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RESEARCH ARTICLE

CLINICAL OUTCOMES AND LIFE EXPECTANCY OF NON-CURATIVE HEPATOCELLULAR CARCINOMA IN MOROCCO

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Abstract

Background and aim: Hepatocellular carcinoma (HCC) is one of the most common and lethal cancers worldwide, with poor prognosis when diagnosed at intermediate or advanced stages. In Morocco, data on clinical outcomes of non-curative HCC remain scarce. This study aimed to evaluate survival outcomes and prognostic factors in Moroccan patients with intermediate and advanced HCC.

Methods: We conducted a retrospective study including 102 patients diagnosed with Barcelona Clinic Liver Cancer (BCLC) stage B or C HCC between January 2015 and August 2023 at Hassan II University Hospital, Fez. Diagnosis was based on EASL imaging criteria or histology when required. Clinical characteristics, liver function (Child-Pugh score), performance status, tumor burden, treatments, and outcomes were analyzed. Survival probabilities were estimated using Kaplan–Meier methods and compared with the log-rank test.

Results: The mean age was 66 years, with a male predominance (59%). Cirrhosis was present in 84.8% of cases, mainly related to hepatitis C (44%) and hepatitis B (16%). At diagnosis, 47% were symptomatic, 12% had portal vein thrombosis, and 20% had extrahepatic metastases. Treatments included transarterial chemoembolization (72.5%), sorafenib (8.8%), immunotherapy (1%), or best supportive care (14.7%). Overall survival at 1 and 3 years was 60.5% and 43.8%, respectively, with a median survival of 26 months. Patients treated with TACE achieved a one-year survival of 75% and a median survival of 27 months, significantly better than supportive care alone (4 months, $p < 0.001$).

Conclusion: In this Moroccan cohort, the prognosis of non-curative HCC was strongly influenced by treatment modality, with TACE offering the best survival benefit. These findings highlight the need for early detection, systematic screening in cirrhotic patients, and improved access to systemic therapies, including immunotherapy, to optimize patient outcomes.

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Introduction:-

Hepatocellular carcinoma (HCC) is the 7th most prevalent cancer in the world and has the second-highest mortality rate, with an estimated 832,000 deaths worldwide in 2020, just below the level of lung cancer[1]. Its incidence is influenced by various risk factors including cirrhosis, chronic hepatitis B or C infection, HIV co-infection, alcoholic- and non-alcoholic fatty liver disease, diabetes, obesity, and smoking [2].

Even with improved treatment protocols and medication, the expected 5-year survival rate of patients with HCC is less than 20%[3].Later-stage HCC is associated with even worse survival rates; patients diagnosed with Barcelona Clinic Liver Cancer (BCLC) stage B have a median survival time of 21.8 months, while BCLC stage C patients have a time of only 6.6 months[4].

The BCLC guidelines (updated in 2022) divided treatment modalities for HCC patients into two categories: curative and palliative therapy. Therapy selection is mainly based on tumor size, number of tumors, the extent of extrahepatic invasion, performance status, biochemical profile, severity of liver disease and complexity of comorbidity. The curative route—surgical resection, liver transplantation (LT), radiofrequency ablation (RFA), and microwave ablation—is specifically preserved for early-stage HCC or a solitary lesion with preserved liver function. The palliative route includes transarterial chemoembolization (TACE), hepatic artery infusion chemotherapy (HAIC), systemic chemotherapy, immunotherapy, and trans-arterial radioembolization (TARE) with Yttrium-90 and is prescribed for intermediate-to-late-stage HCC and those with extra-hepatic involvement or deteriorated and decompensated liver cirrhosis [5].

In Morocco, the lack of a national cancer registry and frequent delays in diagnosis limit the availability of reliable data on survival and treatment options for patients with HCC. In addition, restricted access to certain innovative therapies, such as immunotherapy, makes management even more complex.

Sorafenib, amultikinase inhibitor, as an oral form of systemic therapy for patients with advanced HCC has shown improved survival and time to progression in patients with advanced HCC[6].The aim of our study is to define the life expectancy, the median survival time and the overall survival time at 1 year and 3 years of advanced HCC.

Materials and methods:-

This was a retrospective study including 102 case of advanced HCC diagnosed in the Gastroenterology Department of Hassan II University Hospital Fez between January 2015 and August 2023, including the clinical profiles and data of patients diagnosed with intermediate (BCLC stage B) and advanced HCC (BCLC stage C).

The diagnosis of hepatocellular carcinoma (HCC) was established based on the non-invasive criteria outlined by the European Association for the Study of the Liver (EASL). According to these guidelines, in patients with cirrhosis, HCC can be diagnosed non-invasively when imaging techniquessuch as a four-phase multidetector CT scan or dynamic contrast-enhanced MRIreveal a lesion larger than 1 cm exhibiting the typical hallmark of HCC: arterial phase hyperenhancement followed by washout in the portal venous or delayed phases. In cases where imaging findings are inconclusive, a biopsy is recommended to confirm the diagnosis [7] .

Eligible patients were those diagnosed with intermediate (BCLC B) or advanced (BCLC C) HCC. Patients who had undergone curative treatments such as surgical resection, radiofrequency ablation, or transplantation were excluded. Survival curves were compared using the log-rank test, and multivariate analysis with Cox regression was considered to identify prognostic factors.

The severity of liver damage was assessed using the Child-Pugh score, which evaluates liver function based on five parameters: bilirubin, albumin, prothrombin time, ascites, and encephalopathy. Therapeutic decisions were guided by the patient's overall health status, as determined by the World Health Organization (WHO) performance status classification, the Child-Pugh score, presence of portal vein thrombosis, and existence of extrahepatic metastases.

The treatments we collected data for were as follows: TACE, immunotherapy, radiation therapy, sorafenib and symptomatic therapy.Data entry and analysis of results were performed using the Statistical Package for Social Science (SPSS) software. Survival was estimated using the Kaplan-Meier curve, in collaboration with the

Epidemiology Department of Hassan II University Hospital in Fez.The study was conducted in accordance with ethical principles and with full respect for patient data confidentiality.

Results:-

We collected 102 cases of non curative HCC. The mean age of diagnosis was 66 years [16 years - 87 years], with a slight male predominance of 58.83%. The liver was cirrhotic in 84.8% of cases vs 15.2% non-cirrhotic.
The etiological diagnosis in cirrhotic patients revealed: hepatitis B in 15.68% cases, hepatitis C in 44.11% cases , primary sclerosing chlongitis (PSC) in 1.96% cases, Portal cavernoma in 1.96% cases,Buddchiari syndrome (BCS) in 1.96% cases, Non-alcoholic steatohepatitis (NASH) in 0.98% cases and Alagille syndrome in 0.98% cases.

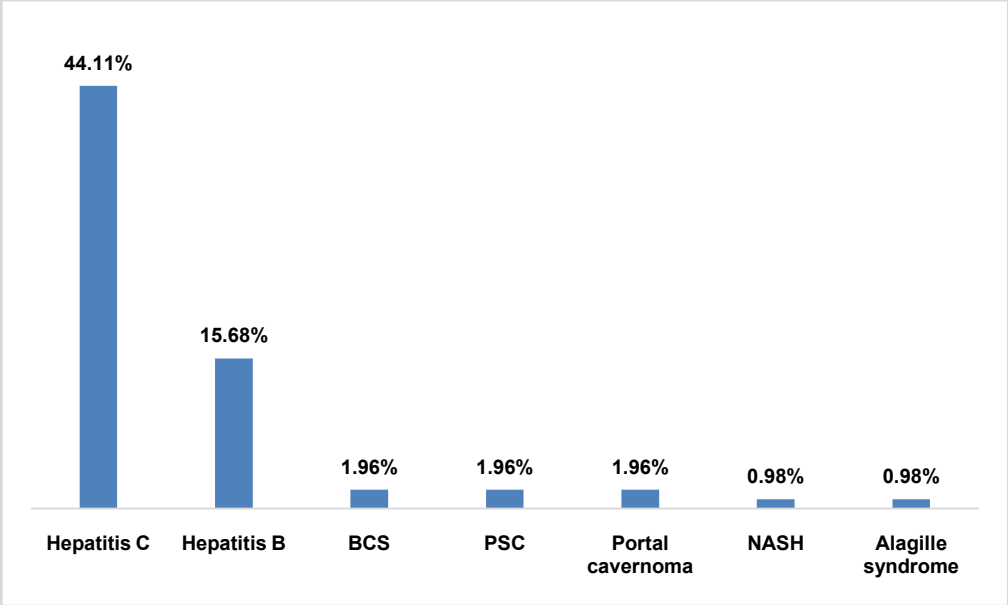

Figure 1: Causes of cirrhosis in patients with HCC

The diagnosis of HCC was made during routine screening in 33.4% cases , incidentally discovered during a radiological examination conducted for another reason in 19.6% cases , or in symptomatic patients in 47.05% cases .
The mean time to diagnosis was 7,58 months [1- 48]. The majority of our patients were in good general condition with WHO performance satuts of 0-1 (89.2%), however, 4.9% of patients had a WHO performance status of 2 and 5.88% of patients had WHO performance status of 3-4 . The CHILD score was < B7 in 66,66% of cases and ≥ B7 in 33.32% of cases, the alpha-fetoprotein AFP was positive in 51.96% with a level ≥ 400 ng/ml in 29.48%.
The positive diagnosis was based on morphologic criteria in 84.8% of cases compared to 15.2% based on histologic criteria. The average size of the HCC was 5.35 cm, ranging from 1.2 cm to 20 cm. A portal vein thrombosis or thrombosis of a branch of the portal vein was identified in 11,76%. Extended work-up revealed extrahepatic metastases in 19.6% of cases. More than half of them were gonglionic.

Table 1: Characteristics of study participants.

Characteristics	Percentage (%)/ Value
Age • < 45 years • 45 - 60 years • > 60 years	**Averageage : 66 years** • 10,78% (n=11) • 24,5% (n=25) • 64,7% (n=66)
Sex: • Male • Female	 • 58,83% (n=61) • 41,17% (n=41)
Liver : • Cirrhotic	 • 84,8% (n= 87)

• Non-cirrhotic	• 15.2% (n= 15)
Post-viral cirrhosis	70.9% (n=81)
Diagnosis of HCC: • Screening • Incidentally discovered • symptomatic patients	 • 33.33% (n=34) • 19.60% (n=20) • 47.05% (n=48)
WHO performance status : • WHO 0-1 • WHO 2 • WHO 3-4	 • 89.21% (n=91) • 4.90% (n=5) • 5.88% (n=7)
Child Pugh score • A (5-6) • B (7-9) • C (10-15)	 • 66.66% (n=68) • 23.52% (n=24) • 9.8% (n=10)
Dignosis of HCC: • Morphologiccriteria • Histologiccriteria	 • 84.8% (n= 86) • 15.2% (n=16)
Size of HCC	5.35 cm
Portal thrombosis	11,76% (n=12)
Extrahepaticmetastases	19.6% (n=21)

All patients were discussed in a multidisciplinary meeting attended by a gastroenterologist, a digestive surgeon, a radiologist, an oncologist, a radiation therapist, and a pathologist.
In our series, 72.5% benefited from chemoembolization with an average of 2 sessions, 8.8% were treated with sorafenib, 1 patient received bevacizumab + atezolimumab immunotherapy, and 14.7% were treated with symptomatic therapy.

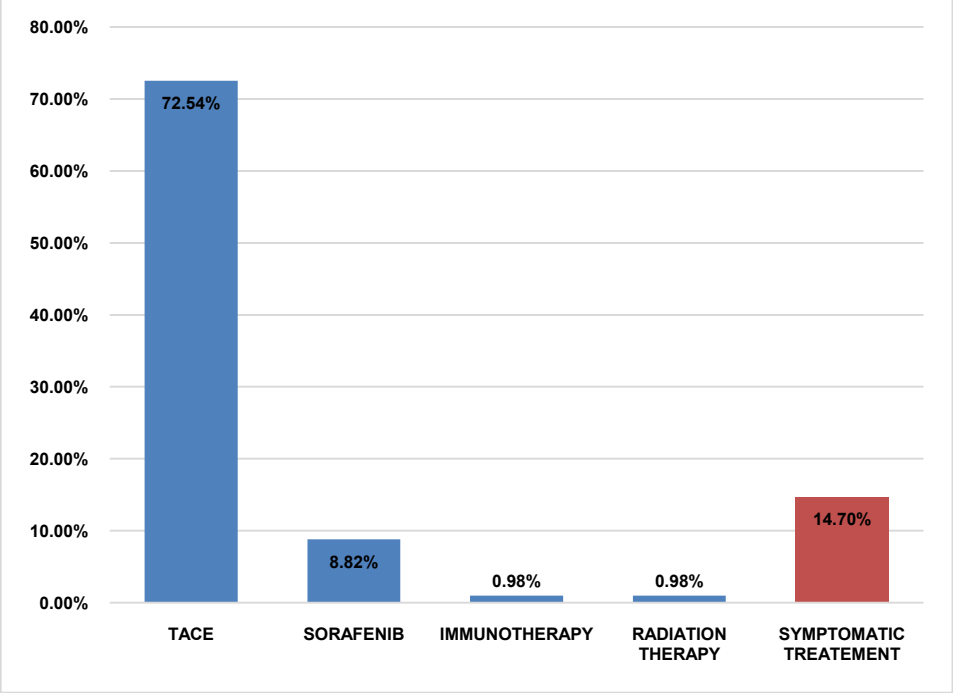

Figure 2: The treatments administered to our patients.

Disease progression was observed in 60.77% vs. 39.23% of patients with response or stabilization, and death was observed in 48.03% vs. 18.6% of patients monitored,

The overall survival rate at 1 year and at 3 years is estimated at 60.5% and 43.8%, respectively. Median survival is estimated at 26 months, with median survival on treatment at 23 months and without treatment at 4 months.
In patients who have undergone TACE, the one-year overall survival rate is estimated at 75%, with a median survival estimated at 27 months.In our study, there is a significant difference in median and overall survival according to treatment with p value at 0.001;

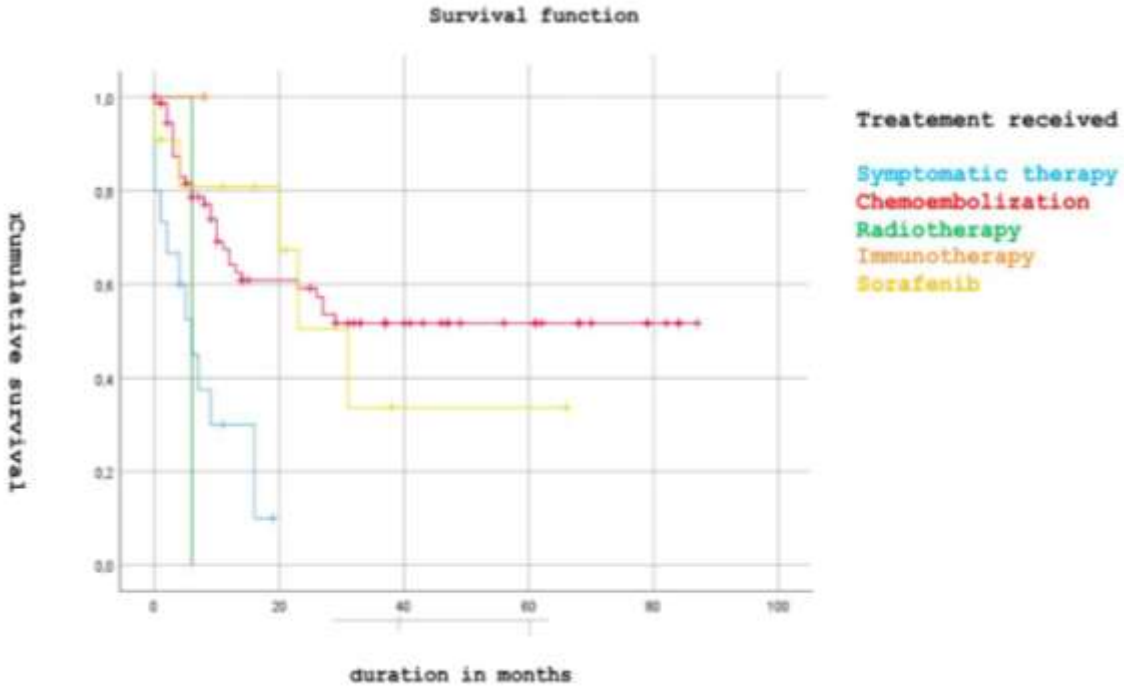

Figure 3: The overall survival curves based on the treatment received.

Discussion:-

Globally, there is an estimation of 830,000 mortality and 906,000 new cases, giving an approximation figure of 1:1 with mortality and incidence of liver cancer. Primary liver cancer is the 3rd most deadly cancer and the 6th most diagnosed cancer overall [8]. In Morocco, hepatocellular carcinoma (HCC) was ranked as the 13th most common cancer and the 9th leading cause of cancer-related death, with an estimated incidence of 1,311 cases in 2020. In the absence of a national cancer registry, these estimates were based on data from the cancer registries of Casablanca and Rabat [9].

Cirrhosis is the primary risk factor for hepatocellular carcinoma (HCC), developing in over 90% of cases on a cirrhotic liver [10]. It can result from various causes, including: Chronic viral infections: such as hepatitis B (HBV) and hepatitis C (HCV). Excessive alcohol consumption. Metabolic diseases: like non-alcoholic steatohepatitis (NASH). Genetic conditions : such as hemochromatosis (iron overload), alpha-1 antitrypsin deficiency, Wilson's disease (copper overload), and, more rarely, autoimmune hepatitis . All types of cirrhosis can lead to HCC, but the risk is particularly high in cases of chronic viral infections, which account for over 80% of HCC cases worldwide [11].

A total of 84,8% of our patients had cirrhosis at the time of HCC diagnosis, which aligns with data from the literature [10,12,13]. Compared to neighboring countries, our survival outcomes appear more favorable. For example, studies conducted in Tunisia and Egypt report median survivals of 15–18 months in advanced HCC, largely due to later diagnosis and limited access to TACE. The relatively higher proportion of BCLC B patients in our series may partly explain the longer survival observed in Morocco.In palliative care, various therapeutic options are available to enhance patient comfort and quality of life.

Transarterial chemoembolization (TACE) is a primary palliative treatment for unresectable hepatocellular carcinoma (HCC), especially at the intermediate stage (BCLC B). The BCLC staging system defines intermediate HCC as presence of multifocal nodules (>3 nodules or a maximum nodule diameter of >3 cm), preserved liver function, no cancer related symptoms,Eastern Cooperative Oncology Group (ECOG) 0, and no macrovascular invasion or extrahepatic spread. The updated BCLC staging system recommends that intermediate-stage HCCs with diffuse, infiltrative, extensive liver involvement do not benefit from TACE, and systemic therapy is the recommended first-line choice for these patients [14].

Two milestone RCTs reported 1-year survival probabilities of 75% and 57% [15], Another systematic review of the treatment efficacy and safety of lipiodol TACE for HCC was published in 2016.It included 10,108 patients in 101 studies, and the results showed a median OS of 19.4 months [16] ,In our study , 72,54% of patients were indicated for TACE ,the one-year overall survival rate is estimated at 78%, with a median survival at 27 months.For nearly a decade, the first-line treatment for advanced HCC (BCLC C- D) was limited to Sorafenib, an anti-angiogenic tyrosine kinase inhibitor (TKI) providing a median overall survival (OS) of 10.7 months [17].

Sorafenib is FDA-approved for the treatment of unresectable HCC based on the results of the phase III SHARP study. In this study, sorafenib demonstrated a significant extension of median overall survival (OS) of 10.7 months compared to 7.9 months in the placebo group (HR: 0.69) (128). Similar results were reported by another phase III study in the Asia-Pacific region (ORIENTAL), with a median OS of 6.5 months for sorafenib compared to 4.2 months in the placebo group (HR: 0.68) [18].In our study , 8,81% of patients were indicated for sorafenib , the one year overall survival rate is estimated at 80%, with a median survival at 19 months.

The results of the phase III IMbrave150 study, comparing the combination of Atezolizumab (an anti-PD-L1 immunotherapy) at a dose of 1200 mg and Bevacizumab (a monoclonal antibody targeting VEGF) at a dose of 15 mg/kg every 3 weeks to Sorafenib treatment, led to a change in first-line treatment recommendations for all patients with advanced HCC. The combination demonstrated improved overall survival of 19.2 months (95% CI 17.0–23.7) compared to 13.4 months with Sorafenib (95% CI 11.4–16.9) ($p < 0.001$) . However, upper gastrointestinal bleeding occurred more frequently with the combination than with Sorafenib (7% vs. 4.5%). Therefore, an endoscopic evaluation is essential before initiating treatment, and preventive treatment for variceal rupture should be implemented if necessary. In light of these results, this combination is now the standard first-line treatment for advanced HCC [19].

In our study 1 patient was indicated for immunotherapy , with an overall survival of 5 months .
14, 7% of our patients had advanced HCC and were not eligible for treatment. All of these patients were placed on symptomatic treatment, with a median survival of 4 months.In our study ,the overall survival rate at 1 year and at 3 years is estimated at 60.5% and 43.8%, respectively. Median survival is estimated at 26 months, with median survival on treatment at 23 months and without treatment at 4 months.

Conclusion:-

The findings of our study highlight the critical need for early detection and appropriate therapeutic strategies in managing advanced HCC, as well as the importance of individualized patient care to optimize outcomes. This underscores the necessity for ongoing research and the development of innovative treatment options to enhance survival rates and improve quality of life for patients facing this challenging diagnosis.The implementation of multidisciplinary approaches that integrate novel therapies and supportive care could further empower healthcare providers to tailor interventions that address the unique needs of each patient.Such strategies may not only improve clinical outcomes but also foster a more compassionate healthcare environment that prioritizes the well-being and dignity of patients throughout their treatment journey.

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