World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(RESEARCH ARTICLE)

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Minimally invasive laparoscopic surgery versus open surgery for hepatocellular carcinoma (HCC)

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World Journal of Biology Pharmacy and Health Sciences, 2025, 22(01), 340-349

Publication history: Received on 16 January 2025; revised on 24 February 2025; accepted on 27 February 2025

Article DOI: https://doi.org/10.30574/wjbphs.2025.22.1.0228

Abstract

Background: In recent decades, the use of laparoscopic liver resection (LLR) has grown significantly. Laparoscopic and open major liver resections for the treatment of hepatocellular carcinoma (HCC) are still not well studied, despite the fact that several authors have said that LLR is safer and more effective than OLR in treating HCC.

Objective: To determine minimally invasive laparoscopic surgery versus open surgery of HCC.

Methods: A cross-sectional study was conducted at Park Hospital, New Delhi, India, which was performed between June 2021 to March 2024, The total number of patients in our study were 120. The number of female patients in our study were 36 and males were 84. For all patients, we did diagnostic tests before surgery blood test, Ultrasound and biopsy. Our main focus was on open surgery versus minimally invasive laparoscopic surgery for hepatocellular carcinoma (HCC). We excluded pregnant women in our study. Data was tabulated and analyzed by SPSS version 27.

Result: In a current study total 120 patients were enrolled. The minimum age of patients were 51 years and the maximum age of the patients were 97 years. The mean age were 66.26±9.339 years. The minimum BMI of patients were 20 kg/m2 and the maximum BMI of the patients were 38 kg/m2 . The mean BMI were 33.48±2.883 kg/m2.

The frequency of weight loss were not present in 54 patients and were present in 66 patients. The frequency of abdominal discomfort were not present 96 patients and were present in 24 patients.The frequency of HCC location in left lobe were 25 and were in right lobe in 95 patients. P-Value were <0.02. The frequency of mass size on ultrasound 2 cm patients were 48, The frequency of mass size on ultrasound 3 cm patients were 46, The frequency of mass size on ultrasound 4 cm patients were 7, The frequency of mass size on ultrasound 5 cm patients were 19. P-Value were less than 0.03.The frequency of open HCC surgery who have large scar, more bleeding and more pain were 120 patients and the frequency of minimally invasive HCC surgery who have less scar, less bleeding and less pain were in 120 patients. In our study P-Value were less than (< 0.05).

Conclusion: Our study found that individuals who have minimally invasive hepatocellular carcinoma (HCC) surgery recover more quickly than those who undergo open surgery. Compared to open surgery, individuals who undergo minimally invasive procedures spend less time in the hospital. Compared to the left lobe of the liver, HCC is more frequent in the right lobe. In patients having liver resection, the risk of surgical wound and organ infections following the procedure is reduced with minimally invasive surgery than with open surgery. The majority of hepatocellular

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carcinoma (HCC) diagnoses were made in elderly patients. In our study, there were more male patients than female ones.

Keywords: Hepatocellular carcinoma (HCC); Minimally invasive liver surgery (MILS); percutaneous radiofrequency ablation (pRFA); Ultrasound (US) and Open surgery (OS)

1. Introduction

The most prevalent primary liver tumor and the third most common cause of cancer-related mortality globally is hepatocellular carcinoma (HCC) [1-2]. The disease's incidence and fatality rates are highest in East Asian countries; in the West, its incidence is also rapidly increasing, and it could soon surpass all other causes as the third leading cause of cancer-related fatalities [3–4]. Chronic liver disease, especially cirrhosis, which is the final result of any ongoing hepatic injury, is the most frequent cause of HCC development. Hepatitis B and C viruses, alcohol, metabolically-associated liver disease, and hepatitis C are the most common contributing factors [5]. Hepatic cancer is usually treated surgically, usually by hepatic resection or liver transplantation [6-7].Hepatic resection is regarded as one of the most successful surgical techniques for hepatic cancer. The first microinvasive hepatic resection operation was reported in the 1990s. The use of minimally invasive techniques for hepatic resection has now been reported by a number of additional specialists [8]. About 80% of instances of HCC are caused by liver cirrhosis [9]. In order to treat localized HCC, surgical excision has therefore gained importance [10]. Previously, patients with single nodules smaller than 3 cm were the only ones recommended for surgery. However, according to updated guidelines, the first line of treatment for patients with a single tumor of any size or up to three nodules smaller than 3 cm is surgical removal [11]. As experience grew, surgeons began utilizing minimally invasive surgical procedures to conduct a variety of challenging liver resections [12]. As of right now, the most acceptable LLR indication has been used to do laparoscopic major liver resection and isolated lesions (≤5 cm) in segments 2 [13-14-15]. The majority of patients with HCC usually have cirrhosis and chronic hepatitis. High portal pressure and impaired coagulation make liver resections challenging for patients with cirrhosis [16]. However, it was discovered that patients with cirrhosis who were assigned to Child-Pugh class B had worse long-term outcomes, as well as more inpatient complications and fatalities [17–18]. In actuality, patients with HCC may now choose minimally invasive liver surgery (MILS) over open surgery. Robotic, laparoscopic, and image-guided ablation therapies are examples of MILS techniques [19–20]. However, whether the minimally invasive method improves long-term oncological results, extends the surgical rationale for the illness, or changes the therapeutic plan for HCC is still up for question. It has been demonstrated that laparoscopic and robotic methods are effective in reducing surgical complications and the risk of liver failure after a hepatectomy [21–22]. Laparoscopic ablation (LA) of HCC is another minimally invasive surgical technique that could increase the justification for surgery. LA may be used on patients who are not candidates for formal liver resection or percutaneous radiofrequency ablation (pRFA). Laparoscopy-based microwave ablation overcomes several technological obstacles. The first obvious advantage is the possibility of more adaptable liver access, which would allow the ultrasonography probe and needle to operate from a variety of angles [23].

2. Material and methods

A cross-sectional study was conducted at Park Hospital, New Delhi, India, which was performed between June 2021 to March 2024, the total number of patients in our study were 120. The number of female patients in our study were 36 and males were 84. For all patients, we did diagnostic tests before surgery blood test, Ultrasound and biopsy. Our main focus was on open surgery versus minimally invasive laparoscopic surgery for hepatocellular carcinoma (HCC). We excluded pregnant women in our study. Data was tabulated and analyzed by SPSS version 27.

- **Inclusion Criteria:** All patients diagnosed with HCC.
- **Exclusion Criteria:** Pregnant women.

3. Results

Table 1 Mean Age and BMI of all the enrolled patients (*n=120*)

Variables	Minimum	Maximum	Mean±SD
Age (Years)	51	97	66.26±9.339
BMI (Kg/m2)	20	38	33.48±2.883

In a current study total 120 patients were enrolled. The minimum age of patients were 51 years and the maximum age of the patients were 97 years. The mean age were 66.26±9.339 years. The minimum BMI of patients were 20 kg/m2 and the maximum BMI of the patients were 38 kg/m2. The mean BMI were 33.48±2.883 kg/m2.

Table 2 Frequency and Percentage of Gender (n=120)

Gender	Frequency	Percent	Valid Percent	Cumulative Percent
F	36	30.0	30.0	30.0
M	84	70.0	70.0	100.0
Total	120	100.0	100.0	

In the above table 2, the frequency of Female patients were 36 and the percentage were 30.0. The cumulative percent were the same 30.0. The frequency of male patients were 84 and the percentage were 70.0. Total number of patients were 100 (100 %) in our study.

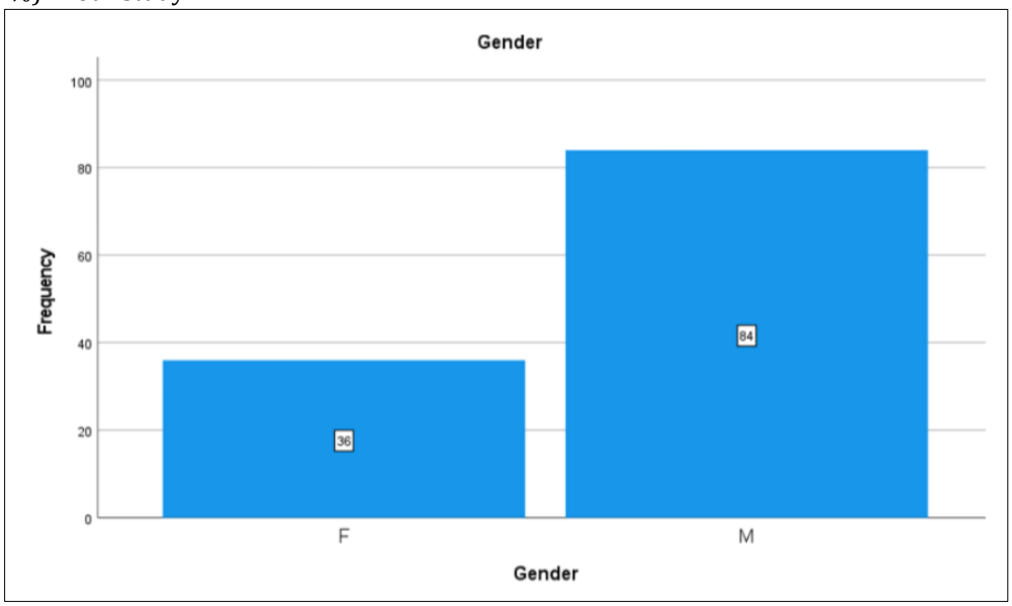

Figure 1 Gender distribution

We can see the male and female patient frequency in the above bar chart.

Table 3 Patient characteristics of enrolled patients (n=120)

Variables	Frequency	Percentage	P-Value
Weight loss			
NO	54	45.0	
YES	66	55.0	
Abdominal Discomfort			
NO	96	80.0	
YES	24	20.0	
Loss of Appetite			
NO	77	64.2	
YES	43	35.8	
Causes			

HBV	76	63.3	0.04
HCV	44	36.7	
Liver Biopsy			
NO	6	5.0	
YES	114	95.0	
HCC Location			
Left Lobe	25	20.8	0.02
Right Lobe	95	79.2	
Mass size on Ultrasound (cm)			
2 cm	48	39.2	
3 cm	46	38.3	
4 cm	5	1.7	
4cm	2	1.7	
5 cm	19	19.0	
Open HCC Surgery			
Large scar, more bleeding, more pain	120	100.0	
Minimally invasive HCC Surgery			
Less scar, Less bleeding, Less pain	120	100.0	
Early detection of HCC oN			
CT Scan	25	20.8	
Ultrasound	95	79.2	
Treatment			
Laproscopic RFA	44	36.7	
Laparoscopic surgery	6	5.0	
Laparoscopic Surgery	6	5.0	
Open Surgery	58	48.3	
Surgical resection	6	5.0	

The current study included a total of 120 patients Minimally invasive laparoscopic surgery versus open surgery for HCC whose characteristics are summarized in Table 3.

The frequency of weight loss were not present in 54 patients and were present in 66 patients. The frequency of abdominal discomfort were not present 96 patients and were present in 24 patients. The frequency of loss of appetitie were not present in 77 patients and were present in 43 patients.

The frequency of causes of HBV were in 76 patients and its percentage were 63.3%. The frequency of causes of HCV were in 44 patients and its percentage were 36.7%. P-Value were <0.04. The frequency of liver Biopsy were not done in 6 patients and were done in 114 patients.

The frequency of HCC location in left lobe were 25 and were in right lobe in 95 patients. P-Value were <0.02.

The frequency of mass size on ultrasound 2 cm patients were 48, The frequency of mass size on ultrasound 3 cm patients were 46, The frequency of mass size on ultrasound 4 cm patients were 7, The frequency of mass size on ultrasound 5 cm patients were 19. P-Value were less than 0.03.

The frequency of open HCC surgery who have large scar, more bleeding and more pain were 120 patients and the frequency of minimally invasive HCC surgery who have less scar, less bleeding and less pain were in 120 patients. The frequency of early detection of HCC on CT Scan were in 25 patients and the frequency were 95 on Ultrasound.

The frequency of treatment laparoscopic RFA were done in 44 patients. The frequency of Laparoscopic surgery were done in 12 patients. The frequency of open surgery were were done in 58 patients. The frequency of surgical resection were done in 6 patients.

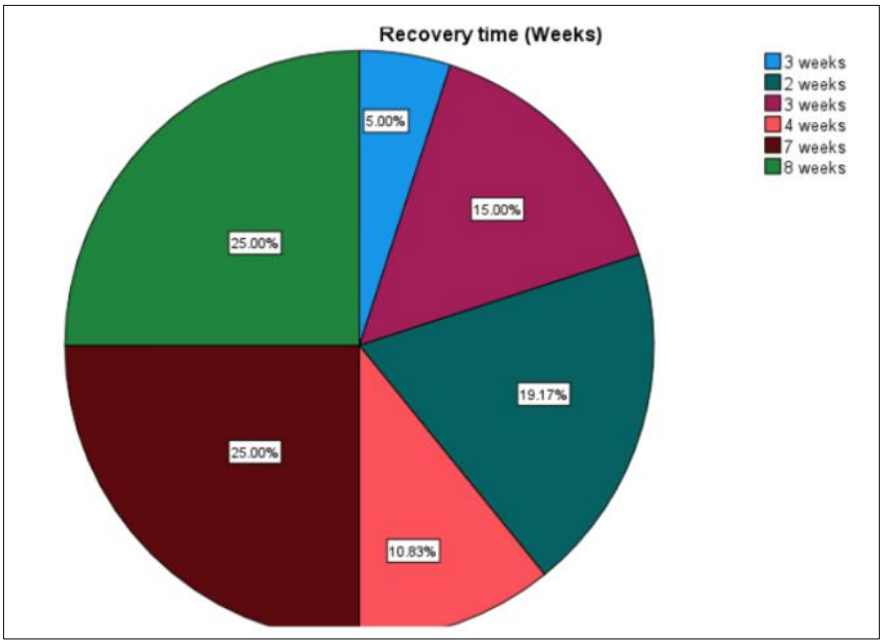

Figure 2 In Figure 2, we can see the recovery time in weeks in percentage

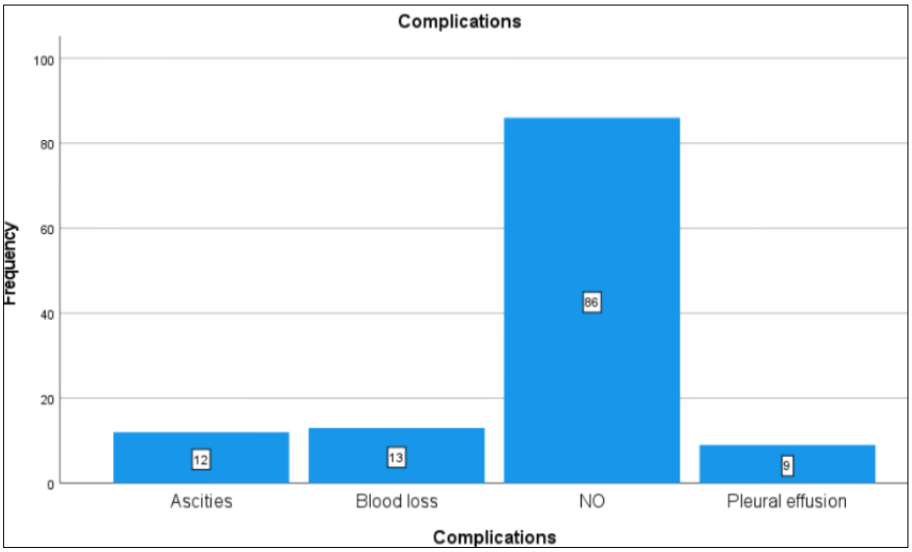

Figure 3 In Figure 3, we can see the bar graph in which we see the percentage of complications of HCC. Ascites were 12%, Blood loss were 13%, Pleural effusion were 9% and no complications in 86% of patients

Figure 4 Minimally invasive laparoscopic surgery of Hepatocellular Carcinoma (HCC)

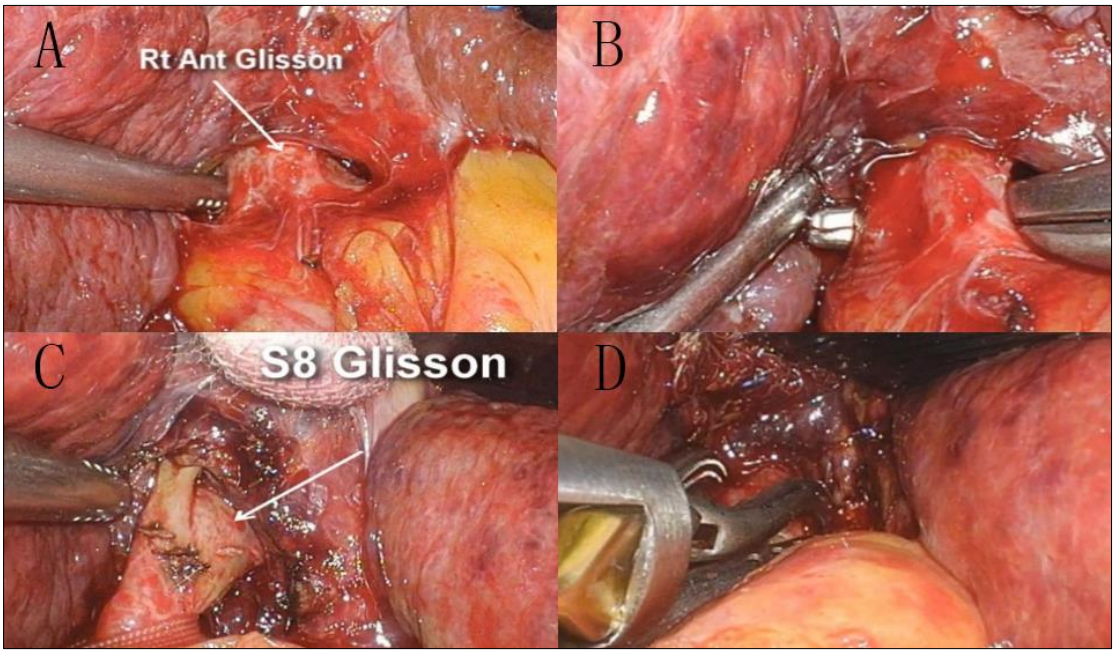

Figure 5 Minimally invasive laparoscopic surgery of Hepatocellular Carcinoma (HCC)

Figure 6 Open surgery for Hepatocellular Carcinoma (HCC)

4. Discussion

In the US and other developed economies, minimally invasive surgical methods are employed, whereas in Europe, less than one in four liver resections are now carried out [24–25]. There is disagreement over the optimal surgical approach for both short- and long-term outcomes, despite the fact that surgical resection remains the cornerstone of treatment for patients with locally advanced HCC [26]. There are established protocols that use minimally invasive surgery (MIS) to remove certain gastrointestinal malignancies. For liver malignancies, multicenter randomized data are available from the COMET trial, which compared open surgery and laparoscopic procedures for 280 patients with colorectal liver metastases [27]. This study found that patients in the laparoscopic surgery arm experienced fewer postoperative issues and hospital stays, even though there was no significant difference in intraoperative blood loss, operating time, or perioperative mortality between the two groups. The results of our study of HCC patients, which demonstrate a notably shorter hospital stay, validate the benefit of MILR for patients' postoperative recovery. Together with the results of several other studies that demonstrated less pain, earlier mobilization, and a quicker return of gastrointestinal function after minimally invasive surgery as opposed to open surgery for a variety of abdominal malignancies, these data extend the advantages of MILR on postoperative recovery to patients with HCC. Due to chronic parenchymal liver injury, 80–90% of cases of HCC have a history of severe fibrosis or cirrhosis. [28]. Laparoscopic determination of the margin distance is more challenging and may have contributed to a higher proportion of positive margins, even if there is still debate regarding the minimum required margin width in HCC. Additionally, tumor detachment from major intrahepatic arteries in HCC has been demonstrated to be oncologically suitable, with survival and recurrence rates equivalent to those of R0 resections [29]. The growth of LLR procedures is associated with the advancement of technology and equipment. During this period, two global consensus conferences have described the current status and future directions of LLR [30–31].

The safety of laparoscopic hepatectomy for big liver carcinoma has been confirmed by a number of papers, despite the lengthy operating duration [32, 33]. According to Goh et al., tumor size has little bearing on either the short- or long-term results [34]. However, only skilled surgeons in referral HPB hospitals are now able to conduct laparoscopic liver resection for big liver tumors due to its technical difficulty. The limited surgical perspective, the inability to manage the underlying cirrhotic or fibrotic liver, and the close proximity to blood and biliary structures make LLR challenging for large tumors. In fact, one of the primary factors influencing the most popular LLR difficulty scores is tumor size, and a recent study by Xiaocui et al. found a link between technical difficulty and long-term outcomes following minimally invasive liver resection [35]. In this case, sharing our actual data regarding the results of LLR for large HCC could provide crucial proof of its efficacy and safety. Both intraoperative and postoperative outcomes, such as in-hospital, short-term, and long-term survival, did not differ significantly. The rate of R0 resection was comparable as well. Interestingly, despite earlier research indicating greater operative times, there were no differences in the operative time either [36]. As previously noted in the literature, the experience of the surgeons and the center most likely plays a significant impact

in this aspect [37]. Despite being non-significant (41% vs. 23.5%, p = 0.11), the rate of blood transfusions was nearly double in the OLR compared to the LLR, which was another intriguing finding. Given the prognostic significance of blood transfusions during liver resection for HCC, more research may concentrate on this area [38, 39].

Additionally, since the beginning of the HPB program, all consecutive cases of massive HCC undergoing surgery at Seoul National University Bundang Hospital were included in our population. Although this is a realistic representation of the day-to-day situation in an HPB referral center, the LLR case's outcomes might even be impacted by the learning curve effect, considering our center's increasing number and technical complexity of laparoscopic liver procedures, which is infamously associated with better outcomes [37]. Results following LLR could therefore be considerably better. Such a feature may be clarified by more research.

There are several restrictions on this study. First, it is susceptible to selection bias due to its retrospective and single-center design. However, all consecutive patients who met the selection criteria were included in order to minimize selection bias. Second, despite the fact that statistical significance differs from clinical significance, the small sample size may have an impact on the statistical results because of the decreased statistical power, which may make it challenging to attain statistical significance [40]. Results should not be misconstrued in this way, as it is widely recognized that the lack of evidence does not imply the absence of it. Contextualizing the clinical setting is necessary when deciding if the lack of evidence is a sufficient reason to alter clinical practice. Since patients with huge HCC are not always suitable for surgery, it is challenging to include a larger sample size. Therefore, in our case, we included patients who had previously had LLR for huge HCC, as has already been described in other centers. Although we do not recommend altering clinical treatment in light of our findings, we think it is critical to publish the initial results that are accessible from routine practice in referral centers in order to support future research. Additionally, we think it's critical to concentrate on how referral centers might choose patients with large HCC for LLR. Designing a multicenter trial could be a future tactic to achieve this goal, although there is a danger of increased heterogeneity. As of right now, this remains the biggest monocentric LLR series for massive HCC. Thirdly, the patients were not matched based on the characteristics of the tumors and the patients [40]

5. Conclusion

Our study found that individuals who have minimally invasive hepatocellular carcinoma (HCC) surgery recover more quickly than those who undergo open surgery. Compared to open surgery, individuals who undergo minimally invasive procedures spend less time in the hospital. Compared to the left lobe of the liver, HCC is more frequent in the right lobe. In patients having liver resection, the risk of surgical wound and organ infections following the procedure is reduced with minimally invasive surgery than with open surgery. The majority of hepatocellular carcinoma (HCC) diagnoses were made in elderly patients. In our study, there were more male patients than female ones.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

Ethical approval was obtained.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] Ferlay, J.; Soerjomataram, I.; Dikshit, R.; Eser, S.; Mathers, C.; Rebelo, M.; Parkin, D.M.; Forman, D.; Bray, F. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int. J. Cancer 2015, 136, E359–E386.

[2] Siegel, R.L.; Miller, K.D.; Jemal, A. Cancer statistics, 2018. CA Cancer J. Clin. 2018, 68, 7–30.

[3] McGlynn, K.A.; Petrick, J.L.; London, W.T. Global Epidemiology of Hepatocellular Carcinoma. Clin. Liver Dis. 2015, 19, 223–238.

[4] Rahib, L.; Smith, B.D.; Aizenberg, R.; Rosenzweig, A.B.; Fleshman, J.M.; Matrisian, L.M. Projecting Cancer Incidence and Deaths to 2030: The Unexpected Burden of Thyroid, Liver, and Pancreas Cancers in the United States. Cancer Res. 2014, 74, 2913–2921.

[5] European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. J. Hepatol. 2018, 69, 182–236

[6] Hwang S, Lee SG, Belghiti J. Liver transplantation for HCC: its role: eastern and Western perspectives. J Hepatobiliary Pancreat Sci. 2010;17(4):443-448.

[7] Capussotti L, Ferrero A, Vigano L, Polastri R, Tabone M. Liver resection for HCC with cirrhosis: surgical perspectives out of EASL/AASLD guidelines. Eur J Surg Oncol. 2009;35(1):11-15.

[8] Vibert E, Kouider A, Gayet B. Laparoscopic anatomic liver resection. HPB (Oxford). 2004;6(4):222-229.

[9] Llovet J.M., Kelley R.K., Villanueva A., Singal A.G., Pikarsky E., Roayaie S., Lencioni R., Koike K., Zucman-Rossi J., Finn R.S. Hepatocellular carcinoma. Nat. Rev. Dis. Primers. 2021;7:6. doi: 10.1038/s41572-020-00240-3.

[10] Di Sandro S., Benuzzi L., Lauterio A., Botta F., De Carlis R., Najjar M., Centonze L., Danieli M., Pezzoli I., Rampoldi A., et al. Single Hepatocellular Carcinoma approached by curative-intent treatment: A propensity score analysis comparing radiofrequency ablation and liver resection. Eur. J. Surg. Oncol. 2019;45:1691–1699. doi: 10.1016/j.ejso.2019.04.023.

[11] Vogel A., Martinelli E., ESMO Guidelines Committee Updated treatment recommendations for hepatocellular carcinoma (HCC) from the ESMO Clinical Practice Guidelines. Ann. Oncol. 2021 doi: 10.1016/j.annonc.2021.02.014.

[12] Vibert E, Kouider A, Gayet B. Laparoscopic anatomic liver resection. HPB (Oxford). 2004;6(4):222-229.

[13] Buell, J.F.; Cherqui, D.; Geller, D.A.; O'Rourke, N.; Iannitti, D.; Dagher, I.; Koffron, A.J.; Thomas, M.; Gayet, B.; Han, H.S.; et al. The international position on laparoscopic liver surgery: The Louisville Statement, 2008. Ann. Surg. 2009, 250, 825–830.

[14] [14]Wakabayashi, G.; Cherqui, D.; Geller, D.A.; Buell, J.F.; Kaneko, H.; Han, H.S.; Asbun, H.; O'rourke, N.; Tanabe, M.; Koffron, A.J.; et al. Recommendations for laparoscopic liver resection: A report from the second international consensus conference held in Morioka. Ann. Surg. 2015, 261, 619–629.

[15] Kawaguchi, Y.; Fuks, D.; Kokudo, N.; Gayet, B. Difficulty of Laparoscopic Liver Resection. Ann. Surg. 2018, 267, 13–17.

[16] Chen, J.; Bai, T.; Zhang, Y.; Xie, Z.-B.; Wang, X.-B.; Wu, F.-X.; Li, L.-Q. The safety and efficacy of laparoscopic and open hepatectomy in hepatocellular carcinoma patients with liver cirrhosis: A systematic review. Int. J. Clin. Exp. Med. 2015, 8, 20679–20689.

[17] Giuliante, F.; Ardito, F.; Pinna, A.D.; Sarno, G.; Giulini, S.M.; Ercolani, G.; Portolani, N.; Torzilli, G.; Donadon, M.; Aldrighetti, L.; et al. Liver Resection for Hepatocellular Carcinoma ≤3 cm: Results of an Italian Multicenter Study on 588 Patients. J. Am. Coll. Surg. 2012, 215, 244–254.

[18] Kabir, T.; Syn, N.L.; Tan, Z.Z.; Tan, H.-J.; Yen, C.; Koh, Y.-X.; Kam, J.H.; Teo, J.-Y.; Lee, S.-Y.; Cheow, P.-C.; et al. Predictors of post-operative complications after surgical resection of hepatocellular carcinoma and their prognostic effects on outcome and survival: A propensity-score matched and structural equation modelling study. Eur. J. Surg. Oncol. (EJSO) 2020, 46, 1756–1765.

[19] Santambrogio, R.; Vertemati, M.; Barabino, M.; Zappa, M.A. Laparoscopic Microwave Ablation: Which Technologies Improve the Results. Cancers 2023, 15, 1814.

[20] Zhu, P.; Liao, W.; Zhang, W.G.; Chen, L.; Shu, C.; Zhang, Z.W.; Huang, Z.Y.; Chen, Y.F.; Lau, W.Y.; Zhang, B.X.; et al. A Prospective Study Using Propensity Score Matching to Compare Long-term Survival Outcomes after Robotic-assisted, Laparoscopic, or Open Liver Resection for Patients with BCLC Stage 0-A Hepatocellular Carcinoma. Ann. Surg. 2023, 277, e103–e111.

[21] Di Benedetto, F.; Magistri, P.; Di Sandro, S.; Sposito, C.; Oberkofler, C.; Brandon, E.; Samstein, B.; Guidetti, C.; Papageorgiou, A.; Frassoni, S.; et al. Safety and Efficacy of Robotic vs Open Liver Resection for Hepatocellular Carcinoma. JAMA Surg. 2023, 158, 46–54.

[22] Angelico, R.; Siragusa, L.; Serenari, M.; Scalera, I.; Kauffman, E.; Lai, Q.; Vitale, A. Rescue liver transplantation after post-hepatectomy acute liver failure: A systematic review and pooled analysis. Transplant. Rev. 2023, 37, 100773.

[23] Cillo, U.; Noaro, G.; Vitale, A.; Neri, D.; D'Amico, F.; Gringeri, E.; Farinati, F.; Vincenzi, V.; Vigo, M.; Zanus, G. Laparoscopic microwave ablation in patients with hepatocellular carcinoma: A prospective cohort study. HPB 2014, 16, 979–986.

[24] Farges O, Goutte N, Dokmak S, Bendersky N, Falissard B, Group AFHS . How surgical technology translates into practice: the model of laparoscopic liver resections performed in France. Ann Surg. 2014;260(5):916-921. discussion 21-2.

[25] Kim Y, Amini N, He J, et al. National trends in the use of surgery for benign hepatic tumors in the United States. Surgery. 2015;157(6):1055-1064.

[26] Benson A.B., 3rd, D'Angelica M.I., Abbott D.E., Abrams T.A., Alberts S.R., Saenz D.A., Are C., Brown D.B., Chang D.T., Covey A.M., et al. NCCN Guidelines Insights: Hepatobiliary Cancers, Version 1.2017. J. Natl. Compr. Cancer Netw. 2017;15:563–573. doi: 10.6004/jnccn.2017.0059.

[27] Fretland A.A., Dagenborg V.J., Bjornelv G.M.W., Kazaryan A.M., Kristiansen R., Fagerland M.W., Hausken J., Tonnessen T.I., Abildgaard A., Barkhatov L., et al. Laparoscopic Versus Open Resection for Colorectal Liver Metastases: The OSLO-COMET Randomized Controlled Trial. Ann. Surg. 2018;267:199–207. doi: 10.1097/SLA.0000000000002353.

[28] Pinnock C.A., Haden R.M. The surgical insult. In: Pinnock C., Lin T., Smith T., editors. Fundamentals of Anaesthesia. 3rd ed. Cambridge University Press; Cambridge, UK: 2009. pp. 105–114.

[29] Donadon M., Terrone A., Procopio F., Cimino M., Palmisano A., Vigano L., Del Fabbro D., Di Tommaso L., Torzilli G. Is R1 vascular hepatectomy for hepatocellular carcinoma oncologically adequate? Analysis of 327 consecutive patients. Surgery. 2019;165:897–904. doi: 10.1016/j.surg.2018.12.002.

[30] Buell JF, Cherqui D, Geller DA, et al. The international position on laparoscopic liver surgery: the Louisville statement, 2008. Ann Surg. 2009;250(5):825–30.

[31] [31] Wakabayashi G, Cherqui D, Geller DA, et al. Recommendations for laparoscopic liver resection: a report from the second international consensus conference held in Morioka. Ann Surg. 2015;261(4):619–29.

[32] [32] Zhou YM, Li B, Xu DH, Yang JM (2011) Safety and efficacy of partial hepatectomy for huge (>/=10 cm) hepatocellular carcinoma: a systematic review. Med Sci Monit 17(3):RA76-83

[33] Dumronggittigule W, Han HS, Komoltri C, D'Silva M, Lee B, Cho JY (2023) Laparoscopic versus open hepatectomy for large hepatocellular carcinoma: a single center propensity-score-matching comparative analysis of perioperative outcomes and long-term survival. Surg Endosc 37(4):2997–3009

[34] Goh BK, Chow PK, Teo JY, Wong JS, Chan CY, Cheow PC et al (2014) Number of nodules, Child-Pugh Status, margin positivity, and microvascular invasion, but not tumor size, are prognostic factors of survival after liver resection for multifocal hepatocellular carcinoma. J Gastrointest Surg 18(8):1477–1485

[35] Lv X, Zhang L, Yu X, Yu H (2023) The difficulty grade of laparoscopic hepatectomy for hepatocellular carcinoma correlates with long-term outcomes. Updates Surg 75(4):881–888

[36] Kabir T, Syn NL, Guo Y, Lim KI, Goh BKP (2021) Laparoscopic liver resection for huge (>/=10 cm) hepatocellular carcinoma: a coarsened exact-matched single-surgeon study. Surg Oncol 37:101569

[37] Cassese G, Han HS, Yoon YS, Lee JS, Lee B, Lee HW et al (2024) Evolution of laparoscopic liver resection in the last two decades: lessons from 2000 cases at a referral Korean Center. Surg Endosc 38(3):1200–1210

[38] Yamamoto J, Kosuge T, Takayama T, Shimada K, Yamasaki S, Ozaki H et al (1994) Perioperative blood transfusion promotes recurrence of hepatocellular carcinoma after hepatectomy. Surgery 115(3):303–309

[39] Giehl-Brown E, Geipel E, Lock S, Dehlke K, Schweipert J, Weitz J et al (2024) Transfusions of packed red blood cells in surgery for liver cancer: predictor of impaired overall survival but not recurrence-free survival—impact of blood transfusions in liver surgery. J Gastrointest Surg 28(4):402–411

[40] Gikandi A, Hallet J, Koerkamp BG, Clark CJ, Lillemoe KD, Narayan RR et al (2024) Distinguishing clinical from statistical significances in contemporary comparative effectiveness research. Ann Surg 279(6):907–912.