CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.7155384

Available online at: http://www.iajps.com *Review Article*

CLINICAL CHARACTERISTICS AND SURVIVAL RATES OF HEPATOCELLULAR CARCINOMA, A SYSTEMATIC REVIEW

Bassam Farhan Alakhras [1], Zahra Mohammed almusa [2], Sarah Mohammed Alqahtani [3], zahra ali alqambar [4], Amal Ahmad Alorabi [5], fatimah ali alqambar [6], Almaha Yousef Alabbad [7], Zainab Ali alQambar [8]

[1]Internal Medicine and Oncology consultant, drbassam88@gmail.com
[2]Medical Intern, Dar Uloom university, Riyadh, Zahraalmusa19@gmail.com
[3]Post Graduate, Vision College of Riyadh, Saudi Arabia, saramalqahtani6@gmail.com
[4]Medical Intern, Dar Uloom university, Riyadh, Zahraqambar@hotmail.com
[5]Post Graduate, Vision College of Riyadh, Riyadh, amal122195@gmail.com
[6]Medical Student, Dar Uloom university, Riyadh, Fatimahqambar@hotmail.com
[7]Post Graduate, Vision College of Riyadh, Almaha1Alabbad@gmail.com
[8]GP, King Abdualziz university, Jeddah, dr.zaq@hotmail.co.uk

Article Received: September 2022 **Accepted:** September 2022 **Published: September** 2022

Abstract:

Background: *Hepatocellular carcinoma (HCC), which accounts for approximately 75% of primary liver tumors, is one of the most serious complications of chronic liver disease. It is now the sixth most common cancer in the world, contributing to the third leading cause of death from cancer.*

Objectives: *The study aims to summarize current evidences regarding clinical characteristics and survival rates of hepatocellular carcinoma*

Methods: *For article selection, the PubMed database were used. All relevant articles relevant with our topic and other articles were used in our review. Other articles that were not related to this field were excluded. The data was extracted in a specific format that was reviewed by the group members.*

Conclusion: *In conclusion, 13 were enrolled for final data extraction. The most common cause of HCC among Medicare patients is NAFLD which was linked to less HCC surveillance reception, early-stage identification, and somewhat worse survival when compared to other etiologies. Viremic HCC patients had lower survival than post-SVR patients and viremic patients who were treated and achieved SVR after HCC diagnosis.*

Key words: *liver, carcinoma, tumor, HCC, hepatocellular carcinom*

Corresponding author:
Bassam Farhan Alakhras,
Internal Medicine and Oncology consultant,
drbassam88@gmail.com

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Please cite this article in Bassam Farhan Alakhras et al, ***Clinical Characteristics And Survival Rates Of Hepatocellular Carcinoma, A Systematic Review.,*** *Indo Am. J. P. Sci, 2022; 09(09).*

INTRODUCTION:

Hepatocellular carcinoma (HCC), which accounts for approximately 75% of primary liver tumors, is one of the most serious complications of chronic liver disease. It is now the sixth most common cancer in the world, contributing to the third leading cause of death from cancer [1]. Incidence has increased globally, most likely due to an increase in chronic hepatitis B and C infections. Every year, over 500,000 people worldwide develop hepatocellular carcinoma (HCC), and nearly as many die from it [2].

In 80% of patients, HCC is secondary to liver cirrhosis, which is the greatest risk factor, hepatitis B virus (HBV), hepatitis C virus (HBC), alcohol, and / or non-alcoholic steatohepatitis (NASH), inherited liver disorder such as hereditary hemochromatosis (HH), 4% of them develop HCC every year, or it occurs incidentally. Advanced age, male gender, obesity, alcohol abuse, diabetes, and family history are all risk factors for developing HCC [3].

HCC pathogenesis is comprised of various genetic/epigenetic aberrations and alterations with numerous signaling pathways, resulting in a known heterogeneity of the disease's biologic and clinical behavior [4]. The majority of specimens are from hepatectomy procedures and thus represent a subset of patients. HCC genetic heterogeneity is quite impressive. Variations within stages of tumor development in a similar patient, such as nodules, as well as diversity within a tumor, exist between patients [5].

The prognosis of hepatocellular carcinoma depends on both tumor burden and liver dysfunction. Tumor-node-metastasis (TNM) does not account for the degree of performance status and liver dysfunction. The Barcelona clinic's staging system for liver cancer is the most popular (BCLC). A poor prognosis is associated with HCC that is poorly differentiated and has high levels of alpha-fetoprotein [65]. Patients with hepatitis B virus-related HCC who have positive serum levels of hepatitis B e antigen (HBeAg) also have a poor prognosis and are more likely to have HCC recurrence [6, 7]. A higher risk for HCC and recurrence is linked to high serum concentrations of hepatitis B virus DNA [8, 9]. A risk factor for the development of HCC and one that is connected to a poor prognosis is diabetes mellitus [10].

In high-risk patients, such as those with chronic hepatitis B virus (HBV) infection and/or cirrhosis, study of the Liver guidelines recommend surveillance with ultrasound every six months. Reducing all-cause mortality and detecting HCC at an early stage when it is treatable are the objectives of surveillance [11, 12]. The study aims to summarize and assess clinical studies identified clinical characteristics, survival rates and prognosis of hepatocellular carcinoma.

METHODS:

Study design

A systematic review of the current evidence on clinical characteristics, survival rates and prognosis of hepatocellular carcinoma is considered a robust way of identifying and synthesizing the peer reviewed articles for evidence in this area to define a cohesive empirical research agenda that builds on prior knowledge. This review will include qualitative evidence only to produce an interpretation. Further, a synthesis of qualitative data aims to generate findings that are meaningful, relevant and appropriate to individuals, to inform a research agenda and ultimately to more effectively practices on clinical characteristics, survival rates and prognosis of hepatocellular carcinoma. The review will use methods of qualitative synthesis to combine, integrate and interpret, where possible, the evidence from the included papers.

Study eligibility criteria

The review will include qualitative peer-appraised studies. Qualitative data from mixed methods-studies was screened for inclusion and included if the qualitative element is pertinent. The study did not include those studies that have been conducted concerning the topic. All peer-reviewed articles published in English, reporting clinical characteristics, survival rates and prognosis of hepatocellular carcinoma was included.

Study Inclusion and Exclusion criteria

The articles were selected based on the relevance to the project, English language and studies with relative objective was considered. All other articles which do not have one of these topics as their primary end, or repeated studies, and reviews studies were excluded. The reviewers will exclude any studies not available in English, conference abstracts, books or grey literature, Studies that included less than 100 patients, and editorial comments. Studies reporting only qualitative data was excluded. Studies that have significant different methodology compared to other studies included were also excluded.

Search strategy

A systematic search strategy was developed through PubMed database using a combination of Medical Subject Headings (MeSH) and controlled vocabulary

to identify peer-reviewed articles on clinical characteristics, survival rates and prognosis of hepatocellular carcinoma.

Selection of study

The ENTREQ guidelines for reporting qualitative systematic reviews was used to demonstrate the selection processes and results. All retrieved studies will initially be imported into Endnote library to assist removing duplicates. After removing the duplicates, the Endnote library was shared between the two reviewers to independently screen the articles by title and abstract, guided by the eligibility criteria. The studies which the two reviewers would have agreed on was subjected to the full-text review. A third reviewer will adjudicate any discrepancies between the two reviewers. The two reviewers independently review the full text of all eligible studies. In the case where there are differences between the two reviewers, consensus was sought through discussion on the differences with the third reviewer. Finally, the full texts of all relevant studies found to meet the inclusion criteria was retained for the final framework synthesis.

Data extraction

Data was independently extracted by two reviewers from eligible studies onto a customized data extraction form and populated with variables pertaining to the study population and phenomena of interest. Double checking and verification of extracted articles was done by the third review author. Study characteristics that were extracted will include name of the first author and year of publication, data collection period and region in which the study was conducted. Specific study details including the study design, study population, sample size, sampling procedures and data collection procedures then were captured. clinical characteristics, survival rates and prognosis of hepatocellular carcinoma was systematically identified.

Data synthesis and analysis

No software was utilized to analyze the data. The reviewers sorted the data by theme and present the themes in the form of an analysis table (chart). The columns and rows of the table reflect the studies, and related themes and enable authors to compare findings of the studies across different themes and subthemes.

RESULTS:

Figure 1 shows the selection and identification of studies. The search of the mentioned databases returned a total of 286 studies that were included for title screening. 198 of them were included for abstract screening, which lead to the exclusion of 52 articles. The remaining 146 publications full-texts were reviewed. The full-text revision led to the exclusion of 137 studies due to difference in study objectives, and 13 were enrolled for final data extraction **(Table 1).**

In Jingli Ding, et al. 2021 study. [13] There were 80,347 patients covered in all For HCC severity at diagnosis, including SEER stage, tumor size, tumor spread, and lymph node involvement, significant decreasing temporal trends were seen (P 0.001 for all). Patients with HCC experienced improvements in OS and DSS over time (P 0.001). In comparison to patients who underwent no surgery, those who received liver-directed treatment (HR = 0.54), hepatic resection (HR = 0.35), or transplantation (HR = 0.14) had considerably longer DSS. The positive effects of a surgical approach, independent of the kind of therapy, were significant across all phases in stratified analyses. Chen JG, et al. 2021[14] study indicated that The 1-, 5-, 10-, and 20-year observed survival (OS) rates from the data set were 18.51%, 6.28%, 4.03%, and 2.84%, respectively, showing a very significant upward trend (P0.01), liver cancer survival rates have significantly increased over three 15-year periods of 1972-1986, 1987-2001, and 2002-. [14]

Patients with cHCC-CC showed comparable incidences of cirrhosis. Patients with cHCC-CC showed an intermediate prognosis between HCC and ICC, with median overall survival (OS) times of 20.5 months, 35.7 months, and 11.6 months (p0.001) for cHCC-CC, HCC, and ICC, respectively. [15]

Overall Survival in Hepatocellular Carcinoma Patients Undergoing Sorafenib Treatment: According to a Polish Experience: Of the 2072 individuals who received treatment, 27.44% (427) of the 1556 male cases examined did not result in death. This population had a 58.16% one-year survival rate, and it had 34.45%, 21.81%, and 9.72% two-, three-, and five-year survival rates, respectively. The 516 females had 25.78% of their cases filtered (133). For this population, the survival rates at 1, 3, and 5 years were 59.30%, 36.27%, 22.47%, and 11.34%, respectively. The curve profiles by sex did not differ significantly according to statistical testing. [16] LS patients had more favorable baseline features and were more commonly diagnosed while being monitored [17]

According to Ratana-Amornpin S, et al. The prevalence of HCC in old women was greater than in younger people (37.0% vs. 23.2%, p=0.049), whereas the younger group had a considerably better 2-year survival rate (65.0% vs. 45.5%, p=0.03). Poor survival rate was substantially correlated with abdominal

discomfort, ascites upon presentation, ruptured hepatoma, advanced-stage HCC, and serum hypoalbuminemia. [18]

Toyoda H, et al. study showed that compared to individuals with chronic HCV, participants with SVR had less advanced CC and worsening liver function. In comparison to patients with persistent HCV, patients with SVR had a considerably better survival rate following diagnosis (1, 3, and 5 year survival rates of 98.2%, 92.5%, and 86.8% versus 89.5%, 74.7%, and 60.8%, respectively; P 0.001). [19]. Wang J, et al. research comprised 271 people with CHC in total. The 1-, 3-, and 5-year OS rates were 52.3%, 27.1%, and 23.3%, respectively, with the median OS being 14 months. [20] in Kim YA, et al research, the percentage of HCC patients that were untreated was 27.6%, down from 33.4% in 2008 to 24.8% in 2013. Untreated patients had higher rates of older age (P 0.001), female gender (P 0.01), distant SEER stage (P 0.001), severe liver disease (P 0.001), and poorer income (P 0.001) compared to treated patients. The hazard ratio for all-cause death when comparing treated and untreated individuals was 3.11. [21]

Karim MA, et al. showed that NAFLD was the most common cause among 5098 HCC patients, accounting for 1813 cases (35.6%). NAFLD was linked to reduced HCC surveillance receipt, poorer early-stage HCC identification, and marginally worse OS when compared to individuals with hepatitis C-related HCC. [22] Cho YY, et al. Study, which aimed to identify Clinical Profiles of Long-Term Hepatocellular Carcinoma Survivors Following Sorafenib Therapy: According to this extensive, multicenter, retrospective investigation, Korean patients had an objective response rate of 9.1% and a proportion of long-term survival of 16.4%. [23] Yeh ML, et al. found that post-SVR HCC patients had greater median survival than viremic patients (153.3 vs. 55.6 months). [24] Li B, Liu A, et al. studied patients survival rate that were treated surgically and found that Viremic HCC patients had lower survival than post-SVR patients and viremic patients who were treated and achieved SVR after HCC diagnosis.

The included studies had different study designs.

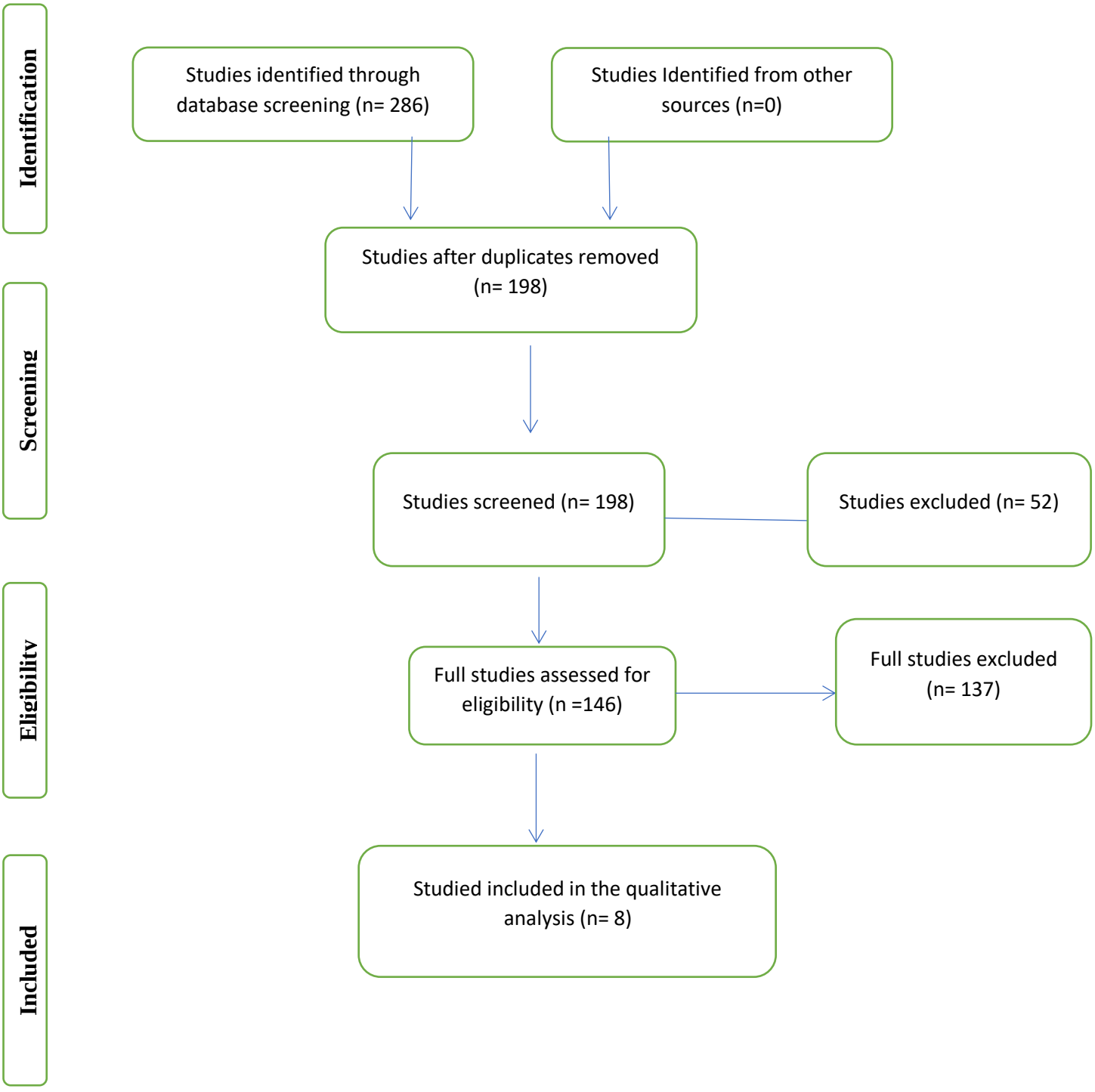

Table 1: Author, country, year of publication, methodology and outcome:

Author, Publishing Year	Methodology	Results	Conclusion
Jingli Ding, et al. 2021 [13]	From 1988 to 2015, individuals with primary HCC were identified using the Surveillance Epidemiology and End Results (SEER) database. Using the Kaplan-Meier technique, overall survival (OS) and disease-specific survival (DSS) were estimated. To calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for prognostic markers and compare survival between patients diagnosed at various times, univariate and multivariate Cox regression models were utilised (per 5-year interval).	There were 80,347 patients covered in all. the proportion of young patients (45 years) and senior patients (75 years) declined with time (P 0.001). For HCC severity at diagnosis, including SEER stage, tumour size, tumour spread, and lymph node involvement, significant decreasing temporal trends were seen (P 0.001 for all). Patients with HCC experienced improvements in OS and DSS over time (P 0.001). Young age, female gender, Hispanic ethnicity, and marital status were factors favouring DSS on multivariate analyses, while a poorer DSS was shown in patients with tumours larger than 5 cm, vascular invasion, and lymph node involvement. In comparison to patients who underwent no surgery, those who received liver-directed treatment (HR = 0.54), hepatic resection (HR = 0.35), or transplantation (HR = 0.14) had considerably longer DSS. The positive effects of a surgical approach, independent of the kind of therapy, were significant across all phases in stratified analyses.	These findings show a considerable increase in patient survival for HCC patients from 1988 to 2015, which may be related to developments in early detection and therapy strategies.
Chen JG, et al . 2021 [14]	From 1972 to 2016, a total of 32,556 patients with liver cancer were recorded. There were both aggressive and passive follow-up techniques used. SPSS22 programme used the life table approach for survival analysis. A significant test was regarded as Wilcoxon (Gehan) statistics. The Joinpoint Regression Program was used to estimate the annual percent change (APC) in relative survival, which was calculated using the SURV programme.	The 1-, 5-, 10-, and 20-year observed survival (OS) rates from the data set were 18.51%, 6.28%, 4.03%, and 2.84%, respectively, while their relative survival (RS) rates were 18.88%, 6.95%, 4.96%, and 4.49%. The 5-year OS and RS rates were 5.93% and 6.54% for 24,338 male patients and 7.34% and 8.15% for 8218 female cases, respectively, with P values less than 0.01. With 5-year OS rates of 2.02%, 4.40%, and 10.76%, 5-year RS rates of 2.18%, 4.83%, and 12.18%, and 10-year OS and RS rates of 0.95%, 3.00%, and 7.02% vs 1.13%, 3.65%, and 8.96%, respectively, showing a very significant upward trend (P0.01), liver cancer survival rates have significantly increased over three 15-year periods of 1972-1986, 1987-2001, and 2002-	The survival rate for liver cancer in Qidong varies significantly by gender and age. Although RWD points to a somewhat worse liver cancer survival rate in this region, significant progress has been made in recent years.
Tang Y, et al 2021 [15]	This study included a total of 1041 eligible patients with pathological diagnoses of cHCC-CC (n=135), HCC (n=698), and ICC (n=208). Cox analysis using univariate and multivariate variables were both used to evaluate significant risk factors. Additional 1:1 matching was done between cHCC-CC and HCC and ICC for significant clinical risk variables. The Kaplan-Meier technique along with the log-rank test was used to	Patients with cHCC-CC showed comparable incidences of cirrhosis, sex, and age with HCC (p0.05) and hepatitis B or C with ICC (p=0.197). Patients with cHCC-CC showed an intermediate prognosis between HCC and ICC, with median overall survival (OS) times of 20.5 months, 35.7 months, and 11.6 months (p0.001) for cHCC-CC, HCC, and ICC, respectively. In matched cohorts, the disease-free survival (DFS) of cHCC-CC was worse than HCC but better than ICC (p0.05), whereas the OS of cHCC-CC was worse than HCC but similar with ICC (p=0.06). Additionally, postoperative transarterial	When matched on albumin level, tumour size, lymph node infiltration, tumour stage, and margin, the long-term survival of cHCC-CC was lower than HCC but similar with ICC. Lack of postoperative TACE and lymph node involvement were linked to a poor outcome for cHCC-CC.

	visualise the survival curves of matched and unmatched cohorts.	chemoembolization (TACE) and lymph node infiltration were separate risk factors for cHCC-CC that were linked to prognosis.	
Straś W, et al. 2021 [16]	Overall Survival in Hepatocellular Carcinoma Patients Undergoing Sorafenib Treatment: A Polish Experience Using the standards of the Polish Drug Program, the assessed group of patients was determined to be eligible for sorafenib treatment. The OS curves were plotted using the Kaplan-Meier technique, and testing was done using the log-rank test. Cox regression was used to do a multivariate analysis of the covariates (sex and age) connected to the patient's time to death.	Of the 2072 individuals who received treatment, 75% (1556) were men and 25% were women (516). 27.44% (427) of the 1556 male cases examined did not result in death (by the date of completing the analysis). This population had a 58.16% one-year survival rate, and it had 34.45%, 21.81%, and 9.72% two-, three-, and five-year survival rates, respectively. The 516 females had 25.78% of their cases filtered (133). For this population, the survival rates at 1, 3, and 5 years were 59.30%, 36.27%, 22.47%, and 11.34%, respectively. The curve profiles by sex did not differ significantly according to statistical testing. Age and OS were not related in any way.	When sorafenib is administered systemically while meeting the established criteria, extremely positive outcomes are possible that are on par with those of the patient subgroups profiled by other authors.
Pelizzaro F, et al. 2021 [17]	intended at evaluating the effect of monitoring on patients with HCC's long-term survival. 1028 cases was chosen with long-term survival (LS group, >5 years) and 2721 controls with short-term survival (SS group, >5 years) from the ITA.LI.CA database. Multivariable logistic regression analysis was used to account for confounding factors in the connection between surveillance and LS. After balancing the baseline features with inverse probability weights, the survival of surveilled patients was given both as observed and adjusted for the lead-time bias, and the comparison of survival between the surveillance and no surveillance groups was also carried out (IPW).	LS patients had more favourable baseline features and were more commonly diagnosed while being monitored (p 0.0001). LS may be predicted independently by surveillance (p 0.0001). Patients who were monitored had substantially longer observed and lead-time corrected survivals than patients who were not monitored (p 0.0001 and p = 0.0008, respectively). No evidence of a difference in survival between the two groups was found in IPW adjusted populations (p = 0.30).	A crucial factor in determining long-term survival in HCC patients is surveillance, which improves early-stage detection and the application of curative therapy. To enhance the prognosis of HCC patients, surveillance systems should be widely implemented.
Ratana-Amornpin S, et al. 2021 [18]	Between January 2009 and January 2019, a retrospective cohort analysis of female HCC patients at Thammasat University Hospital in Thailand was carried out.	There were 187 female HCC patients in total, with a mean age of 65.711.9 years. The prevalence of HCC in old women was greater than in younger people (37.0% vs. 23.2%, p=0.049), whereas the younger group had a considerably better 2-year survival rate (65.0% vs. 45.5%, p=0.03). Poor survival rate was substantially correlated with abdominal discomfort, ascites upon presentation, ruptured hepatoma, advanced-stage HCC, and serum hypoalbuminemia.	Numerous girls are affected by HCC, which typically has a poor prognosis and is identified at an advanced stage, particularly in Thailand and the ASEAN. A poor prognosis is linked to abdominal discomfort, ascites, ruptured HCC, advanced-stage HCC, and serum hypoalbuminemia. In individuals who are at

			risk, early identification of HCC and timely treatment may improve survival rates.
Toyoda H, et al. 2021 [19]	de novo HCC after SVR was described and compared with HCC that formed in individuals with chronic hepatitis C virus (HCV) infection. Characteristics, survival rates, and recurrence rates in 127 patients with initial HCC that developed during persistent HCV infection diagnosed between 2011 and 2015 and 178 patients who developed initial HCC after SVR between 2014 and 2020 were compared. HCC was detected under surveillance in both groups.	Compared to individuals with chronic HCV, participants with SVR had less advanced CC and worsening liver function. In comparison to patients with persistent HCV, patients with SVR had a considerably better survival rate following diagnosis (1, 3, and 5 year survival rates of 98.2%, 92.5%, and 86.8% versus 89.5%, 74.7%, and 60.8%, respectively; P 0.001). The rate of recurrence following curative therapy, however, was comparable among groups. In patients with SVR, liver function improved between the initial HCC diagnosis and recurrence, but it deteriorated in the control group (P 0.001). Additionally, patients with SVR were more likely to obtain curative therapy for recurrence (80.4% versus 47.8%, respectively; P = 0.0008) than those with chronic HCV	Despite identical rates of recurrence following curative therapy, survival of patients with de novo HCC after SVR was considerably greater than that of individuals in whom HCC occurred with chronic HCV infection. Improvements in liver function and a greater incidence of curative therapy for recurrent HCC were factors in this outcome.
Wang J, et al. 2021 [20]	Analysis of Prognostic Factors and Survival Prediction in Patients with Combined Hepatocellular and Cholangiocarcinoma Between 2004 and 2015 was carried out, eligible people were gathered from the Surveillance, Epidemiology and End Results (SEER) database and randomly assigned to the training or verification cohort. To find independent factors connected to OS, univariate and multivariate analyses were conducted. The nomogram was created using multivariate analysis, and the calibration curve and consistency index (C-index) were used to assess how well it predicted outcomes.	This research comprised 271 people with CHC in total. The 1-, 3-, and 5-year OS rates were 52.3%, 27.1%, and 23.3%, respectively, with the median OS being 14 months. In the training and validation cohorts, the corresponding C-indices for the nomogram-based model were 0.76 (95% CI: 0.72-0.81) and 0.72 (95% CI: 0.66-0.79), respectively. The calibration of the nomogram revealed good agreement between the projected and actual 1-, 3-, and 5-year OS rates in both cohorts. In the group receiving surgical therapy, the TNM stage (HR, 1.23; 95% CI: 1.01 - 1.49), and M stage (HR, 1.87; 95% CI: 1.14 3.05) were risk factors. With no statistically significant difference seen, liver transplantation and surgical excision might both greatly increase survival.	For patients with CHC, the pathological grade, TNM stage, and surgery were independent prognostic variables.
Kim YA, et al. 2021 [21]	The purpose of this study was to examine the prevalence, characteristics, and prognosis of untreated hepatocellular carcinoma (HCC) patients over a broad, representative national sample. The National Health Insurance Service (NHIS) database in Korea was used for a cohort research. Between January 2008 and December 2013, 63,668 individuals with newly diagnosed HCC in total were examined. After HCC diagnosis, patients were divided into treatment groups and	The percentage of HCC patients that were untreated was 27.6%, down from 33.4% in 2008 to 24.8% in 2013. Untreated patients had higher rates of older age (P 0.001), female gender (P 0.01), distant SEER stage (P 0.001), severe liver disease (P 0.001), and poorer income (P 0.001) compared to treated patients. The hazard ratio for all-cause death when comparing treated and untreated individuals was 3.11 after complete adjustment. In all pre-defined subgroups, including those with a distant SEER stage and those with significant liver disease, the risk of mortality was greater for untreated individuals. A quarter of individuals with newly diagnosed HCC did not receive any therapy specifically for HCC.	Even among individuals with early-stage diagnoses of HCC, untreated cases are still widespread. Patients with HCC who were not treated had a greater chance of dying than those who were. Reduced income, severe liver disease, older age, and advanced stage were all linked to a lower chance of having HCC therapy.

	no treatment groups using claim codes.		
Karim MA, et al. 2022. [22]	Hepatocellular Carcinoma Associated with Non-Alcoholic Fatty Liver Disease in the United States Clinical Features, e pidemiology and End Results-Medicare database was studied through cohort of HCC patients between 2011 and 2015, and multivariable logistic regression was used to find characteristics related to receiving surveillance, spotting early-stage tumours, and receiving curative therapy. To find variables linked to OS, Cox regression was employe.	NAFLD was the most common cause among 5098 HCC patients, accounting for 1813 cases (35.6%). NAFLD was linked to reduced HCC surveillance receipt, poorer early-stage HCC identification, and marginally worse OS when compared to individuals with hepatitis C-related HCC. NAFLD subgroup analysis revealed that increased OS was linked to early-stage HCC, lack of ascites/hepatic encephalopathy, surveillance, and receipt of curative therapy. Compared to NAFLD patients without concurrent liver illnesses, NAFLD patients with coexisting liver disease were more likely to get monitoring, early-stage identification, curative therapy, and better OS.	The most common cause of HCC among Medicare patients is NAFLD. NAFLD was linked to less HCC surveillance reception, early-stage identification, and somewhat worse survival when compared to other etiologies. To improve the prognosis of patients with NAFLD-related HCC, multifaceted strategies for increasing surveillance uptake are required.
Cho YY, et al. 2021 [23]	Clinical Profiles of Long-Term Hepatocellular Carcinoma Survivors Following Sorafenib Therapy INCLUDED 1,566 individuals with unresectable HCC who had sorafenib therapy between 2007 and 2014 at nine tertiary hospitals in Korea as part of a multicenter, retrospective, cohort analysis. The patients were divided into two groups: long-term survivors (greater than two years of survival; n = 257), and controls (n = 1309). The prognostic variables that affected long-term survival were the main results.	The majority of the patients (83.8%) were male and had stage C liver cancer at the Barcelona clinic (BCLC-C) and chronic hepatitis B (77.3%). 9.0 months represented the median overall survival. According to the mRECIST criteria, eight patients (0.4%) experienced a full response following therapy, whereas 139 patients (8.8%) experienced a partial response. Metformin usage (adjusted hazard ratio, hand-foot skin reaction, and concurrent treatment with chemoembolization or radiation were prognostic variables that predicted long-term survival.	Korean patients had an objective response rate of 9.1% and a proportion of long-term survivorship of 16.4%.
Yeh ML, et al. 2021 [24]	Retrospective analysis of overall survival rates in 1389 HCC patients with HCV infection included 1088 patients with HCV viremia at HCC diagnosis and 301 patients whose HCC developed after HCV eradication (post-SVR HCC) (viremic HCC). Propensity score-matching techniques were also used to assess overall survival in the two groups.	When HCC was diagnosed, post-SVR HCC patients had improved liver function, lower alpha-fetoprotein levels, early BCLC stages, and a greater likelihood of surgical therapy. They were also older, less obese, and less likely to be cirrhotic. Post-SVR HCC was not independently related with survival on multivariate analysis, although overall, post-SVR HCC patients had greater median survival than viremic patients (153.3 vs. 55.6 months). On a sub-analysis, however, it was discovered that patients with viremic HCC who later got anti-viral therapy and attained SVR had a greater median survival than patients with post-SVR HCC.	The greater overall survival of post-SVR HCC patients was driven by advantages in clinical and tumour characteristics at HCC diagnosis; however, HCV eradication after HCC formation was also linked to increased survival.
Li B, Liu A, et al. 2021 [25]	After invasive therapy, the prognostic significance of serum markers in hepatocellular carcinoma was assessed. Six blood indicators for HCC patients following treatment—fetoprotein (AFP), fetoprotein-L3 (AFP-L3),	The findings showed that whereas patients with greater GP73, ALT, and TBil had longer RFS (p = 0.000, 0.020, and 0.019), those with higher AFP and AFPL3 had shorter RFS (p = 0.016 and 0.004). High levels of GP73, ALT, TBil, and low levels of ALB were associated with a substantially increased death rate (p=0.035,	Viremic HCC patients had lower survival than post-SVR patients and viremic patients who were treated and achieved SVR after HCC diagnosis. Favorable

	Golgi protein73 (GP73), alanine aminotransferase (ALT), albumin (ALB), and total bilirubin—were examined using real-world data (RWD). 104 cases were utilised to examine overall survival, and a total of 268 cases were enlisted to study recurrence-free survival (RFS).	0.008, and 0.005, respectively). GP73 and ALT were shown to be independent prognosis variables for RFS, while ALB and ALT were found to be independent prognostic factors for OS, according to multivariate analysis. In early-stage HCC, subgroups analysis revealed that GP73 had superior predictive values to other serum markers (p = 0.023).	clinical and tumour characteristics contributed to better survival among patients with post-SVR HCC compared to patients who developed HCC while being viremic overall. The evidence favours prompt antiviral therapy for HCV patients both before and after the diagnosis of HCC.

DISCUSSION:

Results demonstrate that there has been a considerable rise in the number of patients with localised illness and an earlier peak in the age distribution, which is likely a result of improvements in early diagnosis in this patient population. As evidence that therapeutic efforts, including but not limited to advances in imaging techniques and newly emerging therapeutic options with a curative intent, contributed to this temporal improvement in HCC survival, the period of initial diagnosis retained its independent significance in predicting survival on multivariate analysis and was significant in subgroup analyses in patients diagnosed with localised and regional disease. [13,26,27]

With an overall 5-year survival rate of 34.6%, liver resection can be safely undertaken for multinodular hepatocellular carcinoma (HCC) in the presence of cirrhosis. A countrywide multicenter retrospective study encompassing 18,275 of 42,573 genuine HCC patients who had hepatectomy revealed that the 1, 3, and 5 years overall survival rates were, respectively, 73.2%, 28.8%, and 19.6%. According to data from Shanghai, the 5-year survival rate for clinical resection patients may reach 36.2%, and for small HCC resection cases, it can reach 64.9%. From 1958 to 1970, the overall 5-year survival rate was 4.8%; from 1971 to 1983, it was 12.2%; and from 1984 to 1996, it was 50.5%. For small HCC resection patients, the rates were 33.3%, 52.4%, and 67.1%, respectively, throughout the three time periods. [14]

Many advanced primary liver cancers were treated with sorafenib therapy as an alternate strategy. Because sorafenib was linked to diarrhoea and hand-foot syndrome, a recent comprehensive analysis found that it was not superior to hepatic arterial infusion chemotherapy in patients with advanced HCC. In addition, capecitabine was advised as an alternative to adjuvant chemotherapy after biliary tract malignancy was surgically removed. Regarding cHCC-CC, there was just one research that documented the use of molecular targeted treatment, but it was unable to show that it was superior in terms of recurrence or survival. [15]

In the view of therapy, surgical resection is the most effective method to improve the survival rate, with high 5-year rate up to 63% in Korea,5 and even reached to 93.4% in patients with solitary HCC less than 2 cm in diameter in Taiwan.28 These findings have shown that the level of clinical treatment of liver cancer has indeed improved over the past few decades, among which surgery and small liver cancer have the best therapeutic effects. [14]

According to the articles, the OS of the sorafenib-treated patients ranged from 7 months to 8.7 months, 9.7 months, 11.5 months, 15.3 months, 15.8 months, and even 17.4 months. The tumour growth stage, liver function, overall patient health, and the presence of portal thrombosis in the groups under study all affect the outcomes. Age, sex, race, general health, the B or C stage of the Barcelona Clinic Liver Cancer (BCLC staging) classification, the presence of extrahepatic spread (EHS), macroscopic vascular invasion (MVI), the number and size of the tumours, the cause of cirrhosis, bilirubin, albumin, ALBI (albumin-bilirubin grade), NLR (neutrophil-to-lymphocyte ratio), Child-Pugh score, AFP. [16, 28-35]

In various studies, the percentage of HCC patients who do not get a particular anticancer therapy range from 10% to more than 60%. In the US, individuals were less likely to get HCC-specific therapy if they were elderly, non-Caucasian, and had low socioeconomic position, poor liver function, and poor performance status. In line with these results, we also discovered

that older patients, those with severe liver disease, and those with lower incomes had reduced treatment likelihoods. After correcting for confounding variables, female patients had a greater probability of not receiving HCC therapy. Similar to other research, it found that gender inequality showed up in both lower health spending and poorer health outcomes for women compared to males. [21,36,37]

CONCLUSION:

In conclusion, 13 were enrolled for final data extraction. The most common cause of HCC among Medicare patients is NAFLD. NAFLD was linked to less HCC surveillance reception, early-stage identification, and somewhat worse survival when compared to other etiologies. Viremic HCC patients had lower survival than post-SVR patients and viremic patients who were treated and achieved SVR after HCC diagnosis.

There is considerable increase in patient survival for HCC patients recently, which may be related to developments in early detection and therapy strategies. However, HCC surveillance should not be limited to solely post-SVR patients with cirrhosis, as 30% of post-SVR HCC patients did not have known cirrhosis at the time of HCC onset. When sorafenib is administered systemically while meeting the established criteria, extremely positive results were obtained.

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