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Prioritizing Hepatocellular Carcinoma Management Strategies and Their Impact on the Outcome of Treatment in Egypt: A Single-Centre Real-Life Retrospective Cohort Study

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ABSTRACT

Background: *Hepatocellular carcinoma (HCC) is a significant health concern worldwide, with low- and middle-income countries bearing the brunt of its high incidence and mortality. In such settings, the priority of curative, locoregional, and systemic therapies is heavily reliant on multidisciplinary team (MDT)-guided decision-making.*

From August 2018 to August 2025, a retrospective cohort study was conducted on adult patients with confirmed HCC who were managed through specialized MDT at Ain Shams University Hospitals in Egypt. Patients were categorized as either interventional radiology, surgical, systemic therapy, or best supportive care pathways according to MDT recommendations. The results incorporated overall survival (OS), disease free survival (DFS), and radiologic response estimated using modified Response Evaluation Criteria in Solid Tumors (mRECIST).

Out of the 686 eligible patients, 155 received interventional radiology treatment, while 156 received surgical therapy, 181 received systemic therapy, and 200 received best supportive care. After radiofrequency ablation, the mean OS in interventional radiology was 26.4 months, while the average OS was 31.7 months after transarterial chemoembolization, with no significant difference between

modalities. The most successful long-term outcomes were achieved through surgical management, with liver transplantation achieving near international standards for 5-year OS, despite the need to depend on living donors. Systemic therapy did not improve outcomes, with the median OS of about 5 months, a result of advanced disease stage (hepatic decompensation), portal vein invasion, and restricted access to immunotherapy.

The allocation of resources to HCC treatment through MDT-guided prioritization allows for a rational allocation and results in comparable outcomes, despite resource constraints. To improve outcomes in low-resource settings, it is imperative to incorporate tumor biology into the selection criteria and expand early detection and access to modern systemic therapies.

Keywords
HCC, Hepatocellular Carcinoma, Multidisciplinary Team, Liver Transplantation, Interventional Radiology, and Systemic Therapy.

Introduction
The leading cause of cancer deaths worldwide is hepatocellular carcinoma (HCC), which is the most prevalent type of primary liver cancer [1,2]. According to recent estimates worldwide, liver cancer is one of the leading causes of cancer death in a significant number of countries, and its frequency is expected to increase further in the coming decades due to population growth and aging [3]. Despite the fact that several of the pathogens responsible for HCC can be prevented, the projected surge in case numbers will put more pressure on healthcare systems, especially those located in low- and middle-income countries (LMICs).

HCC epidemiology is marked by geographical heterogeneity, which refers to differences in the prevalence of viral hepatitis, metabolic risk factors, environmental exposures, and access to surveillance programs [4]. The primary cause of hepatitis infection in Egypt and other parts of the Middle East has been viral, leading to its late-stage appearance and low acceptance of curative measures. Treatment options for HCC in the Middle East and North Africa are primarily focused on surgical resection, local ablation, and liver transplantation due to chronic hepatitis C virus infection. The treatment of malignancy and cirrhotic liver through liver transplantation can result in favorable long-term survival under strict selection criteria [5]. This is a theoretical advantage. Egypt, unlike other countries where there is no established deceased donor program or organ availability, has to rely on living donor liver transplantation and alternative treatment strategies for organ transplantation. However, this situation remains limited [6].

Locoregional therapies, such as transarterial chemoembolization, radiofrequency ablation, and new embolization techniques, are crucial in controlling the disease for various HCC stages. Besides palliative intent, these methods are becoming more common as a way to bridge the gap between patients and their eligibility for surgery or transplantation [7]. Patients who are not suited for locoregional therapy have access to more systemic treatments, such as tyrosine kinase inhibitors and immune checkpoint inhibitor combinations. However, their efficacy is heavily influenced by liver function in addition to disease stage and treatment accessibility [8].

HCC causes significant socioeconomic and quality-of-life challenges for those affected, in addition to clinical factors. The disparity in survival rates, particularly among socioeconomically disadvantaged groups, is partly due to advanced liver dysfunction, treatment-related side effects, and financial difficulties [9,10]. These challenges emphasize the need for a multidisciplinary approach that considers both oncologic benefit and patient-centered and system-level approaches.

The cornerstone of modern care is the multidisciplinary team-based approach to HCC management. The integration of expertise across disciplines in MDTs enables personalized treatment selection and sequencing, which is particularly important in limited resources. A large Egyptian tertiary referral center is the site of the study, which assesses treatment outcomes for patients with HCC managed

Patients and Methods
This retrospective study was conducted in the Tropical Medicine Department, Ain Shams University Hospitals, Cairo, Egypt, in the period from August 2018 to August 2025.

The study population: All HCC patients who presented to the multidisciplinary team(MDT) and registered on the database of the Hepatoma Group of the Tropical Medicine Department and were directed for treatment to the Interventional Radiology Unit, the Viral Hepatitis Research and Treatment Unit, and Ain Shams Center for Organ Transplantation during the study period Ain Shams Center for Organ Transplantation (ASCOT) were eligible to be included in the study provided they fulfill the inclusion criteria.

Inclusion criteria
- Patients above 18 years old present to Ain Shams University Hospitals with a confirmed HCC diagnosis.
- HCC patients with complete data in the database.

Exclusion criteria
- Patients with missing data.
- Patients with other advanced comorbidities that developed after providing HCC management, which may impact the outcome of the disease.

Sample size calculation
The study included all the medical records in the database for the patients with HCC who presented to the Hepatoma Group at the Tropical Medicine Department, the Viral Hepatitis Research and Treatment Unit, and Ain Shams Center for Organ Transplantation (ASCOT) Ain Shams University Hospital, during 7 years from August 2018 to August 2025 (at least 500 patients).

The retrieved data included:
- The full history, clinical examination results, and laboratory

data (CBC, ESR, alpha fetoprotein, HCV antibodies, HBsAg, HBsAb, etc.).

- The reports of the imaging studies were retrieved, including abdominal US. spiral triphasic abdominal CT and/or triphasic abdominal MRI.
- The multi-disciplinary team's decision for the treatment strategy recommended for each case was retrieved, and the result of the treatment for each case was retrieved. All the details of the treatment, whether surgical, interventional radiology methods, or treatment with systemic therapy, were retrieved.
- The data of cases unfit to receive any of the above treatment lines and were recommended to have the best supportive care. All retrieved data were subjected to statistical analysis.
- The outcome of treatment was analyzed on an individual basis by using the following parameters:

Overall Survival (OS), Progression Free Survival (PFS), an objective measurement for the improvement of the tumor after treatment, e.g., the modified Response Evaluation Criteria in Solid Tumors (mRECIST), was used whenever possible [11].

Statistical analysis

Data were analyzed using SPSS version 26. Continuous variables were presented as mean ± standard deviation (SD), and median and interquartile range (IQR). Categorical variables were summarized as frequency and percentage. Survival analysis was conducted using the Kaplan–Meier method to estimate overall survival (OS) and disease-free survival (DFS).

Ethical considerations

The current research was conducted in accordance with good clinical practice and the principles outlined in the Declaration of Helsinki, following approval of the research protocol by the Faculty of Medicine, Ain Shams University Ethical Committee (FMASU REC), which holds a Federal Wide Assurance Number (FWA 00017585). The research protocol approval number is: FMASU R192/2025. The informed consent requirement was waived by FMASu REC on the basis that the research was conducted retrospectively on retrieved recorded data for anonymous cases.

Results

In the present study, eight hundred HCC patients presented to the HCC MDT at Ain Shams University Hospitals in the period from August 2018 to January 2025. One hundred and fourteen cases were excluded due to incomplete investigations and loss for follow-up. The other six hundred and eighty-six patients were allocated to the lines of treatment based on the HCC staging according to the guidelines. One hundred and fifty-five cases were directed to the interventional radiology treatment arm, one hundred and fifty cases were directed to the liver transplantation treatment arm, one hundred and eighty-one cases were directed to the systemic therapies arm, and two hundred cases were directed to the best supportive care.

The results of the interventional radiology treatment, liver transplantation treatment, and systemic therapies arms are presented as follows:

Interventional Radiology Treatment Arm Results (Tables 1-6)

Most patients were males (56%), with a mean age of 59.2-61.5 years, and a mean follow-up time of 18.5 months.

Table 1: Distribution of patients with HCC treated with radiological intervention. N=155 patients.

Variable	No.	%		
Gender				
Male	87	**56.1**		
Female	68	43.9		
Occupation				
Manual worker	106	68.4		
Administrative	2	1.3		
Medical occupation (nurses, dentists, lab worker)	47	30.3		
Residence				
Rural	138	89		
Urban	17	11		
Comorbid condition				
Hypertension	34	**21.9**		
Diabetes mellitus	7	**4.5**		
Presenting symptom				
Fever	138	89		
Right hypochondrial pain	17	11		
Number of lesions				
Single	113	72.9		
Two lesions	11	7.1		
Multiple	31	20.0		
Site				
Right lobe	150	96.8		
Left lobe	5	3.2		
Number of radiological interventions				
One	86	55.5		
More than one	69	44.5		
	Mean	SD	Range	**95% CI**
Age	**60.4**	7.0	40-78	59.2-61.5
Body weight	78.8	7.5	56-102	77.6-79.9
Body mass index	26.7	7.7	21-36	25.4-27.9

Table 2: Overall survival of patients according to the type of initial intervention.

Overall	Number of deaths	Mean estimate	Standard error	95% CI
RF N=33	8	26.4	1.6	23.2-29.5
TACE N=122	40	31.7	1.3	28.9-34.4

Log rank test 0.8 P=0.3

Our results showed no statistically significant difference in overall survival means among TACE intervention compared to RF although the 2 years' survival rate for initial therapy RF patients is 27.3% with 95% CI (13.2-45.5), While the 2 years' survival rate for initial therapy with TACE is 18.9% with 95% CI (12.3-26.9) (Figures 1-2).

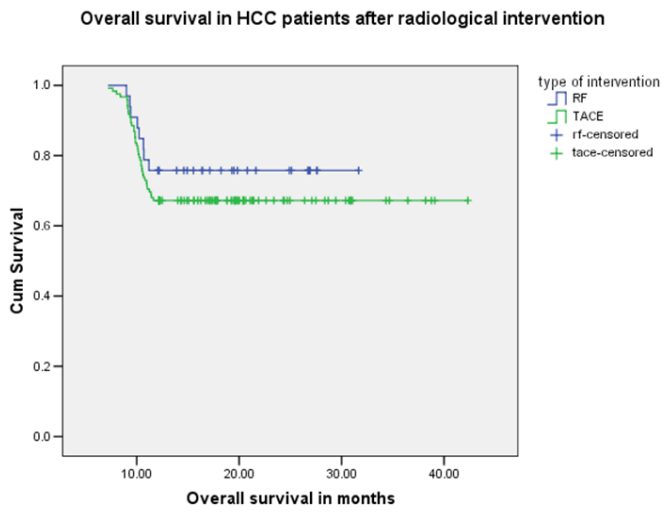

Figure 1: Overall survival in HCC patients after interventional radiology treatment.

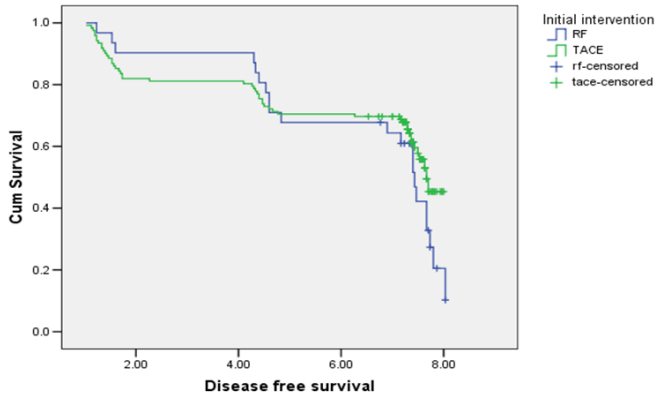

Figure 2: Disease free survival curve after initial interventional radiology treatment.

Table 3: Disease-free survival of patients according to the type of initial intervention.

DFS	Number of events	Mean estimate	Standard error	95% CI
RF N=31	21	6.35	0.3	5.6-7.1
TACE N=122	50	6.24	0.2	5.7-6.6

Log rank test 1.2 P=0.2

Table 4: Overall survival of patients according to the number of interventions received.

Overall	Number of events	Mean estimate	Standard error	95% CI
One N=86	24	33.2	1.5	30.1-36.3
More than one N=69	24	24.1	1.2	21.7-26.5

Log rank test 0.6 P=0.4

There is a higher mean overall survival among patients receiving one intervention compared to patients receiving multiple interventions with no significant difference statistically by the log-rank test (Figure 3).

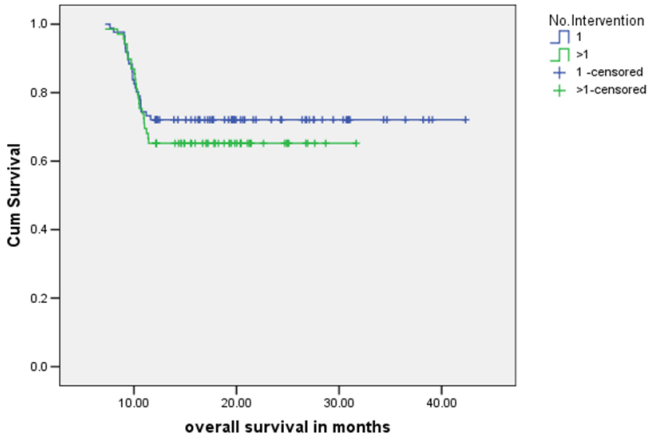

Figure 3: Overall survival curve after interventional radiology treatment according to the number of received interventions.

Table 5: Disease-free survival of patients according to the number of interventions received.

DFS	Number of events	Mean estimate	Standard error	95% CI
One N=85	4	**7.8**	0.09	7.7-8.0
More than one N=68	67	4.4	0.3	3.7-5.0

Log rank test 132.6 P=0.000

P<0.01 is highly significant

This table shows a higher mean survival among patients receiving one intervention (7.8 months) compared to those receiving more than one intervention (4.4 months), with a highly statistically significant difference.

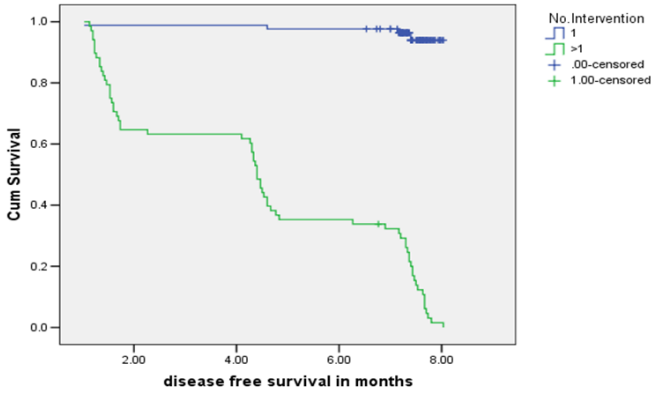

Figure 4: Disease-free survival curve of interventional radiology arm patients according to the number of received interventions.

Results of the Liver Transplantation Treatment Arm:(Tables 6-8)

Table 6: Demographic, Etiology, and Clinical Characteristics of Patients (n = 155).

Variable	Category	N (%)
Gender	Male Female	139 (89.7) 16 (10.3)
Age (years)	Mean ± SD; Range(min.-max.) Median (IQR)	53.59 ± 7.49; 53 (14–67) 55 (49–59)
Etiology	HCV HBV Combined Others	129 (83.2) 11 (7.1) 4 (2.6) 19 (12.3)
Comorbidities	DM HTN	63 (40.6) 36 (23.2)
Ascites	Yes No	92 (59.4) 63 (40.6)
Hepatic Encephalopathy	Yes No	33 (21.3) 122 (78.7)

Figure 5: Survival Curve (10-year follow-up) for surgical treatment arm patients.

Table 7: Tumor Characteristics, Staging, Treatments, and Outcomes (n = 155).

Variable	Category	N (%)
Tumor Site	Rt lobe Lt lobe Bi-Lober	85 (54.8) 26 (16.8) 41 (26.5)
Tumor Size (cm):	Mean ± SD; Range (min.-max.) Median (IQR)	3.25 ± 1.38; 8.5 (0.5–9) 3.0 (2.5–4.0)
Number of Focal Lesions	One Two ≥ Three	73 (47.1) 39 (25.2) 43 (27.7)
HCC Grade	Complete Necrosis Grade 1 Grade 2 Grade 3 Grade 4	25 (16.1) 8 (5.2) 113 (72.9) 4 (2.6) 5 (3.2)
Tumor Number	1 2 3	49 (31.6) 40 (25.8) 66 (42.6)
Size (cm)	Mean ± SD; Range (min.-max.) Median (IQR)	3.0 ± 1.72; 9.3 (0.1–9.4) 2.70 (1.80–3.80)
Microvascular Invasion	Yes No	18 (11.6) 137 (88.4)
Staging Criteria	MILAN UCSF Beyond UCSF	97 (62.6) 52 (33.5) 6(3.9)
Treatment Modalities	Microwave RF TACE Alcohol injection Combined Resection hepatectomy Down staging Bridging	4 (2.6) 21 (13.5) 42 (27.1) 2 (1.3) 32 (20.6) 6 (3.9) 59 (38.1) 40 (25.8)
Response (mRECIST)	Complete Partial Stable Progressive	134(86.5) 12 (7.7) 3 (1.9) 6 (3.9)

Recurrence	Yes No	13 (8.4) 142 (91.6)
Time to recurrence (months)	Mean ± SD; Range (min.-max.) Median (IQR)	24.9 ± 24.7; 86.6 (0.7–87.3) 16.4 (11.1–28.0)
Recurrence Site (n=13)	Hepatic Extrahepatic Both hepatic and extrahepatic	0(0.0) 11 (84.6) 2 (15.4)
Survival Status	Alive Died	104 (67.1) 51 (32.9)
Death Cause (n=51)	HCC recurrence Other	12 (23.5) 39 (76.5)
Overall Survival months	Mean ± SD; Range (min.-max.) Median (IQR)	**88.4 ± 49.7; 149.5 (0.2–149.6)** **120.0 (24.3–120.0)**
Disease-free Survival months	Mean ± SD; Range (min.-max.) Median (IQR)	**87.1 ± 50.5; 149.5 (0.2–149.6)** **120.0 (19.2–120.0)**

Table 8: Early vs. Late Recurrence Distribution Across Clinical and Treatment Variables (n = 13).

Variable	Category	Early Recurrence (n = 3)	Late Recurrence (n = 10)	Total (n = 13)
Age	Mean ± SD	54.0 ± 7.211	52.1 ± 8.762	52.54 ± 8.18
Focal lesion numbers	one	3 (50.0%)	3 (50.0%)	6 (46.2%)
	Two	0 (0.0%)	5 (100.0%)	5 (38.5%)
	≥Three	0 (0.0%)	2 (100.0%)	2 (15.3%)
Size	Mean ± SD	4.167 ± 2.0207	4.33 ± 2.6684	4.29 ± 2.45
Child Class	A	2 (33.3%)	4 (66.7%)	6 (46.2%)
	B	0 (0.0%)	4 (100.0%)	4 (30.8%)
	C	1 (33.3%)	2 (66.7%)	3 (23.1%)
HCC Grade	Complete necrosis	0 (0.0%)	1 (100.0%)	1 (7.7%)
	Grade 2	3 (25.0%)	9 (75.0%)	12 (92.3%)
Tumor number	1	1 (50.0%)	1 (50.0%)	2 (15.4%)
	2	1 (33.3%)	2 (66.7%)	3 (23.1%)
	3	1 (12.5%)	7 (87.5%)	8 (61.5%)
Tumor size	Mean ± SD	3.4 ± 2.15174	4.38 ± 2.07086	4.15 ± 2.04
Alfa-fetoprotein	Mean ± SD	10.9 ± 14.38	94.37 ± 156.26	75.11 ± 140.3
Microvascular Invasion	No	3 (27.3%)	8 (72.7%)	11 (84.6%)
	Yes	0 (0.0%)	2 (100.0%)	2 (15.4%)
Staging Criteria	MILAN	1 (25.0%)	3 (75.0%)	4 (30.8%)
	UCSF	2 (28.6%)	6 (71.4%)	7 (53.8%)
	Beyond	0 (0.0%)	2 (100.0%)	2 (15.4%)
Treatment Modalities	RF	0 (0.0%)	1 (100.0%)	1 (7.7%)
	TACE	1 (25.0%)	3 (75.0%)	4 (30.8%)
	Combined	1 (20.0%)	4 (80.0%)	5 (38.5%)
	Downstaging	2 (40.0%)	3 (60.0%)	5 (38.5%)
	Bridging	0 (0.0%)	5 (100.0%)	11 (84.6%)
Alfa-fetoprotein Before Transplantation	Mean ± SD	66.5 ± 51.95	29.14 ± 31.55	37.76 ± 38.27
Response (mRECIST)	Complete response	2 (18.2%)	9 (81.8%)	11 (84.6%)
	Partial response	0 (0.0%)	1 (100.0%)	1 (7.7%)
	Progressive disease	1 (100.0%)	0 (0.0%)	1 (7.7%)
Overall Survival months	Mean ± SD	45.9 ± 34.2	38.4 ± 39.6	40.11 ± 37.17
Disease-free Survival months	Mean ± SD	5.7 ± 4.7	30.7 ± 25.5	24.91 ± 24.73

- Early Recurrence: Recurrence within the first year after transplantation
- Late Recurrence: Recurrence after the first year from transplantation

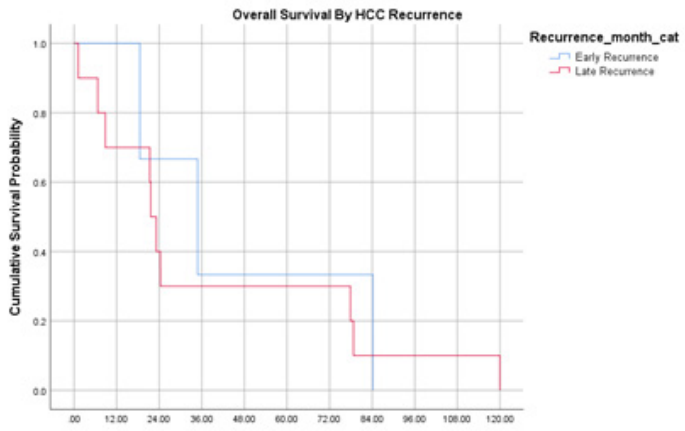

Figure 7: Overall Survival for Surgical Arm Patients with HCC recurrence.

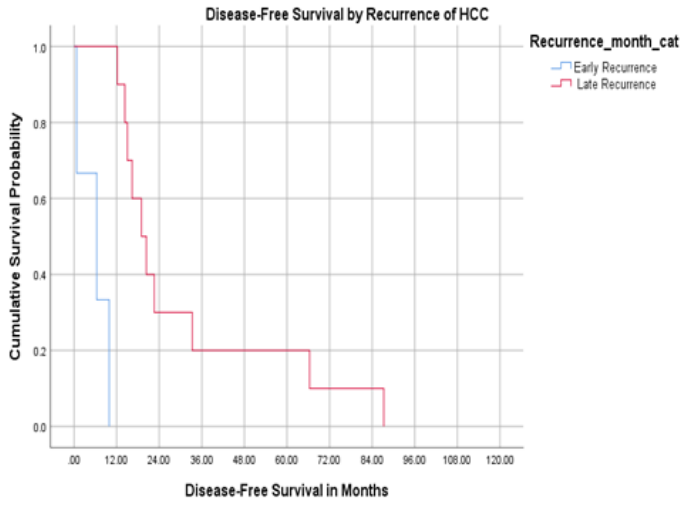

Figure 8: Disease-free survival curve comparing early and late recurrence.

Results of the Systemic Therapy Arm: (Tables 9-16)

Table 9: Demographic and Clinical Characteristics of Patients (n = 181).

Variable	Category	N (%)
Age (years)	Mean ± SD Median (IQR)	62.77 ± 8.29 62 (57.5–69)
Gender	Male	134 (74.0%)
	Female	47 (26.0%)
Etiology	HCV	163 (90.1%)
	HBV	6 (3.3%)
	Others (e.g., Budd-Chiari Syndrome and Cryptogenic)	10 (5.6%)
Comorbidities	Diabetes Mellitus (DM)	63 (34.8%)
	Hypertension (HTN)	56 (30.9%)
	Thyroid Disease	1 (0.6%)
	Cardiac Disease	20 (11.0%)
	Renal Impairment	2 (1.1%)

Table 10: Laboratory Parameters (n = 181).

Variable	Mean ± SD	Median (IQR)
Hemoglobin	12.5 ± 1.9	12.5 (11.0-13.9)
Total Leukocyte Count (×10^3/µL)	6.15 ± 2.54	5.9 (4.1–8.9)
Platelets (×10^3/µL)	195.8 ± 106.0	170 (90–257)
AST (U/L)	56.44 ± 35.42	45 (32–69)
ALT (U/L)	41.24 ± 27.71	32 (25–49)
Serum Albumin (g/dL)	3.68 ± 0.52	3.60 (3.35–4.00)
Total Bilirubin (mg/dL)	1.03 ± 0.43	0.90 (0.70–1.08)
Serum Creatinine (mg/dL)	0.93 ± 0.58	0.90 (0.70–1.10)
INR	1.16 ± 0.19	1.14 (1.07–1.28)
Alfa-fetoprotein (ng/mL)	18,826 ± 107,284	380 (49–2889)
ALBI score	-2.32 ± 0.50	-2.30 (-2.68 _ -2.02)

Table 11: Tumor Characteristics and Clinical Data (n = 181).

Variable	Category / Statistic	N (%)
Number of Focal Lesions	One	91(50.3%)
	Two	36(19.9%)
	Three	47(26%)
	≥ four	7 (3.9%)
Tumor Site	Right lobe	123(68%)
	Left lobe	57(31.2%)
	Bilobar	1(0.6%)
Tumor Size (cm)	Mean ± SD Median (IQR)	7.56 ± 4.43 6.5 (4.0–10.0)
Portal Vein Invasion (PVI)	No	47 (26.0%)
	Yes	134 (74.0%)
PVI Type (n=134)	Segmental	1 (0.6%)
	Right or left	65 (35.9%)
	Main portal	68 (37.6%)
Abdominal Lymph Nodes	Yes	73 (40.3%)
	No	108 (59.7%)
Extrahepatic Spread	Yes	44 (24.3%)
	No	137 (75.7%)
Child-Class	A5	87 (48.1%)
	A6	58 (32.0%)
	B7	36 (19.9%)
BCLC Stage	B	18 (9.9%)
	C	163 (90.1%)
MELD Score	Mean ± SD Median (IQR)	8.97 ± 2.4 9.0 (7-10)

Table 12: Previous Interventions Provided to the Systemic Therapy Arm Patients (n=181).

Variable	Category	N (%)
Denovo patients (Who didn't receive previous interventions)		169 (93.3%)
Locoregional	Radiofrequency Ablation	1 (0.6%)
	Trans arterial Chemoembolization (TACE)	5 (2.8%)
	Trans arterial Radioembolization (TARE)	2 (1.1%)
Surgical	Hepatectomy	4 (2.2%)

Table 13: Treatment Used and Outcomes in the Systemic Therapy Arm patients (n varies).

Variable	Category	N (%)
Tyrosine kinase inhibitors (TKIs)	Sorafenib	150 (82.9%)
	Regorafenib	20 (11.0%)
Immunotherapy	Atezolizumab + Bevacizumab	19 (10.5%)
	Durvalumab + Tremelimumab	12 (6.6%)
Therapy Duration (Days)	**Mean ± SD**	165.37 ± 209.43

Table 14: Therapy Response Markers and Follow-Up Metrics (n=181).

Time	Variable	N (%)	
At 3 months	**AFP (ng/mL): Mean ± SD**	**6269.74 ± 30777.39**	
	mRECIST Response	**Partial Response**	37 (20.4%)
		Stable Disease	57 (31.5%)
		Progressive Disease	26 (14.4%)
		Not estimated	61 (33.7%)
At 6 months	**AFP (ng/mL): Mean ± SD**	**474.08 ± 2130.44**	
	mRECIST Response	**Partial Response**	14 (7.7%)
		Stable Disease	25 (13.8%)
		Progressive Disease	12 (6.6%)
		Not estimated	130 (71.8%)
At 9 months	**AFP (ng/mL): Mean ± SD**	**176.78 ± 779.92**	
	mRECIST Response	**Partial Response**	6 (3.3%)
		Stable Disease	8 (4.4%)
		Progressive Disease	6 (3.3%)
		Not estimated	161 (89%)
At 12 months	**AFP (ng/mL): Mean ± SD**	**34.51 ± 201.94**	
	mRECIST Response	**Partial Response**	4 (2.2%)
		Stable Disease	4 (2.2%)
		Progressive Disease	7 (3.9%)
		Not estimated	166 (91.7%)

Table 15: Therapy Response According to the Received Therapy (n=181).

Time	mRECIST Response	TKI (n=150) N (%)	Immunotherapy (n=31) N (%)
At 3 months	**Partial Response**	31 (20.7%)	6 (19.4%)
	Stable Disease	45 (30.0%)	12 (38.7%)
	Progressive Disease	21 (14.0%)	5 (16.1%)
	Not estimated	53 (35.3%)	8 (25.8%)
At 6 months	**Partial Response**	11 (7.3%)	3 (9.7%)
	Stable Disease	17 (11.3%)	8 (25.8%)
	Progressive Disease	8 (5.3%)	4 (12.9%)
	Not estimated	114 (76.0%)	16 (51.6%)
At 9 months	**Partial Response**	5 (3.3%)	1 (3.2%)
	Stable Disease	4 (2.7%)	4 (12.9%)
	Progressive Disease	5 (3.3%)	1 (3.2%)
	Not estimated	136 (90.7%)	25 (80.6%)
At 12 months	**Partial Response**	4 (2.7%)	0 (0.0%)
	Stable Disease	3 (2.0%)	1 (3.2%)
	Progressive Disease	7 (4.7%)	0 (0.0%)
	Not estimated	136 (90.7%)	30 (96.8%)

Table 16: Treatment Discontinuation and Patients' Survival.

Variable	Category	N (%)
Treatment Continuation	**Continued treatment**	18 (9.9%)
	Discontinued treatment	156(86.2%)
Cause of Treatment Discontinuation (n=156)	**Side effects**	40 (25.6%)
	Decompensation	55 (35.3%)
	Progression	30 (19.2%)
	Upper GI Bleeding	2 (1.3%)
	Loss of follow-up	22 (14.1%)
	Died	7 (4.5%)
Survival Time (months)	**Mean ± SD; Range (min.-max.)** **Median (IQR)**	6.83 ± 6.10; 35.5 (1-36.5) 5.00 (3.00–8.05)
Disease-Free Survival (months)	**Mean ± SD** **Median (IQR)**	6.2 ± 5.8 4.03 (3.00–7.33)

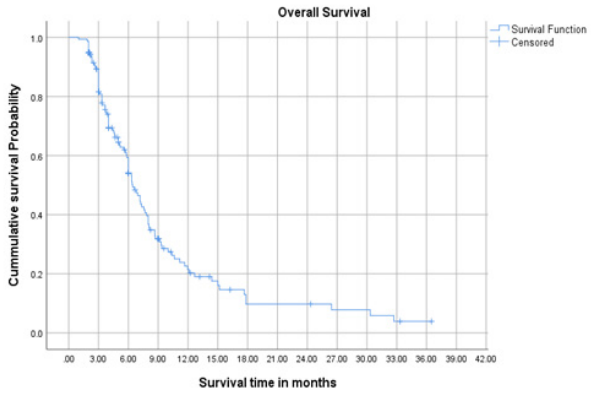

Figure 9: Overall Survival Curve for the Systemic Therapy Arm Patients.

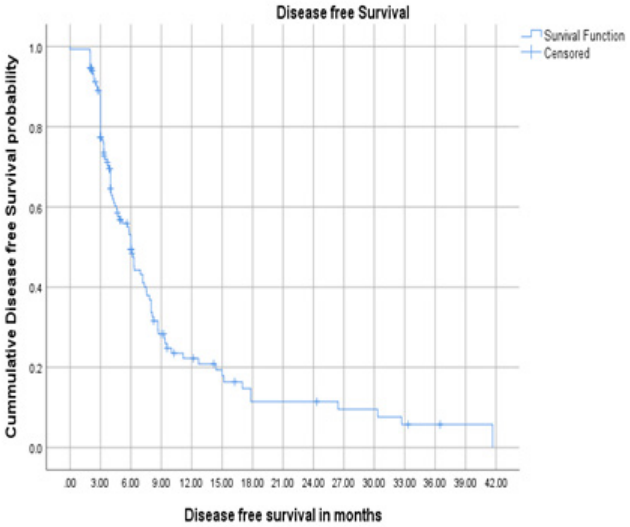

Figure 10: Disease-Free Survival Curve for the Systemic Therapy Arm Patients.

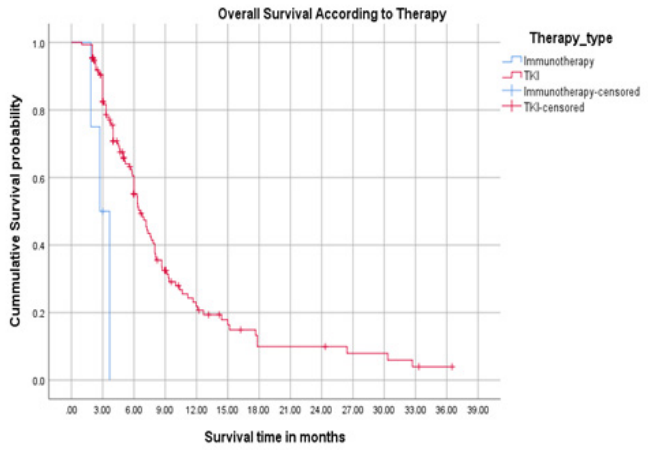

Figure 11: Overall Survival Curve According to the Used HCC Therapy.

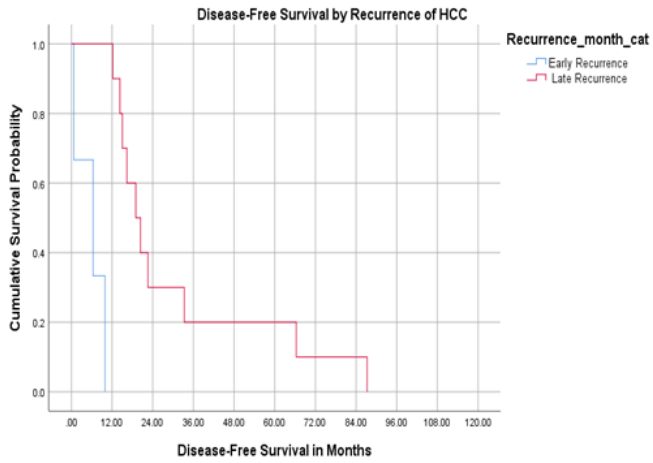

Figure 12: Disease-Free Survival Curve According to the Recurrence of HCC.

Discussion

This research endeavor aimed to investigate the role of an integrated team in prioritizing HCC treatment at Ain Shams University Hospital, a high-risk healthcare facility in Egypt that represents low- and middle-income countries with limited resources.

HCC management has been optimized by multidisciplinary teams (MDTs), which draw on the expertise of specialists from diverse medical fields such as hepatologists, radiologists, surgeons, oncologists and nurse coordinators [12,13]. This approach is also seen as an important aspect. The precise evaluation of MDT evaluation ensures accurate diagnosis and staging, as it takes into account the intricate relationship between tumor burden, liver function, underlying liver disease, and patient performance status, which sets the basis for selecting appropriate therapy lines [14]. Research has consistently shown that MDT involvement significantly increases the availability of curative treatments such as resection, ablation, and transplantation, while also improving compliance with guideline-based treatment pathways, decreasing undertreatment, and making it easier to target specific therapeutic sequences [15,16].

The association between Multidisciplinary Care (MDC) and improved survival rates highlights the potential benefits of treating HCC patients in a multidisciplinary care setting [17].

Elkassas et al. [18] identified significant shortcomings in multidisciplinary HCC management in the Middle East and North Africa (MENA). A lack of consistency, fragmented referral networks, limited access to diagnostic tools, and inadequate public awareness are major obstacles to achieving optimal patient care.

Treatment lines worldwide have embraced multidisciplinary team (MDT) models that combine expertise from various fields such as Hepatology-based medicine, Hepatobiliary surgery, medical oncology, Interventional radiology, Radiological analysis, Pathology, and palliative care. The collaborative nature of MDTs is especially advantageous in HCC, where the presence of chronic liver disease and malignancy necessitates precise staging and customized treatment planning [19,20]. MDTs optimize treatment priority by systematically matching available treatments across different modalities [21] without any artificial intervention.

MDTs play an even more important role in Egypt and the MENA region, where HCC continues to be burdensome for many patients, often with advanced or intermediate cases. The prevalence of hepatitis C sequelae, metabolic syndrome, and variable screening uptake is largely attributed to regional epidemiology, which has led to delayed diagnosis and locoregional or systemic therapies instead of curative options [22,23]. The National Egyptian recommendations explicitly advocate for mandatory MDT review in all HCC cases to promote standardization, equitable access, and optimal outcomes [24].

Ain Shams University Hospitals in Egypt established the first multidisciplinary team to treat hepatocellular carcinoma in March 2002. Ever since then there has been a weekly meeting to review the patient's data and make decisions about treatment. Initially, there were no other treatments except locoregional radiofrequency ablation and trans arterial chemoembolization. Following that, the MDT meetings were attended by surgeons and clinical oncologists. The diagnosis was primarily based on imaging criteria in the triphasic spiral CT. If it was necessary, the samples were sent to the pathologist for testing. This is still in progress. The surgical intervention, resection or liver transplantation is performed at Ain Shams Specialized Hospital. Following the presidential initiative in March 2022 for the early detection and treatment of HCC, Sorafenib was introduced as 1st-line therapy and Regorafinib as 2nd line in April 2021, followed by the introduction of Atezolizumab and Bevacizumab in July 2024 and Durvalumabu and Tremelimumab in January 2025. Egyptian patients can receive HCC immunotherapy for free from the Egyptian Ministry of Health (MOH) and Health Insurance Organization as per the current regulations.

In our cohort of 155 patients undergoing interventional radiology for HCC (mean age 60.4 years, 72.9% single lesions, mean follow-up 18.5 months), observed mean overall survivals after radiofrequency

ablation and TACE were 26.4 and 31.7 months respectively, with no statistically significant difference between modalities. Patients treated with a single intervention had significantly longer disease-free survival than those requiring multiple interventions (7.8 vs 4.4 months; P<0.01). These outcomes compare favorably with many published Egyptian series — which report median survivals for mixed TACE cohorts commonly in the range ~12–18 months 25 and align with the pattern reported from well-resourced tertiary centers in the MENA region and globally when adjusted for stage and liver function [22]. The apparent advantage in our cohort likely reflects a more favorable case mix (high proportion of single lesions and preserved liver function), high IR expertise and MDT care, whereas national averages are lowered by late presentation and heterogeneous access to IR services.

Across our cohort, the use of radiofrequency ablation followed by trans arterial chemotherapy led to similar overall survival rates, while disease-free life expectancy was significantly higher in those who required a single intervention. The outcomes reinforce the idea that repeated locoregional operations typically indicate more aggressive tumor biology or deteriorating liver reserve, which aligns with both regional and international research [25,26].

In this cohort, the most long-lasting survival outcomes were achieved through surgical means, specifically liver transplantation. Despite the use of donor transplantation as the primary method, global standards were set for long-term survival, emphasizing the efficiency of surgical techniques and multidisciplinary approach. In Africa, the first successful liver transplantation (LT) was performed on a 6-year-old child who received the transplant of an Egyptian mother's left lateral segment of her liver. Living donor liver transplant (LDLT) was the 74th procedure reported worldwide [27]. In 2001, the Egyptian Medical Syndicate established regulatory frameworks that enabled new LDLT programs to be implemented. The first case was performed in August of that year [28,29].

While executive regulations were still pending, the Egyptian Parliament passed legislation in 2010 that acknowledged brain death and allowed cadaveric organ transplantation. Socially acceptable notions of brain death remain a major obstacle to expanding the practice of donor donation from deceased individuals [30,31]. In Egypt, 17 active liver transplantation centers are present, performing roughly 370 liver transfusions each year in both public and private healthcare sectors [32].

The prognostic value of recurrence was closely linked to biological factors, including alpha-fetoprotein elevation and microvascular invasion, rather than just tumor size or number.

This observation aligns with the growing international evidence supporting the move away from selection criteria based on morphology and towards more biology-based models of transplant candidacy [33].

Long-term survival rates for liver transplants are high, as demonstrated by the current Egyptian cohort: 94.9% for 1-year OS, 78% for 3-yearOS, and 74.5% for 5-yearOSS. Compared to the current study, survival rates at Egyptian transplant centers are similar or slightly lower. The published Egyptian series exhibits 3- and 5-year OS of 65-75% and 20-30% recurrence rates, particularly given the high prevalence of HCV and the advanced stage of cirrhosis at listing [34].

The process of downstaging tumors using locoregional therapy before transplantation provides a good indication against aggressive tumor that may still progress, while tumor cells with better histology are more likely to respond to treatment and do well after orthotopic liver transplanted [35].

There was a recurrence rate of 25.4% in our cohort of patients, mostly occurring within the first two postoperative years.

Our findings confirm the pivotal role of liver transplantation (LT) as the most effective curative treatment for selected HCC patients but also highlight the persistent challenge of post-transplant recurrence.

Our study also demonstrates that more than half of the recurrences occurred in patients who were initially within Milan criteria, echoing Egyptian reports that morphology-based criteria alone underestimate biological aggressiveness. Accordingly, Egyptian transplant teams increasingly incorporate AFP dynamics, radiologic response, and multidisciplinary assessment—approaches aligned with international directions but still limited by resource constraints [32].

Outcomes from major transplant programs in Saudi Arabia, Turkey, and Iran demonstrate comparable survival patterns, with 5-year OS between 70–80% and recurrence rates of 10–20% in carefully selected candidates [36,37]. Our cohort's 5-year OS of 74.5% is consistent with regional benchmarks, although the recurrence rate of 25.4% is slightly higher than the upper regional average. This difference may be attributable to: Higher prevalence of HCV-related cirrhosis in Egypt, delayed referral and large tumor burden, higher AFP levels and greater incidence of microvascular invasion and dependence on living donor liver transplantation (LDLT) in Egypt compared with cadaveric programs in Gulf countries.

International outcomes for LT in HCC typically show excellent long-term survival. In the landmark work by Mazzaferro et al. [38], 5-year OS reached 70%, a benchmark that continues to define global expectations. More recent Western series report 5-year OS exceeding 80%, with recurrence rates <15% when biological selection criteria are applied [39,33].

The strong predictive effect of AFP ≥400 ng/mL and microvascular invasion in our results mirrors international evidence emphasizing tumor biology over morphology [33,40].

The fact that preoperative locoregional therapy did not significantly affect survival in our cohort aligns with international data

emphasizing that response, rather than treatment type, predicts recurrence [41,42].

The results of the systemic therapy group in the current study were disappointing because of the disease's advanced stage and poor liver function of most patients at diagnosis.The high percentage of patients presenting with portal vein invasion and extrahepatic metastasis, together with frequent interruptions of treatment because of hepatic decompensation, explains the poor survival.

The Egyptian cohort studied here consisted of 181 patients with HCC, of whom most (90.1%) were diagnosed with BCLC stage C, having tumor load with portal vein invasion and extrahepatic metastasis of 74% and 24%, respectively. These characteristics reflect the persistently late presentation of HCC in Egypt, consistent with national studies that have noted high rates of advanced-stage diagnosis driven by underlying HCV predominance and delayed surveillance [43].

While partial radiologic and biochemical responses were documented, overall survival remained substantially shorter than that reported in pivotal clinical trials, illustrating the persistent gap between trial efficacy and real-world effectiveness in LMIC settings [44,45].

Comparison with regional and global data emphasizes both progress and persistent disparities. While outcomes for locoregional and surgical therapies in specialized centers can approximate international standards, access to early diagnosis, transplantation, and modern systemic agents remains uneven. MDTs play a critical mitigating role by tailoring treatment strategies to realistic local capabilities and by facilitating appropriate sequencing, including transitions between locoregional and systemic approaches as disease evolves [22].

While the total number of HCV infections is expected to decline, the number of cases with more advanced liver diseases is expected to increase. As the infected population ages, HCV-infected individuals will advance to cirrhosis, decompensated cirrhosis, and hepatocellular carcinoma (HCC). This suggests that strategies are required to manage the expected increase in HCV disease burden [46].

Therapeutic choices in Egypt are shaped by affordability, availability, and national guidelines. In this cohort, sorafenib remained the main systemic agent (82.9%), while regorafenib and immunotherapy combinations (atezolizumab–bevacizumab and durvalumab–tremelimumab) were used in smaller proportions (11% and 17%, respectively). Overall survival (OS) in this study was modest, with a median of 5 months and a median disease-free survival (DFS) of 4 months. High early discontinuation rates due to decompensation (35.3%) and toxicity (25.6%) further highlight the fragile baseline liver function typical in Egyptian patients with long-standing HCV-related cirrhosis.

In a study from Saudi Arabia, Atezo+Bev had a median OS of 20.94 months, followed by nivolumab at 19.79 months, and finally sorafenib at 11.77 months (HR 1.014, 95% CI 0.79–1.31, p = 0.918). Median overall survival (OS) varied by treatment: patients receiving Atezo+Bev showed the longest OS, followed by nivolumab and sorafenib. No statistically significant difference was observed in survival [47].

The present cohort's OS of 5 months positions Egypt at the lower end of regional performance, largely attributable to more advanced disease stage, heavier tumor burden, and more compromised liver function at presentation. However, in another study from sub-Saharan Africa on HCC patients on top of HBV infection, the median survival in patients treated with Sorafenib or TACE was 94 days (IQR 24 – 121) and 352 days (IQR 30 – 436), respectively [48].

However, the lack of sustained disease control beyond 6–9 months in this cohort reflects treatment discontinuation, resource constraints, and late-stage disease.

International trials have consistently shown substantially better outcomes than observed in this Egyptian real-world cohort. For example: Sorafenib (SHARP trial): median OS 10.7 months [49], Atezolizumab + Bevacizumab (IMbrave150): median OS 19.2 months, PR 27% [45], and Durvalumab + Tremelimumab (HIMALAYA trial): median OS 16.4 months [8], in comparison, this cohort's OS of 5 months and PR rate of ~20% highlight the persistent gap between controlled trial outcomes and real-world results in low- and middle-income countries (LMICs) such as Egypt. Contributing factors include high rates of portal vein invasion, advanced BCLC stage, limited immunotherapy access, and poorer baseline liver function—especially reflected by the high ALBI scores and rates of treatment discontinuation due to decompensation.

Importantly, the magnitude of AFP decline observed at 3–12 months in this cohort—dropping from a median of 380 ng/mL to 34 ng/mL—suggests that some patients achieved meaningful biochemical responses even with TKI therapy, aligning with data suggesting AFP trends are predictive of outcomes [49].

Conclusion

This study demonstrates that multidisciplinary team–guided prioritization is a critical determinant of effective HCC management in resource-limited healthcare settings. Within the Egyptian context, where late presentation, high cirrhosis burden, and constrained access to transplantation and modern systemic therapies remain common, structured MDT decision-making enabled rational allocation of available treatment modalities and optimization of patient outcomes.

Locoregional therapies provided meaningful survival benefit when applied to appropriately selected patients and remain an essential component of intermediate-stage HCC management. Surgical treatment, particularly liver transplantation, achieved the most durable long-term outcomes despite reliance on living donors,

highlighting the feasibility of achieving results comparable to international benchmarks through careful selection and coordinated care. However, post-treatment recurrence was driven predominantly by tumor biological aggressiveness rather than morphologic criteria alone, underscoring the limitations of size- and number-based staging systems.

Outcomes following systemic therapy were modest and reflected advanced disease stage, impaired hepatic reserve, and treatment discontinuation related to liver decompensation. These findings illustrate the persistent gap between clinical trial efficacy and real-world effectiveness in low- and middle-income countries and reinforce the need for earlier diagnosis and expanded access to contemporary systemic agents, including immunotherapy.

Collectively, the results support a transition toward biologically informed, MDT-driven treatment algorithms that integrate tumor markers, radiologic response, and liver function alongside conventional staging. Strengthening surveillance programs, institutionalizing multidisciplinary care pathways, and improving access to advanced therapies are essential steps to narrowing outcome disparities and improving long-term survival for patients with HCC in Egypt and similar healthcare environments.

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