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Outcome of MAFLD-related HCC in Egyptian patients: a single center study

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Abstract

Background Globally, MAFLD becomes in the top list of causes of liver disease. Its effect ranges from steatosis, metabolic steato-hepatitis to MAFLD-related cirrhosis and hepatocellular carcinoma. There is a growing evidence that MAFLD-related HCC seems to be different from HCCs of other causes pathologically, so the purpose of our study was to assess the effect of MAFLD on the prognosis of HCC regarding outcome after management of HCC and survival rate in comparison to a group of patients with HCV-related HCC.

Results Twenty-nine patients with MAFLD related HCC were included in group A, while 58 patients with HCV related HCC were enrolled as group B. Both groups were matched regarding age and gender. The mean age in group A and B was 58.86 (±8.47) years and 60/05(± 6.83) years respectively. Comparison between both groups regarding tumor burden and characteristics of HCC, type of management, and post intervention follow-up showed no significant statistical difference between both groups except for lymph node metastases which was higher in patients with HCV related HCC with $p = 0.045$. Also, a significant difference between both studied groups regarding AFP was detected; the median of AFP in MAFLD-related HCC was (7.2 ng/ml) but much higher in HCV-related HCC group (129.2 ng/ml) with $p = 0.001$.

Conclusion Our data showed no significant difference between the two studied groups regarding outcome of HCC or survival rate except for AFP level before and after management which was higher in HCV patients related HCC. Although both of inclusion and exclusion criteria were strict to the criteria, so the number of participants in the research were not large enough; to our knowledge, this is the first study on MAFLD-HCC in Egypt and Africa. More studies on prospective bases are essentially needed to stand on solid conclusion about the nature and outcome of MAFLD-related HCC.

Keywords Metabolic (dysfunction) associated fatty liver disease, Hepatitis C viral infection, Hepatocellular carcinoma

Background

Hepatocellular carcinoma (HCC) is the most common form of liver cancer accounts for 90% of cases [1]. Globally, metabolic associated fatty liver disease (MAFLD) is becoming the fastest growing etiology of HCC, particularly in the West [2].

The incidence of MAFLD varies geographically ranging from 6% to 35%. it is more prevalent in Western countries (20–30%) than in Eastern countries (10–20%) [3], while in in Middle East countries, the reported average rates for MAFLD incidence was 8.9% [4].

The pathogenesis MAFLD is characterized by lipid accumulation in liver which progress to inflammation and considerable liver injury [5]. It can progress to steato-hepatitis which is a major risk factor for cirrhosis and HCC, but HCC can also arise in absence of cirrhosis [6].

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MAFLD differs from other causes of HCC, such as chronic viral hepatitis, in that there are, up till now, no simple, highly effective treatment directed against MAFLD [7]. There is also no simple compatible way to diagnose MAFLD in patients with cirrhosis and HCC because MAFLD may have "burned out," with hepatic steatosis no longer evident in advanced stage. Moreover, patients with MAFLD often have other comorbidities, which may preclude cancer-directed therapy or increase the risk of complications after therapy [8, 9]. However, these factors affecting the natural history of MAFLD-related HCC compared to other causes of HCC are still not clear, and awareness among the affected people is still poor [10].

MAFLD-related HCCs seems to be pathologically different from HCCs of other causes pathologically, as they are mostly well-differentiated, single hepatic focal lesions, with inflammatory infiltration and less incidence of distant metastases. Also, the size of MAFLD-related HCC is generally larger than the HCCs related to otheretiologies [10].

However, the studies that compare the outcomes of HCC patients according to the etiologies of HCC is scarce. Therefore, this study aimed to compare the outcome and survival rate of MAFLD-related HCC patients and those of HCV-related HCC patients.

Patients and methods

This is a single-center retrospective comparative cross sectional study, between January 2015 and December 2020, to assess the outcome of metabolic dysfunction-associated fatty liver disease (MAFLD) in patients with HCC at HCC specialized outpatient clinic, Tropical Medicine Department at Ain Shams University Hospitals, and to study the impact of MAFLD on the prognosis of HCC and survival rate in comparison to a group of patients with HCV related HCC.

Ethics approval and informed consent

The study was approved by the Ethics committee of the Faculty of Medicine, Ain Shams University, Egypt (assurance no. FWA00017585). Data were retrieved from the file system of the studied patients with preservation of the rights and privacy of patients' data. The requirement for consent was waived by an ethics committee as the study was retrospective and data were recruited from patients' files.

A total number of patients that visited our HCC specialized clinic from January 2015 to December 2020 were 2448 cases; 2125 were HCC cases due to different etiologies; from them, all patients meeting the new MAFLD criteria as an only the cause of HCC were 29 patients (1.36%) that included and named as group (A) and then compared to a group of the double number of HCC (58) patients due to HCV that chosen by simple random method and was named as group (B) (Fig. 1).

Data were retrieved from the file system of the included patients. HCC was diagnosed based on American Association for the Study of Liver Diseases criteria [11].

Clinical assessment at the time of presentation to our HCC clinic included personal history and baseline demographics data, e.g., age at diagnosis and gender, and features of the metabolic syndrome, e.g., body mass index (BMI), type 2 diabetes mellitus, hyperlipidemia, use of anti-dyslipidemia drugs, and hypertension.

Laboratory investigations included were complete blood count, serum creatinine, serum bilirubin, serum albumin, prothrombin time, alanine aminotransferase, aspartate aminotransferase, and alpha-fetoprotein (AFP).

In addition, laboratory investigation for the MAFLD-related HCC group was recorded such as HBA1C, serum triglycerides, serum cholesterol, low density lipoproteins, and high density lipoproteins.

Degree of decompensation (Child–Pugh stage) and MELD scores were calculated.

Radiological investigations were done by expert radiologists for HCC including ultrasonography, Doppler, and triphasic abdominal computed tomography (CT) scan to confirm the diagnosis of HCC by presence of arterial enhancement of the focal lesion followed by washout in porto-venous and delayed phases**.** Magnetic resonance imaging abdomen with diffusion for inconclusive or atypical cases [12] .

Hepatic steatosis was identified as a diffuse increased hepatic parenchymal

echogenicity "bright liver" compared to renal cortex and splenic

parenchyma, hepatomegaly, or intrahepatic vascular blurring on ultrasound [13].

The tumor characteristics included Barcelona Clinic Liver Cancer (BCLC) staging, number and site of hepatic focal lesions, size of largest lesion at diagnosis, and total sizes of all HFLs. Also, data included if there was vascular invasion by HCC, lymph nodes metastases, or distant metastases.

Tumor response after intervention was assessed according to mRECIST (modified Response Evaluation Criteria in Solid Tumors) assessment for hepatocellular carcinoma [14].

Patients were followed from the date of diagnosis with HCC to either date of death or last follow-up; then, we analyzed the cumulative survival rate that was represented in months for all enrolled patients.

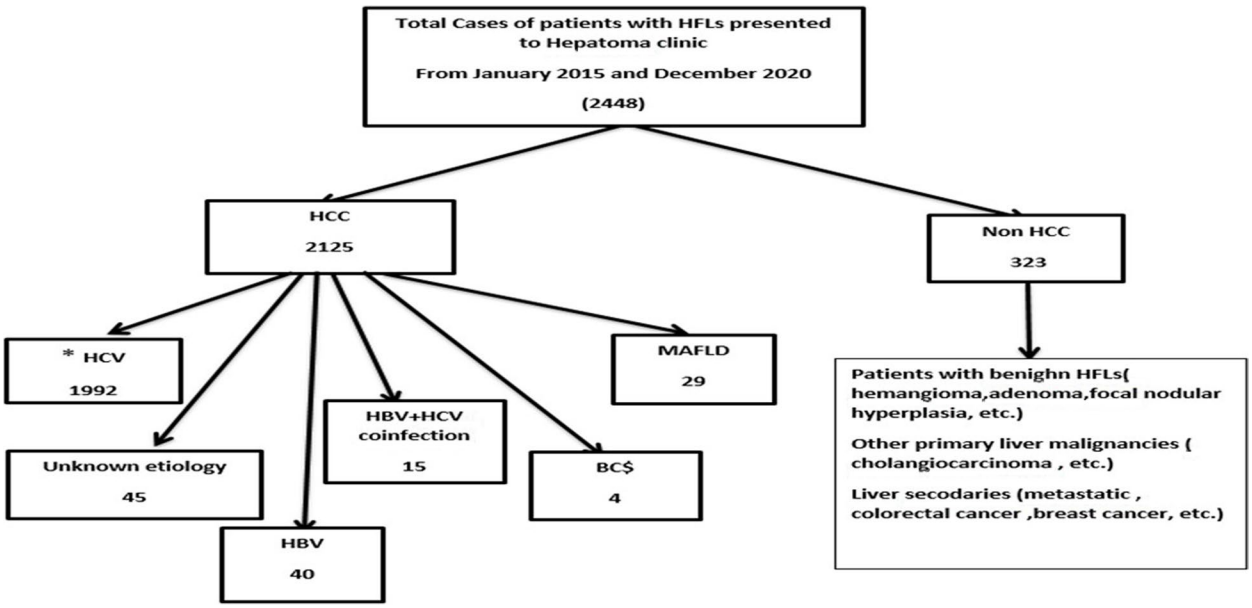

Fig.1 Flow chart of the study *1992 patients with HCC caused by HCV only were introduced to our Heptoma group between January 205 and December 2020, after exclusion of the patients that didn't meet the inclusion criteria (age, comordities like DM and HTN, overnight obesity, etc.) or patients who missed the follow up, 650 patients were found to be meeting the inclusion criteria if our study from which we randomly chose 58 patients (double number of HCC due to MAFLD). Abbreviations: HCV, Hepaptitis C virus, HBV Hepatitis B virus, BCS Budd chiari syndrome, MAFLD Metabolically associated fatty liver disease

Inclusion criteria patients with MAFLD-related HCC group (A)

All patients with excluded other causes of HCC and meeting the new MAFLD criteria presented at a hepatoma specialized outpatient clinic Tropical Medicine Department at Ain Shams University Hospitals from January 2015 to December 2020 with age range of 18–70 years.

The new MAFLD criteria [15]

The presence of hepatic steatosis and anyone of the following 3 metabolic risks, including overweight/obesity, presence of diabetes mellitus, and evidence of metabolic dysregulation (e.g., dyslipidemia and hypertension)

Exclusion criteria of group (A)

Exclusion criteria of group (A) were as follows: other causes of HCC (HCV, HBV, autoimmune hepatitis, Budd Chiari syndrome, Wilson disease, hemochromatosis, etc.), incomplete files, missed follow-up, or not fulfilling the above inclusion criteria.

Inclusion criteria of patients with HCV-related HCC group (B) (HCV-related HCC)

HCC patients on top of HCV-related liver cirrhosis.

Exclusion criteria of group (B)

Exclusion criteria of group (B) were as follows: patients younger than 18 years old or above age of 70 years**,** other causes of HCC, presence of hepatic steatosis, overweight or obesity, hypertension, diabetes mellitus, and dyslipidemia.

Data management and statistical analysis

The collected data was revised, coded, tabulated, and introduced to a PC using Statistical package for Social Science (SPSS 23). Data was presented, and suitable analysis was done according to the type of data obtained for each parameter.

i. Descriptive statistics: mean, standard deviation (± SD), and range for parametric numerical data, while median and interquartile range (IQR) for

non-parametric numerical data. Frequency and percentage of categorical data.

ii. Analytical statistics:Student *t*-test for parametric numerical data. Mann Whitney test for non-parametric numerical data. Chi-square and Fisher's exact tests for the relationship between two qualitative variables. Kaplan-Meier survival analysis is a descriptive procedure for examining the distribution of time-to-event variables. A p value < 0.05 was adopted to interpret the significance of statistical tests.

Results

Basic demographic characteristic of patients in both groups that were matched as regards age and gender (Table1)

Regarding the child score of the patients, in group (A), the mean child score was 6.48 ± 2.26, with 22 patients (75.86%) within child class A, 1 patient (3.45%) child class B, and 6 patients (20.69%) child class C, while in group (B), the mean child score was 6.71 ± 2.19, with 40 patients (68.97%) within child class A, 8 patients (13.79%) child class B, and 10 patients (17.24%) child class C. The difference between both groups regarding both child score and child class was not statistically significant ($P = 0.658$ and 0.324 respectively). Furthermore, regarding the BCLC staging system, most of the patients of group (A) were BCLC B (34.48%), while in group (B), 29.32% of the patients were BCLC B, and 27.59% were BCLC D with no significant statistical difference between both groups ($p = 0.952$; Table1).

Table 1 Baseline characteristics of the two studied groups

		Group		Test of significant	
		Group (A)	Group (B)		
		Mean ± SD *N* (%)	Mean ± SD *N* (%)	*p* Value	Sig.
Age in years		58.86 ± 8.47	60.05 ± 6.83	0.482[(T)]	NS
Gender	Female	9 (31.03%)	13 (22.41%)	0.383[(C)]	NS
	Male	20 (68.97%)	45 (77.59%)		
MELD value		10.34 ± 4.91	11.02 ± 4.75	0.540[(T)]	NS
MELD code	<= 9	17 (58.62%)	34 (58.62%)	1.00[(F)]	NS
	10–19	10 (34.48%)	19 (32.76%)		
	20–29	2 (6.9%)	5 (8.62%)		
Child score		6.48 ± 2.26	6.71 ± 2.19	0.658[(T)]	NS
Child class	A	22 (75.86%)	40 (68.97%)	0.324[(C)]	NS
	B	1 (3.45%)	8 (13.79%)		
BCLC	C	6 (20.69%)	10 (17.24%)		
	A1	3 (10.34%)	6 (10.34%)	0.952[(F)]	NS
	A2	5 (17.24%)	11 (18.97%)		
	A4	2 (6.9%)	2 (3.45%)		
	B	10 (34.48%)	17 (29.31%)		
	C	3 (10.34%)	6 (10.34%)		
	D	6 (20.69%)	16 (27.59%)		

[(T)] Student *t*-test of significance

[(C)] Chi-Square test of significance

[(F)] Fisher's exact test of significance

Table 2 Comparison between important laboratory investigations of both studied groups

	Group		Test of significant	
	Group (A)	Group (B)		
	Mean ± SD Median (IQR)	Mean ± SD Median (IQR)	*p* Value	Sig.
Creatinine (mg/dl)	0.99 ± 0.31	0.99 ± 0.37	0.966[(T)]	NS
Total bilirubin (mg/dl)	1 (0.9–1.9)	1.25 (0.9–2)	0.319[(M)]	NS
Direct bilirubin (mg/dl)	0.4 (0.2–0.9)	0.6 (0.2–1)	0.377[(M)]	NS
AST (IU/L)	62 (49–70)	55 (40–72)	0.749[(M)]	NS
ALT (IU/L)	42 (29–52)	44.5 (32–66)	0.326[(M)]	NS
Serum albumin (gm/dl)	3.44 ± 0.7	3.34 ± 0.61	0.502[(T)]	NS
INR	1.21 ± 0.24	1.25 ± 0.29	0.490[(T)]	NS
White blood count (10^3/uL)	6.9 (4.2 –8)	6.3 (3.8–7.8)	0.715[(M)]	NS
Hemoglobin (gm/dl)	11.41 ± 1.89	12.27 ± 1.92	0.050[(T)]	NS
Platelets (10^3/uL)	159 (90–240)	132 (90–202)	0.290[(M)]	NS
Alpha-fetoprotien (ng/dl)	7.2 (3.9–83.4)	129.2 (12.2–715)	0.002[(M)]	S

[(T)] Student *t*-test of significance

[(M)] Mann-Whitney test of significance

Abbreviations: AST aspartate transaminase, *ALT* alanine transaminase, *INR* international normalized ratio

Regarding laboratory investigations of the enrolled patients as shown in Table 2, statistically significant difference was observed between the two studied groups in AFP level only. The median level of AFP was significantly higher in group (B) (129.2 ng/dl; IQR 12.2–715 ng/ml) than in group (A) which had a median level of 7.2 ng/dl (IQR 3.9–83.4) with p value = 0.002.

The current study shows different types of management and interventions received by patients of the studied groups. In group (A), 12 patients (41.38%) underwent trans-arterial-chemoembolization (TACE), 6 patients (20.69%) underwent radiofrequency ablation (RFA), 1 patient (3.45%) underwent microwave ablation (MWA), 1 patient (3.45%) underwent surgical resection of HCC, 3 patients (10.34%) received sorafenib, and the decision of the other 6 patients (20.69%) was best supportive treatment, while in group (B), 25 patients (43.1%) underwent TACE, 12 patients (12.07%) underwent RFA, 2 patients (3.45%) underwent MWA, 2 patients (3.45%) underwent surgical resection, 6 patients (10.34%) received sorafenib,

Table 3 Comparison of type of first intervention of the studied groups ($N = 87$)

		Group		Fisher's exact test	
		Group (A) $N = 29$	Group (B) $N = 58$		
		N (%)	*N* (%)	*p* Value	Sig.
Type of intervention	TACE	12 (41.38%)	25 (43.1%)	0.926	NS
	RFA	6 (20.69%)	7 (12.07%)		
	MWA	1 (3.45%)	2 (3.45%)		
	Resection	1 (3.45%)	2 (3.45%)		
	BST	6 (20.69%)	16 (27.59%)		
	Sorafenib	3 (10.34%)	6 (10.34%)		

Abbreviations: *N* number,*TACE* trans-arterial chemoembolization, *RFA* radiofrequency ablation, *MWA* microwave ablation, *BST* best supportive treatment, *AFP*alpha-fetoprotein

and 16 patients (27.59%) had best supportive treatment (BST) as shown in Table 3.

Furthermore, we found no significant statistical difference between the two groups regarding type of management received by the patients with $p = 0.926$.

Regarding the first follow-up data of the studied patients after their first intervention, there were no statistical significant differences between both groups except for AFP level; group (A) had a median AFP level of 7.1 (IQR 3.7–22) ng/ml, while group (B) had a median AFP level of 21.8 (IQR 2.8–43) ng/ml as shown in Table 4.

Moreover, regarding mRECIST after 1 month of the intervention, group (A) had 23 patients who underwent intervention or received sorafenib; from them, 7 patients (30.43%) showed complete response (CR), 13 patients (56.52%) showed partial response (PR), 2 patients (8.7%) had stationary disease (SD), and only 1 patient (4.35%) showed progressive disease (PD), while in group (B), 42

Table 4 Follow-up 1 month after first intervention

		Group		Test of significant	
		(A) $N = 23$	(B) $N = 42$		
		N (%) Median (IQR) Mean ± SD	*N* (%) Median (IQR) Mean ± SD	*p* Value	Sig.
mRECIST after 1 month	CR	7 (30.43%)	10 (23.81%)	0.808[F]	NS
	PR	13 (56.52%)	23 (54.76%)		
	SD	2 (8.7%)	4 (9.52%)		
	PD	1 (4.35%)	5 (11.9%)		
Performance status	0	19 (82.61%)	36 (85.71%)	0.867[F]	NS
	1	2 (8.7%)	4 (9.52%)		
	2	2 (8.7%)	2 (4.76%)		
Creatinine(mg/dl)		0.9 (0.7–1)	0.9 (0.7–1.1)	0.912[M]	NS
White blood cells (10^3/uL)		6.9 (4.2–8)	6.25 (4–7.8)	0.602[M]	NS
Hemoglobin (gm/dl)		11.71 ± 1.83	12.49 ± 1.79	0.099[T]	NS
Platelets (10^3/uL)		174 (110–240)	122 (98–176)	0.076[M]	NS
Total bilirubin (mg/dl)		1 (0.9–1.1)	1.1 (0.9–1.5)	0.330[M]	NS
Albumin (gm/dl)		3.48 ± 0.43	3.37 ± 0.41	0.295[T]	NS
INR		1.13 ± 0.21	1.2 ± 0.27	0.279[T]	NS
AFP (ng/dl)		5.5 (4.2–40)	40 (8–280)	0.007[M]	S
Hepatic encephalopathy	No	23 (100%)	42 (100%)		
	Yes	0 (0%)	0 (0%)		
Ascites	No	21 (91.3%)	35 (83.33%)	0.474[F]	NS
	Yes	2 (8.7%)	7 (16.67%)		
Child score		5.78 ± 1.44	6.24 ± 1.54	0.249[T]	NS
Child class	A	20 (86.96%)	35 (83.33%)	1.00[F]	NS
	B	1 (4.35%)	3 (7.14%)		
	C	2 (8.7%)	4 (9.52%)		

[F] Fisher's exact test of significance

[M] Mann-Whitney test of significance

[T] Student *t*-test of significance

patients underwent intervention, 10 patients (23.81%) showed complete response (CR), 23 patients (54.76%) showed partial response (PR), 4 patients (9.52%) had stationary disease (SD), and 5 patients (11.9%) showed progressive disease (PD) with no statistical significant difference regarding between both groups $P = 0.808$ as described in Table 4.

Also, we found no statistical differences between the studied groups as regard the other post intervention laboratory investigations, performance status, child score, or child class.

As for the second intervention of the enrolled patients and follow-up, we found 16 patients from group (A) who underwent therapeutic intervention for HCC, while 31 patients from group (B) underwent therapeutic intervention for HCC with no statistical significant difference between both groups ($p = 0.688$). In group (A), 9 patients (56.25%) underwent TACE, 2 patients (12.5%) underwent RFA, 3 patients (18.75%) received sorafenib, and 2 patients (12.5%) had BST, while in group (B), 18 patients (58.06%) underwent TACE, 5 patients (16.13%) underwent RFA, 2 patients (6.45%) received sorafenib, and 6 patients (19.35%) had BST as shown in Table 5.

There was also no statistical significant difference as regard to mRECIST after 1 month of this second intervention with *P* value of 0.688 and 0.364 respectively as mentioned in Table 5.

Regarding survival from time of diagnosis with HCC, group (A) had 72.41% of 1-year survival, but in group (B), 58.62% had 1-year survival with no significant statistical difference in between.

Furthermore, there was no significant statistical difference between both groups regarding the survival from time of diagnosis of HCC until the end of the study in June 2022; 8 patients (27.59%) of group (A) were alive, while the other 21 (72.41%) died. In group (B), 13 patients (22.41%) were still alive, while the other 45 patients (77.59%) died as shown in Fig. 2.

Table 5 Comparison of second intervention and follow-up mRECIST after 1 month of the two studied groups ($N = 47$)

		Group		Fisher's exact test	
		Group (A) 16	Group (B) 31		
		N (%)	*N* (%)	*p* Value	Sig.
Intervention	TACE	9 (56.25%)	18 (58.06%)	0.688	NS
	RF	2 (12.5%)	5 (16.13%)		
	BST	2 (12.5%)	6 (19.35%)		
	Sorafenib	3 (18.75%)	2 (6.45%)		
mRECIST after 1 month	CR	2 (14.29%)	8 (32%)	0.364	NS
	PR	10 (71.43%)	16 (64%)		
	SD	1 (7.14%)	0 (0%)		
	PD	1 (7.14%)	1 (4%)		

Abbreviations: *CR* complete response, *PR* partial response, *SD* stationary disease, *PD* progressive disease, *mRECIST* modified response evaluation criteria in solid tumors

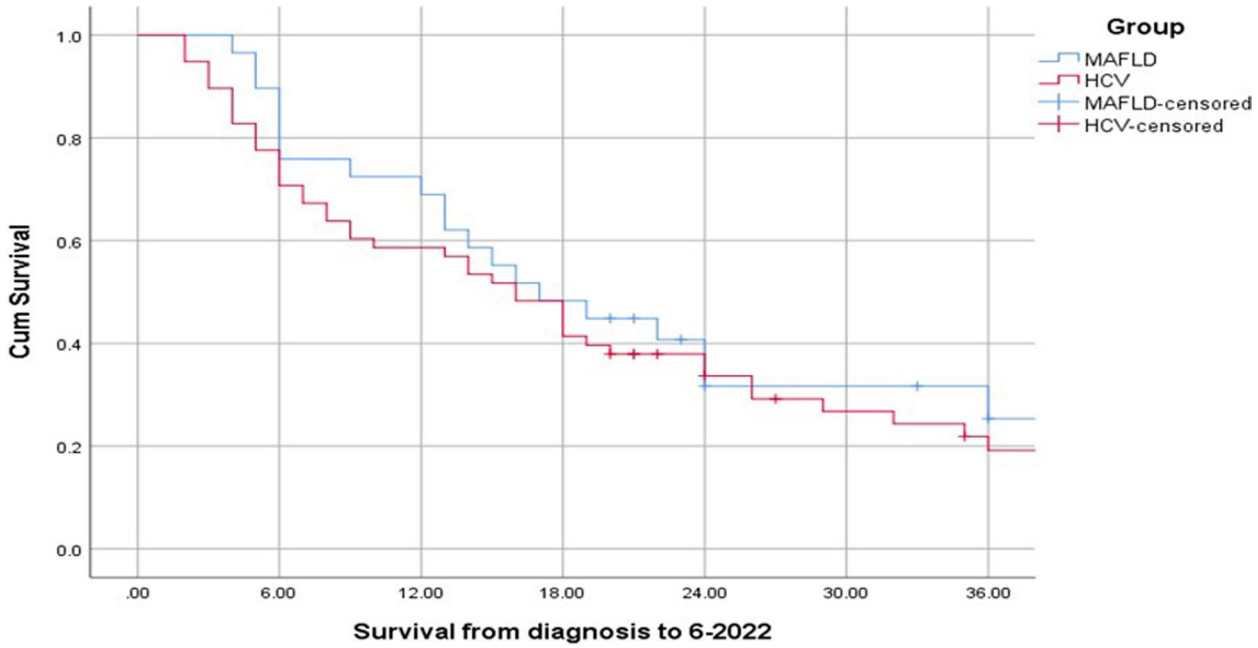

Fig 2 Kaplan-Meier curve showing comparison of survival of both groups from the time of diagnosis with HCC till 6-2022

Moreover, as regard to the total months of survival from diagnosis of HCC to June 2022, group (A) showed a median of 17 months (IQR 9–24), while group (B) showed a median of 16 months (IQR 6–26) with no significant statistical difference between the two groups as shown in Fig. 2.

Discussion

Prevalence of MAFLD is alarmingly growing worldwide in all different populations, and it also becomes an important leading cause of cirrhosis and HCC which needs to be identified and characterized from all aspects [16].

In the present study as regard the different types of management and interventions received in patients of the studied groups, we found in group (A) that 12 patients (41.38%) underwent trans-arterial-chemoembolization (TACE), 6 patients (20.69%) underwent radiofrequency ablation (RFA), 1 patient (3.45%) underwent microwave ablation (MWA), 1 patient (3.45%) underwent surgical resection of HCC, 3 patients (10.34%) received sorafenib, and the decision of the other 6 patients (20.69%) was best supportive treatment (BST).

These results somehow agreed to Chen and colleagues' study [7] in which MAFLD-related HCC patients who underwent trans-arterial chemoembolization were 43.2%, 6.4% patients received systemic therapy, and 28.8% patients received best supportive care, and these results disagreed with our findings in patients who underwent ablation only and resection of HCC (8.8%, 24%) respectively.

Paradoxically, Myers et al. reported that 21% of their enrolled MAFLD-related HCC cases underwent tumor resection,14% underwent RFA, 44% underwent TACE, 14% received systemic therapy, 27% received best supportive care, and 3% underwent liver transplantation [17].

These results regarding the therapeutic treatment also disagreed with a study conducted in 2022 by Nguyen and colleagues on MAFLD-related HCC patients where 33.3 % of the patients underwent resection,16.7% underwent DEB-TACE, 5.6% of patients underwent RFA, 2.8% underwent MWA, 2.8% received sorafenib, and 30.6% received best supportive care [18].

Different results were described by Ahn et al. who reported that 50% of MAFLD-related HCC cases underwent TACE, 19.6% underwent surgical resection, 16.1% received sorafenib, 14.3% received BST, and no one underwent RFA [19]. The median survival of MAFLD-related HCC in this study was 14 months [95% CI, 2.0–26.0] [18].

Meanwhile, in a study of Piscaglia et al. [20], different patterns of tumor burden and liver function led to partially different treatment allocations in the two studied groups. More patients with MAFLD-HCC than HCV-HCC were eligible for liver resection (19.3% versus 10.6%, $P = 0.002$), but more also underwent only supportive care (26.2% versus 12.3%, $P < 0.001$). Percutaneous ethanol injection was adopted more often in HCV patients (9.3 versus 1.4%, $P = 0.002$). However, the overall rate of patients submitted to curative treatments (surgical resection, transplantation, or percutaneous ablation) was similar in the two populations (45.5% versus 49.1% in HCV-HCC, $P =$ non-significant).

Our study showed no significant statistical difference regarding the survival between patients of both groups during 1 year from their diagnosis with HCC ($p = 0.184$).

In the current study, the mean total months of survival from diagnosis with HCC to December 2022 was 19.14 months and median (IQR) of 16 (6–24) months. MAFLD-related HCC patients had mean total months of survival of 17 (9–24) months, while HCV-related HCV patients had mean total months of survival of 16 (6–26) months with no significant statistical value between both groups ($p = 0.522$).Of note this study, the outcomes such as survival of the two groups appeared to be similar. However, MAFLD-induced HCC patients are more likely to have metabolic syndrome-related disease. These patients are expected to have a shorter lifespan because comorbid diseases that would affect the survival.

These results are partially close to results of the study conducted by Nguyen and colleagues where patients with MAFLD-related HCC had a median survival time of 17.2 months, compared with 23.5 months in those with non-MAFLD-related HCC [18].

Paradoxically, Myres and colleagues' study that was conducted in 2021 on 76 patients with MAFLD-related HCC concluded that the median survival of the MAFLD related HCC cases was 101(46–106) weeks which is much higher than what we found in our study [17]; this could be attributed to the type of their study which was prospective cohort over a longer period of patients' enrollment and follow-up.

Moreover, Piscaglia et al. showed that survival rate at 1 year was 76.4% in MAFLD-related HCC and 84.2% in HCV-related HCC and crude mean survival differed statistically between the two groups, being 27.2 months (95% CI 23.5–30.9) in the MAFLD patients and 34.4 months (95% CI 32.7–36.0) in the HCV patients ($P = 0.015$) [20]. These outcomes might have resulted from a later diagnosis in patients who did not undergo surveillance or a later referral of MAFLD-HCC patients to the study centers with a more advanced tumor stage rather than to a more aggressive tumor biology. Moreover, retrospective studies cannot record definite data about duration of risk factors in MAFLD patients before enrollment to the study centers which may affect exact time of diagnosis, analysis, and outcome of HCC.

Regarding mRECIST after 1 month of the intervention, there is no statistical significant difference regarding RECIST between both groups. Also, we found no statistical differences between the studied groups as regard the other post-intervention laboratory investigations, performance status, child score, or child class. As regard first follow-up after the first intervention, there were no statistical significant differences between both groups except for AFP level; group (A) had a median AFP level of 7.1 (IQR 3.7–22) ng/ml, while group (B) had a median AFP level of 21.8 (IQR 2.8–43) ng/ml.

Meanwhile, regarding follow-up after second intervention, our results showed that 16 patients from group (A) underwent therapeutic intervention for HCC, while 31 patients from group (B) underwent therapeutic intervention for HCC with no statistical significant difference between both groups. There was also no statistical significant difference between the 2 groups as regard to mRECIST after 1 month of this second intervention with *P* value (0.688 and 0.364) respectively.

With regard to the limitations to the current study, the single center nature of the study may limit the generalizability of our results. The study design was a retrospective data collection based on medical files. Moreover, a limited number of the studies compare MAFLD with HCV as an etiology with HCC as regard to post-intervention follow-up; further, comparable studies were needed in the future to assess difference in tumor burden and outcomes between both etiologies.

Conclusion

Studies of MAFLD related HCC are still controversial; however, the current study revealed no significant statistical difference in the outcome of HCC or survival rate among patients with MAFLD-related HCC and patients with HCV-related HCC. Although both of inclusion and exclusion criteria were strict, so the number of participants were not large enough. To our knowledge, this is the first study on MAFLD-HCC in Egypt and Africa; future prospective studies on multi centers are required to focus on MAFLD patients, and strict surveillance program timing is also needed for the early detection and treatment of MAFLD-related HCC.

Abbreviations

MAFLD	Metabolic dysfunction–associated fatty liver disease
HCC	Hepatocellular carcinoma
BMI	Body mass index
CTP	Child-Turcotte-Pugh
BCLC	Barcelona clinic liver cancer
HFL	Hepatic focal lesion
DM	Diabetes mellitus
HTN	Hypertension
AFP	Alphafeto-protein
PVT	Portal vein thrombosis
TACE	Trans-arterial-chemoembolization
RFA	Radiofrequency ablation
MWA	Microwave ablation
BST	Best supportive treatment
mRECIST	Modified Response Evaluation Criteria in Solid Tumors
CR	Complete response
PR	Partial response
SD	Stationary disease

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Not applicable.

Authors' contributions

A.E.D., M.S., and E.B. designed the work. H.F. and Y.A. collected the data and did the statistical analysis. D.Z. and I.M. wrote the manuscript. All authors revised and accepted the manuscript.

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None to declare.

Availability of data and materials

Data related to this study are available whenever needed/requested.

Declarations

Competing interests

The authors report no conflicts of interest in this work.

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