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Survival Rates of Hepatocellular Carcinoma BCLC-B Patients who Underwent Hepatic Resection at UP-PGH: A 10-Year Single-Center Experience

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Rationale/Objective: Hepatic Resection (HR) has emerged as a potentially curative treatment for HCC, particularly in Barcelona Clinic Liver Cancer – B (BCLC-B) patients, even though Transarterial Chemoembolization (TACE) is the standard of care according to the BCLC staging system. This study aimed to investigate the characteristics, survival rates and outcomes of patients who underwent HR for HCC BCLC-B at a single center over a 10-year period.

Methods: Patients who were diagnosed HCC BCLC-B and had undergone HR from January 2011 to December 2021 were analyzed. Only complete records with long-term follow-up were included in the study. The authors described patient characteristics, calculated overall survival rates, and assessed associations between patient, disease factors, and survival.

Results: Of 344 patients who underwent HR, 20 of them had complete records with long-term follow-up. This cohort had a median age of 57, predominantly male (70%), exhibiting a median alpha-fetoprotein (AFP) level of 230.5 ng/mL and an average of 4 nodules. Lymphovascular invasion was evident in 65%, with 85% displaying negative primary tumor margins. Major hepatectomy was the primary procedure (50%), followed by bisegmentectomy (40%) and trisegmentectomy (10%). The 1, 2 and 3-year survival rates post-hepatic resection (HR) for HCC BCLC-B stood at 65%, 35% and 25% respectively.

Conclusion: The study shows that the institution's treatment approach for BCLC-B HCC patients achieved acceptable 3-year survival rates, and the median overall survival rate observed are comparable with global data. This study highlights hepatic resection as a potential curative option for BCLC-B HCC patients.

Key words: Hepatocellular carcinoma, BCLC-B, survival rates, hepatectomy

Hepatocellular carcinoma (HCC), the most prevalent primary liver malignancy, is associated with cirrhosis in approximately 80% of cases. Despite advances in understanding its pathogenesis and improvements in diagnostic and surgical techniques, HCC incidence is rising, and prognosis remains poor.[1,2] Given the high rates of recurrence and mortality, effective treatment is essential for improving long-term survival. Various therapeutic approaches, including liver transplantation, Transarterial Chemoembolization (TACE), radiofrequency ablation, and hepatectomy, are employed in HCC management. Notably, hepatectomy—or hepatic resection (HR)—has demonstrated potential as a curative strategy, offering enhanced long-term survival and local disease control, underscoring its importance in HCC treatment.[3] The Barcelona Clinic Liver Cancer (BCLC) algorithm is a widely recognized staging system for HCC. In its initial stages (BCLC-0 & BCLC-A), the algorithm recommends liver resection for HCCs. For BCLC-B patients, TACE remains the preferred treatment for individuals with well-preserved liver function, while those who do not meet the criteria are typically managed with systemic therapy. Recent studies have also demonstrated the efficacy and safety of liver resection in patients with BCLC-B, with comparable and better outcomes observed compared to TACE.[4]

The Philippine General Hospital (PGH), as a tertiary government hospital, plays a crucial role in managing patients with liver diseases, particularly hepatocellular carcinoma (HCC). Equipped with a dedicated liver surgery unit and a well-established multidisciplinary team, PGH has been managing a substantial number of liver cancer cases, with HCC being the most common type.

This study aimed to describe the outcomes of patients diagnosed with BCLC B HCC who underwent hepatic resection at the Division of Hepatobiliary and Pancreatic

Surgery of the University of the Philippines – Philippine General Hospital (UP-PGH) from January 2011 to December 2021. Specifically, the study will describe demographic, clinical and pathologic characteristics of patients who have undergone hepatic resections. It will determine the 1, 2 and 3-year overall survival rates and median overall survival among intermediate stage HCC of these patients. It will identify patient-specific factors (age, functional status, and liver function) and disease-specific factors (tumor grade or differentiation, alpha-feto protein (AFP) values, the size and number of hepatic masses, type of surgery done and resection margins) which may have a significant impact on the survival rates of patients with intermediate stage HCC.

Methods

The study is a retrospective cohort involving review of medical records. All patients fulfilling the inclusion criteria were included in the study. The Philippine General Hospital was the selected study site due to the high volume of patients which may fulfill the study inclusion criteria and the availability and accessibility of medical records to be reviewed for data collection.

Inclusion Criteria

The study included patients who underwent hepatic resections (segmentectomy, bisegmentectomy, trisegmentectomy, right and left trisectionectomy, right hepatectomy, and left hepatectomy) for intermediate stage Hepatocellular Carcinoma from January 1, 2011 to December 31, 2021 whose medical records could be retrieved were included in the study.

Exclusion Criteria

Patients aged less than 19 years old. Patients whose medical records were incomplete or could not be retrieved were excluded from the study. Patients whose data could not be accessed via the ISIS and/or civil registry of the Philippine Statistics Authority.

Definitions

Intermediate stage (BCLC-B) is defined as multifocal HCC (exceeding BCLC-A criteria) with preserved liver function, no cancer-related symptoms (Performance Score 0) and no vascular invasion or extrahepatic spread. As well known, the magnitude of tumor burden may be quite heterogeneous in this stage, and prognosis is also influenced by alpha feto protein (AFP) concentration and the degree of liver function impairment even if still belonging to Child-Pugh class A.[4]

Hepatic Resection (HR) refers to the surgical removal of all or the portion of the liver. Major hepatic resections are termed from the segmental anatomic description of the liver that will be removed. (e.g., Segmentectomy (1 segment), Bisegmentectomy (2 segments), Trisectionectomy: (6 segments), right and left Hepatectomy: 4 segments), as recorded in the patient's operative record.

Tumor Recurrence is defined as radiologic evidence of a new tumor, regardless of size and location, on surveillance ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI) as recorded in the patient chart.

Resection Margin Status is defined as positive if tumor is present within 1 cm from the hepatic surgical margin site as recorded in the patient's pathology report.

Data Collection

Patients were identified using the Integrated Surgical Information System (ISIS) operation query function using the keywords 'hepatectomy' and 'segmentectomy' for the period of January 1, 2011 to December 31, 2021, and was further screened by limiting the final clinical and histopathologic diagnoses of Hepatocellular Carcinoma.

The identified records were retrieved from the UPPGH Medical Records Division, including charts from inpatient admissions and outpatient consults, laboratory and histopathologic examination results, operative techniques, and other available in-hospital data sources. Data collection was performed by the principalinvestigator. Individual demographics, stage and characteristics of primary disease, timing of development of hepatocellular carcinoma, treatment courses applied, histopathologic features, and

other patient-specific and disease-specific factors was compiled for each patient and recorded using a standard data collection form. Individual patient mortality data was requested from the Philippine Statistics Authority (PSA) by determining which study subjects have died and have been issued death certificates, as well as when the patients were registered. The list of patients (complete name and birthdate) was counter checked with the civil registry by the PSA. Those with documented death certificates were confirmed as mortalities while those without death certificates were assumed to be alive at the time of the study.

Data Management

Data were encoded in a digital spreadsheet and summarized in a table. Patient and disease characteristics were processed and expressed as mean values with standard deviations for continuous variables, or as counts and frequency rates for discrete variables. Survival was expressed in months, while time-specific survival rates such as 1-year, 2-year, and 3-year survival rates which were an all-cause mortality rate and were expressed as percentages. Survival status was based on the presence or absence of a death certificate as declared by the PSA, with patients with a death certificate, regardless of cause were classified as dead on the date indicated on the death certificate and those without a death certificate were classified as alive. Overall survival was determined as the interval from hepatic resection until the date of death, or survivorship at data acquisition. For patients whom the date of death or current survival could not be ascertained, surrogate measures, such as the date of last consult or last diagnostic examination done, were taken and interpreted as the endpoint of survival. Other outcome measurements including morbidity and mortality rates were derived from the available data.

Data analysis was done using statistical software (Epi Info), comparing the different patient- (age, functional status, and liver function) and disease-specific factors (tumor grade or differentiation, increased AFP values, the size and number of hepatic masses, type of surgery, and resection margins) determined by specific survival outcome cut-off levels (e.g. patients overall survival less than and greater than 24 months). Baseline characteristics of study patients were presented by mean (standard deviation) for continuous variables and frequency (percentage) for categorical variables. Differences of medians between groups were determined using pairwise Mood's median test. Differences of medians among multiple groups were determined using Mood's median test and pairwise Mood's median test as post-hoc test. Holm-Bonferroni method was used to adjust p-values for multiple comparisons. Factors with significant differences between groups (p value ≤ 0.05) were identified as potentially predictive of survival outcomes.

Results

A total of 344 HCC patients were identified (Figure 1), of which 106 were identified to be at the BCLC-B stage. Of these, 20 hepatic resections were performed, whereas the remainder received TACE and, in a few cases, systemic chemotherapy and radiation therapy. These 20 patients were included in the final data collection and analysis as the other identified cases had either unretrievable records or incomplete data regarding long-term follow-up and outcomes. The follow-up information was incomplete for some cases as not all patients were followed up until disease recurrence.

The study presents the characteristics and outcomes of patients who underwent hepatic resection for BCLC-B HCC in a single center over a 10-year period. The

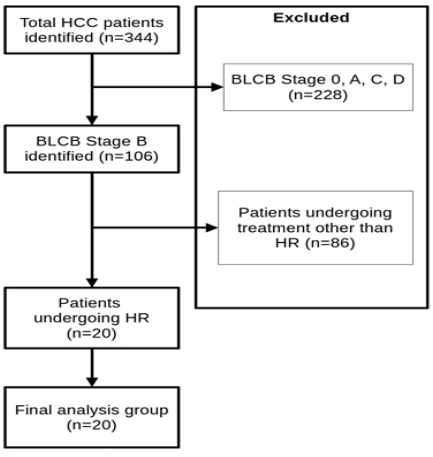

Figure 1. Flow diagram of HCC BCLC Stage B patients undergoing HR at UP Philippine General Hospital from January 1, 2011 to December 31, 2021.

characteristics of the patients are summarized in Table 1.

The median age of the patients was 57 years, with a range of 35-84 years (SD 15.19). The median AFP level was 230.5 ng/mL, with a range of 2.35-2001 ng/ml (SD 667.24). The median number of nodules was 4, with a range of 3-4 (SD 0.31). The median largest size of hepatic nodules was 12.5 cm, with a range of 5.6 – 22 cm (SD 4.06). The median Model for End-Stage Liver Disease (MELD) score was 8, with a range of 7-14 (SD 2.28). (Table 1)

Seventy percent were male and 30% were female. In terms of tumor differentiation, 25% were well-differentiated, 50% were moderately-differentiated, and 25% were poorly-differentiated. Lymphovascular invasion was present in 65% of the patients, and the margin status of the primary tumor was negative in 85% of the cases. Most patients (50%) underwent hepatectomy, while 40% underwent bisegmentectomy and 10% underwent trisegmentectomy. All patients had a Childs Pugh score of A, while none had a score of B. Two patients (10%) were Hepatitis B surface antigen (HBsAg) negative and did not have hepatitis infection, while 18 patients (90%) were positive. (Table 1)

There were no cases of post-operative morbidity, liver-specific morbidity, or 30-day mortality after HR. In terms of overall survival, the 1-year overall survival rate was 65%, which decreased to 35% and 25% at 2-year and 3-year follow-up, respectively. The median overall

Table 1. Baseline demographic, surgical and histopathologic characteristics of study population, UPPGH, 2011-2021.

Characteristic	Median	Range (SD)
Age (years)	57	57 (15.19)
Alpha fetoprotein (AFP) (ng/mL)	230.5	1998.65 (667.24)
Number of nodules	4	1 (0.31)
Largest size of hepatic nodules (cm)	12.5	16.4 (4.06)
MELDS	8	7 (2.28)
Characteristic	**Number**	**(%)**
Gender		
Male	14	70
Female	6	30
Tumor differentiation		
Well differentiated	5	25
Moderately differentiated	10	50
Poorly differentiated	5	25
Lymphovascular invasion		
Absent	7	35
Present	13	65
Margin status of primary tumor		
Negative	17	85
Positive	3	15
Hepatic resection type		
Bisegmentectomy	8	40
Trisegmentectomy	2	10
Hepatectomy	10	50
Childs Pugh Score		
A	20	100
B	0	0
HBsAg		
Positive	2	10
Negative	18	90

survival was 17.19 months, with a wide range of 130.85 months (SD 40.04). (Table 2)

The age of the patients was stratified into two categories: ≤50 years and >50 years, and there was no statistically significant difference in the OS between the two groups (P =0.64). Similarly, there was no significant difference in the OS between male and female patients (P = 1). (Table 3)

When patients were categorized by AFP level (≥1000 ng/mL vs <1000 ng/mL), and there was no significant difference in the OS between the two groups (P = 0.61). There was no statistically significant difference in the OS among well-differentiated, moderately differentiated, and poorly differentiated tumors (P = 0.67). (Table 3) Lymphovascular invasion was categorized as absent or present, and overall survival (OS) appeared lower in patients with lymphovascular invasion than in those without, although this difference was not statistically significant (P = 0.16). When patients were categorized by margin status, the analysis showed a trend toward lower OS in patients with positive margins, although this result was not statistically significant (P = 0.06). (Table 3)

The type of hepatic resection was categorized as bisegmentectomy, trisegmentectomy, or hepatectomy, and there were no significant differences in median OS among these groups (p = 0.11). MELD score was categorized as ≤12 or >12, and while there was a trend toward lower OS in patients with a higher MELD score, this result was not statistically significant (p = 0.14). Finally, the HBsAg status was categorized as positive or negative, and there was no significant difference in the OS between the two groups (p = 0.14). (Table 3) .

In summary, the data indicate that the association between patient and disease-specific factors did not reach the conventional threshold for statistical significance, highlighting the need for further investigation with larger sample sizes.

Discussion

Incidence rates of liver cancer have increased over the previous three decades and are projected to rise to 1,361,080 by 2040 (+61.9% total change). Hepatocellular carcinoma (HCC) constitutes most primary liver cancers.

It is the 5th most prevalent malignancy globally and the second leading cause of cancer-related mortality.[1] With almost ten thousand new cases in 2020, liver cancer ranked fourth in cancer incidence in the Philippines and is the second major cause of cancer mortality.[2] HCC survival rates are low because to the advanced disease stage at

Table 2. Outcome parameters in study population, UPPGH, 2011-2021.

Outcome	Number	(%)
Post-operative morbidity after Resection		
None	20	100
With morbidity	0	0
Liver-specific morbidity after Resection		
None	20	100
With morbidity	0	0
30-day mortality after Resection		
None	20	100
With mortality	0	0
1-year overall survival	13	65
2-year overall survival	7	35
3-year overall survival	5	25
Outcome	**Median**	**Range (SD)**
Overall survival (months)	17.19	130.85 (40.04)

Table 3. Comparison of overall survival between groups based on clinical variables, UPPGH, 2011-2021. OS in months.

Characteristic	OS (SD)	p-value
Age		$p = 0.64$
≤50 years	20.1(29.65)	
>50 years	15.6 (9.99)	
Gender		$p = 1$
Male	17.51 (31.07)	
Female	17.19 (5.61)	
Alpha fetoprotein		$p = 0.61$
≥1000 ng/mL	14.93 (28.25)	
<1000 ng/mL	18.77 (16.59)	
Tumor differentiation		$p = 0.67$
Well differentiated	30.08 (52.10)	
Moderately differentiated	15.26 (11.48)	
Poorly differentiated	20.1 (14.09)	
Lymphovascular invasion		$p = 0.16$
Absent	62.9 (39.86)	
Present	11.57 (12.54)	
Margin status		$p = 0.06$
Negative	20.1 (26.55)	
Positive	4.3 (2.70)	
Hepatic resection type		$p = 0.11$
Bisegmentectomy	20.34 (31.89)	
Trisegmentectomy	5.1 (-)[a]	
Hepatectomy	13.25 (9.96)	
MELD Score		$p = 0.14$
≤12	15.6 (24.88)	
>12	98.45 (-)[a]	
HBsAg		$p = 0.14$
Positive	17.18 (26.56)	
Negative	4.3 (2.7)	

[a]*SD could not be calculated due to uniform data or small sample size.*

diagnosis. The median survival time for untreated HCC ranges from 3 to 9 months, with 5-year death rates as high as >95% every year and a mean age-standardized survival rate of roughly 12% after five years.[4]

The prognostic determinants of survival in patients with hepatocellular carcinoma (HCC) undergoing liver resection have been extensively investigated in various studies. In the present study, a comprehensive analysis was performed to investigate the association between multiple clinical factors, including age, gender, alphafetoprotein level, tumor differentiation, lymphovascular invasion, margin status, hepatic resection type, MELD score, HBsAg status and overall survival (OS) posthepatectomy. None of these factors demonstrated significant prognostic value for

OS. Margin status showed a trend toward association with OS, but the result was not statistically significant ($p = 0.06$). Conversely, Kamiyama, et al. conducted a study to evaluate the prognostic significance of tumor number and the AP-factor, a metric encompassing both tumor size and serum alpha-fetoprotein levels, as predictors of OS after hepatectomy. Their findings demonstrated that patients with a tumor number of ≤3 and/or an AP-factor $< 1 \times 10^5$ had acceptable 5-year OS rates after hepatectomy, while higher tumor numbers and AP-factors were correlated with progressively lower survival rates.[3]

Furthermore, the present study reinforces the existing literature that emphasizes the clinical relevance of numerous prognostic factors in determining the survival outcomes of HCC patients following liver resection. Prior studies have identified poor tumor differentiation, microvascular invasion (MVI), and advanced BCLC stage as key predictors of shorter OS and DFS after hepatectomy for HCC.[5,6,7] A meta-analysis by Sun, et al. showed anatomical resection (AR) significantly improves 5-year survival rates (RR: 0.76, 95% CI:
0.65–0.89, $p < 0.01$) and DFS (HR: 0.64, 95% CI: 0.45–0.91, $p < 0.05$).[5] Hu, et al. further demonstrated that in high-risk MVI patients, AR reduces recurrence and mortality rates regardless of tumor size, emphasizing its prognostic advantage in these cases.[6] Zheng, et al. underscores the impact of microvascular invasion (MVI) on hepatocellular carcinoma (HCC) prognosis, showing poorer outcomes for MVI-positive patients. Anatomical resection improves 5-year DFS (37.72% vs. 27.51%, $p < 0.001$) and OS (61.7% vs. 59.17%, $p < 0.001$) compared to non-anatomical resection. Standardized MVI diagnostic criteria and predictive models are crucial for optimizing treatment and improving survival outcomes.[7]

In this study, patients with a negative margin status had a five-fold longer OS than those with positive margin status, although the difference was not statistically significant ($p=0.06$). This finding is consistent with the study by Wang, et al., which showed that liver resection with a wider surgical margin (>2 mm) significantly improved recurrence-free and overall survival rates compared to a narrow margin (≤2 mm). These results suggest that the determination of surgical margin should be tailored based on both tumor and background liver factors.[8] Wide surgical margins significantly improve outcomes for HCC patients with MVI. Additionally, a metanalysis done by Zheng, et al., showed better 5-year OS (76.3% vs. 56.8%) and DFS (71.1% vs. 25.4%) with margins ≥1 cm[7]. Wide surgical margins have demonstrated superior OS and recurrence-free survival outcomes in HCC patients, underscoring their importance in optimizing surgical strategies.

This study, conducted at Philippine General Hospital, is consistent with other Asian studies that have evaluated the efficacy of HR in treating BCLC-B hepatocellular carcinoma (HCC). Its results demonstrate that HR patients have a 1-, 2- and 3-year overall survival rate of 65%, 35% and 25%, respectively, with a median survival time of 17.19 months. Present study aligns with Zhou, et al.'s meta-analysis, which demonstrated significantly improved 1-year, 3-year and 5-year overall survival (OS) rates for surgical resection (SR) compared to TACE in patients with large hepatocellular carcinoma (HCC) (1-year OS: OR = 2.19; 3-year OS: OR = 3.47; 5-year OS: OR = 2.72; $p < 0.001$).[9] Similar to findings by Hsu, et al., which demonstrated that surgical resection (SR) offered superior long-term survival compared to TACE in HCC patients beyond the Milan criteria, results of the present study highlight the effectiveness of HR as a treatment modality. Hsu, et al. reported that SR significantly improved survival outcomes, with a 2.56-fold reduced risk of long-term mortality compared to TACE ($p < .001$).[10] Both studies underscore the critical role of surgical intervention in achieving better long-term survival outcomes, even in more advanced or challenging HCC cases.

Current findings further reinforce the potential of HR as a priority treatment, particularly in resource-constrained settings where access to advanced therapies like liver transplantation may be limited. In another Taiwanese retrospective study conducted by Lin, et al., HR was shown to be as safe as TACE with significantly better survival rates in BCLC-B/Child-Pugh A HCC patients, with a 3-year overall survival rate of 49% compared to just 2% for the TACE group.[11] Taken together, these findings suggest that HR may offer survival benefits for BCLC-B HCC patients in select cases; however, TACE remains the guideline-recommended treatment due to broader applicability and lower patient selection constraints.

However, some studies highlight significant survival benefits associated with optimized therapeutic strategies for BCLC-B HCC patients. Varghese, et al. demonstrated that combining TACE with Sorafenib improves overall survival, increasing it to 16 months in BCLC-B patients compared to 9 months with TACE alone.[12] Ding, et al. reported a median survival of 30 months for TACE-only patients, further extended beyond 60 months with sequential treatments like radiofrequency ablation (RFA) following TACE in patients with a partial response.[13] These studies emphasize that optimized therapeutic strategies, including TACE combined with sorafenib or sequential treatments like RFA following TACE, demonstrate substantial survival benefits for patients with BCLC-B hepatocellular carcinoma versus TACE alone.

Providing acceptable standards of care for indigent HCC patients in the Philippines remains a challenge for most government institutions. The increasing cost of locoregional therapy (e.g. TACE) for patients with BCLC B HCC has added to the economic burden of treatment. In contrast to Colorectal and Breast Carcinoma, HCC is not covered by the Z benefits package of the Philippine Health Insurance Corporation (PHIC), the country's socialized universal health coverage provider. Although this study is not a cost analysis, it is worth noting that a single TACE session in the Philippines costs between PHP70,000 and PHP 200,000, depending on the institution and patient needs.[14] TACE often requires multiple sessions (2-3 sessions) depending on the size and number of liver lesions, significantly increasing the total cost. In contrast, hepatic resection is a one-time procedure, with a single upfront cost that is generally lower than the cumulative expenses of multiple TACE sessions, making it a potentially more cost-effective option for suitable patients. However, the high cost of TACE can still be a barrier for the underprivileged, which could marginalize people with resectable BCLC B HCC who could have a chance of achieving satisfactory survival rates if managed according to current standards of care.

This study has several limitations that may affect the validity and generalizability of its findings. The small sample size and single-center design restrict the applicability of results to broader populations. The retrospective nature of the study introduces potential selection and other biases. Additionally, the exclusion of important confounding variables limits the ability to draw causal inferences. The short follow-up period reduces the capacity to evaluate long-term outcomes in HCC patients. Furthermore, the study did not assess quality of life, an essential measure in cancer research, nor did it evaluate the cost-effectiveness of treatment modalities, a critical factor in resource-limited settings like the Philippines. These limitations should be considered when interpreting the results and applying them to other contexts.

Conclusions

The study found that the Institution's treatment approach for BCLC-B HCC patients resulted in an acceptable 3-year survival rates and median overall survival rates comparable to similar cases worldwide. Additionally, the study investigated multiple prognostic factors to identify their association with OS after hepatectomy, but none were found to be statistically significantly associated with OS. Hepatic resection (HR) may be an effective treatment for BCLC-B HCC patients, offering a safety profile and a comparable superior long-term survival rate to TACE.

References

1. El-Serag HB. Hepatocellular carcinoma. N Engl J Med 2011 Sep 22;365(12):1118–27. doi: 10.1056/NEJMra1001683.
2. Philippines Department of Health. Philippine cancer facts and estimates 2020 [Internet]. 2020 [cited 2024 Nov 16]. Available from: https://doh.gov.ph/sites/default/files/statistics/PFCE2020.pdf
3. Kamiyama T, Orimo T, Wakayama K, Shimada S, Nagatsu A, Yokoo H, et al. Survival outcomes of hepatectomy for stage B hepatocellular carcinoma in the BCLC classification. World J Surg Oncol 2017 Aug 22;15(1):156. doi: 10.1186/s12957-017- 1229-x.
4. Reig M, Forner A, Rimola J, Ferrer-Fàbrega J, Burrel M, Garcia-Criado Á, et al. BCLC strategy for prognosis prediction and treatment recommendation: The 2022 update. J Hepatol 2022 Mar;76(3):681-93. doi: 10.1016/j.jhep.2021.11.018.
5. Sun Z, Li Z, Shi XL, He XW, Chen J, Song JH. Anatomic versus non-anatomic resection of hepatocellular carcinoma with microvascular invasion: A systematic review and meta-analysis. Asian J Surg 2021 Sep;44(9):1143–50. doi: 10.1016/j.asjsur.2021.02.023.
6. Hu H, Qi S, Zeng S, Zhang P, He L, Wen S, et al. Importance of microvascular invasion risk and tumor size on recurrence and survival of hepatocellular carcinoma after anatomical resection and non-anatomical resection. Front Oncol 2021 Apr 611: 621-2. doi: 10.3389/fonc.2021.621622.

7. Zheng Z, Guan R, Jianxi W, Zhao Z, Peng T, Liu C, Lin Y, Jian Z. Microvascular invasion in hepatocellular carcinoma: A review of its definition, clinical significance, and comprehensive management. J Oncol 2022 Mar 30;2022:9567041. doi: 10.1155/2022/9567041.
8. Wang H, Yu H, Qian YW, Cao ZY, Wu MC, Cong WM. Impact of surgical margin on the prognosis of early hepatocellular carcinoma (≤5 cm): A propensity score matching analysis. Front Med (Lausanne). 2020 May 7;7:139. doi: 10.3389/ fmed.2020.00139.
9. Zhou L, Zhang M, Chen S. Comparison of surgical resection and transcatheter arterial chemoembolization for large hepatocellular carcinoma: A systematic review and meta-analysis. Ann Hepatol 2023;28(2):100890. doi: 10.1016/j.aohep.2022.100890.
10. Hsu CY, Hsia CY, Huang YH, Su CW, Lin HC, Pai JT, et al. Comparison of surgical resection and transarterial chemoembolization for hepatocellular carcinoma beyond the Milan criteria: A propensity score analysis. Ann Surg Oncol 2012 Mar;19(3):842–9. doi: 10.1245/s10434-011-2060-1.
11. Lin CT, Hsu KF, Chen TW, Yu JC, Chan DC, Yu CY, et al. Comparing hepatic resection and transarterial chemoembolization for Barcelona Clinic Liver Cancer (BCLC) stage B hepatocellular carcinoma: Change for treatment of choice? World J Surg 2010 Sep;34(9):2155–61. doi: 10.1007/s00268-010-0598-x.
12. Varghese J, Kedarisetty CK, Venkataraman J, Srinivasan V, Deepashree T, Uthappa MC, et al. Combination of TACE and Sorafenib improves outcomes in BCLC stages B/C of hepatocellular carcinoma: A single-centre experience. Ann Hepatol 2017 Mar-Apr;16(2):247–54. doi: 10.5604/16652681.1231585.
13. Ding YJ, Chang TS, Shen CH, Kuo LM, Hsu SL, Chen YH, et al. Survival benefit of sequential curative treatment for TACE suitable BCLC stage B HCC patients. Sci Rep 2024;14:22588. doi: 10.1038/s41598-024-72767-4.
14. Hepatology Society of the Philippines. The Philippine Clinical Practice Guidelines for the Diagnosis and Management of Hepatocellular Carcinoma 2021 [Internet]. 2021 [cited 2024 Nov 16]. Available from: https://hsp.org.ph/wpcontent/uploads/2021/10/1-The-Philippine-Clinical-Practice-Guidelines-for-the-Diagnosis-and-Management-of-Hepatocellular-Carcinoma-2021.pdf