fr/fr/ statistiques/2011101?geo=DEP-973 [accessed 05 july 2025].

- [23] Dossier complet Département De La Guadeloupe (971) Insee, https://www.insee. fr/fr/statistiques/2011101?geo=DEP-971#chiffre-cle-8 [accessed 05 july 2025].
- [24] Dossier complet Département du Val-de-Marne (94) Insee https://www.insee.fr/fr/statistiques/2011101?geo=DEP-94#chiffre-cle-4 [accessed 05 july 2025].
- [25] Démographie des professionnels de santé DREES. https://drees.shinyapps.io/ demographie-ps [accessed 05 july 2025].
- [26] Trois Guadeloupéens sur 10 ont renoncé ou retardé des soins en 2019 Insee Analyses Guadeloupe –50, https://www.insee.fr/fr/statistiques/5390716#titrebloc-8 [accessed 05 july 2025].
- [27] Un tiers des Guyanais ont retardé ou renoncé à un soin médical en 2019 Insee Analyses Guyane –52, https://www.insee.fr/fr/statistiques/5391092#figure2 [accessed 05 july 2025].
- [28] Benard J, Lafrance MJ, Gordien E, Amaral L, Levrero M, Zoulim F, et al. Hepatitis B virus-associated hepatocellular carcinoma is still a matter of concern in the French Caribbean Island of Guadeloupe. Clin Res Hepatol Gastroenterol 2021;45:101706. https://doi.org/10.1016/j.clinre.2021.101706.
- [29] Droz JP, Couppié P, Fayette J. La cancérologie en guyane : un défi à. Juin 2024;111 (6):597-607. https://doi.org/10.1016/j.bulcan.2024.02.018.
- [30] Vo-Quang E, Vignier N, Adenis A, Adriouch L, Lucarelli A, Guarmit B, et al. Tackling a worrisome rate of lost to follow-up among migrants with hepatitis B in French Guiana. Infect Dis Now 2024;54(7):104974. https://doi.org/10.1016/j. idnow.2024.104974.
- [31] Allaire M, Goumard C, Lim C, Le Cleach A, Wagner M, Scatton O. New frontiers in liver resection for hepatocellular carcinoma. JHEP Rep 2020;2(4):100134.. https://doi.org/ 10.1016/j.jhepr.2020.100134.
- [32] Reig M, Forner A, Rimola J, Ferrer-Fàbrega J, Burrel M, Garcia-Criado Á, et al. BCLC strategy for prognosis prediction and treatment recommendation: the 2022 update. J Hepatol 2022;76(3):681–93. https://doi.org/10.1016/j.jhep.2021.11.018.
- [33] Aubert Lydéric, Carvalho Luisiane, Suivant Claudine, Vaux Sophie, Picohe Corinne. Cécile Brouard et al. Surveillance des hépatites B et C aux Antilles et en Guyane. Bulletin De Veille Sanitaire 2017;2:02-17.
- [34] Brouard C, Saboni L, Gautier A, Chevaliez S, Rahib D, Richard JB, et al. HCV and HBV prevalence based on home blood self-sampling and screening history in the general population in 2016: contribution to the new French screening strategy. BMC Infect Dis 2019;19(1):896. https://doi.org/10.1186/s12879-019-4493-2.
- [35] Nacher M, Epelboin L, Bonifay T, Djossou F, Blaizot R, Couppié P, et al. Migration in French Guiana: implications in health and infectious diseases. Travel Med Infect Dis 2024;57:102677. https://doi.org/10.1016/j.tmaid.2023.102677.
- [36] Santé Publique France. Surveillance des hépatites B et C. 2025, https://www.santepubliquefrance.fr/import/surveillance-des-hepatites-b-et-c [accessed 05 july 2025]
- [37] Sung JJY, Tsoi KKF, Wong VWS, Li KCT, Chan HLY. Meta-analysis: treatment of hepatitis B infection reduces risk of hepatocellular carcinoma. Aliment Pharmacol Ther 1 2008;28(9):1067–77. https://doi.org/10.1111/jj.1365-2036.2008.03816.x.
- [38] Kim JH, Sinn DH, Kang W, Gwak GY, Paik YH, Choi MS, et al. Low-level viremia and the increased risk of hepatocellular carcinoma in patients receiving entecavir treatment. Hepatology 2017;66(2):335–43. https://doi.org/10.1002/hep.28916.
- [39] Brichler S, Nahon P, Zoulim F, Layese R, Bourcier V, Audureau E, et al. Non-virological factors are drivers of hepatocellular carcinoma in virosuppressed hepatitis B cirrhosis: results of ANRS CO12 CirVir cohort. J Viral Hepat 2019;26(3):384–96. https://doi.org/10.1111/jvh.13029.
- [40] Carrilho FJ, Paranaguá-Vezozzo DC, Chagas AL, Alencar RS, de SM, da Fonseca LG. Epidemiology of liver cancer in Latin America: current and future trends. Semin Liver Dis 2020;40(2):101–10. https://doi.org/10.1055/s-0039-3399561.
- [41] Piñero F, Costa P, Boteon YL, Duque SH, Marciano S, Anders M, et al. Results of liver transplantation for hepatocellular carcinoma in a multicenter Latin American cohort study. Ann Hepatol 2018;17(2):256–67. https://doi.org/10.5604/ 01.3001.0010.8648.
- [42] Sudre C, Duplan H, Bukasakakamba J, Nacher M, Peyre-Costa P, Sabbah N. Diabetes care in French Guiana: the gap between national guidelines and reality. Front Endocrinol (Lausanne) 2021;12:789391. https://doi.org/10.3389/fendo.2021.789391.
- [43] Massicard M, Drak Alsibai K, Nacher M, Sabbah N. Nutritional and socioeconomic determinants of overweight and obesity in the French Amazon: the health barometer study. Front Endocrinol (Lausanne) 2022;13:849718. https://doi.org/ 10.3389/fendo.2022.849718.