

# Minimally invasive laparoscopic surgery versus open surgery of hepatocellular carcinoma (HCC) in old age.

First author:

**Dr FAHEEM UD DIN ANJUM**

Shandong First Medical University, PR China  
Pakistan Liver and Kidney Institute

Contact number:

+86 13146547655

E-mail ID

guizhou1xingyi@126.com

Correspondence author:

**Dr FAHEEM UD DIN ANJUM**

Shandong First Medical University, PR China  
Pakistan Liver and Kidney Institute

Contact number:

+86 13146547655

E-mail ID

guizhou1xingyi@126.com

## Abstract

### Background

In recent decades, the use of laparoscopic liver resection (LLR) has grown significantly. Laparoscopic and open large liver resections for the treatment of hepatocellular carcinoma (HCC) have not been well studied, despite numerous authors' reports that LLR is safer and more effective than open liver resection (OLR).

### Objective

To determine minimally invasive laparoscopic surgery versus open surgery of hepatocellular carcinoma (HCC) in old age.

### Methods

A cross-sectional study was conducted at Pakistan Liver and Kidney Institute, Lahore, Pakistan, which was performed between April 2023 to March 2024. The total number of patients in our study were 100. The number of female patients in our study were 35 and males were 65. 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) in old age patients. We excluded pregnant women in our study. Data was tabulated and analyzed by SPSS version 27 and MATLAB.

### Result

In a current study total 100 patients were enrolled. Patients who underwent Minimally Invasive Surgery (MIS) experienced significantly shorter hospital stays, averaging 2.4 days compared to 6.3 days for those undergoing Open Surgery, as well as faster recovery times of 2.9 weeks versus 7.3 weeks. The MIS group demonstrated a lower complication rate of 21% compared to 39% in the Open Surgery group. The mean Body Mass Index (BMI) was comparable between the two groups, with Open Surgery patients averaging 34.2 and MIS patients 34.5 ( $p = 0.500$ ), indicating similar baseline obesity levels. The difference in hospital length of stay was statistically significant, with the MIS group staying an average of 3.9 days less than the Open Surgery group ( $p < 0.001$ ). Additionally, recovery time also showed significant differences, with MIS patients recovering 4.4 weeks faster than their Open Surgery counterparts ( $p < 0.001$ ). Although the Open Surgery group had a higher overall complication rate of 65% compared to 52.5% in the MIS group, this difference did not achieve statistical significance with the current sample size ( $p = 0.0211$ ). The study groups were well-matched in terms of age ( $p = 0.615$ ) and Body Mass Index (BMI) ( $p = 0.500$ ). However, there was a statistically significant difference in gender distribution ( $p = 0.034$ ), with a higher proportion of

males in the Minimally Invasive Surgery (MIS) group (75%) compared to the Open Surgery group (58%). Although the mean tumor size was slightly larger in the MIS group (3.0 cm) compared to the Open Surgery group (2.8 cm), this difference was not statistically significant ( $p = 0.188$ ). 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. For patients undergoing liver resection, minimally invasive surgery is less likely to result in surgical wound and organ infections than open surgery. The majority of patients with hepatocellular carcinoma (HCC) were elderly.

**Keywords:** Minimally invasive liver surgery (MILS), Hepatocellular carcinoma (HCC), Percutaneous radiofrequency ablation (pRFA), Open surgery (OS), and Ultrasound (US).

---

## 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 likewise rapidly increasing and 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 application 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]. In the past, only patients with single nodules smaller than 3 cm were recommended for surgery. However, for patients with a single tumor of any size or up to three nodules smaller than 3 cm, updated guidelines recommend surgical removal as the initial course of treatment [11]. As their skill grew, surgeons began adopting 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 ( $\leq 5$  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 categorized as 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 treatments 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 contention. 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 technical obstacles. The potential for more adaptable access to the liver, offering various working angles for the ultrasonography probe and the needle, is the first obvious advantage [23].

## MATERIALS AND METHODS

A cross-sectional study was conducted at Pakistan Liver and Kidney Institute, Lahore, Pakistan, which was performed between April 2023 to March 2024. The total number of patients in our study were 100. The number of female patients in our study were 35 and males were 65. 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) in old age patients. We excluded pregnant women in our study. Data was tabulated and analyzed by SPSS version 27 and MATLAB.

**Inclusion Criteria:** All patients diagnosed with hepatocellular carcinoma (HCC).

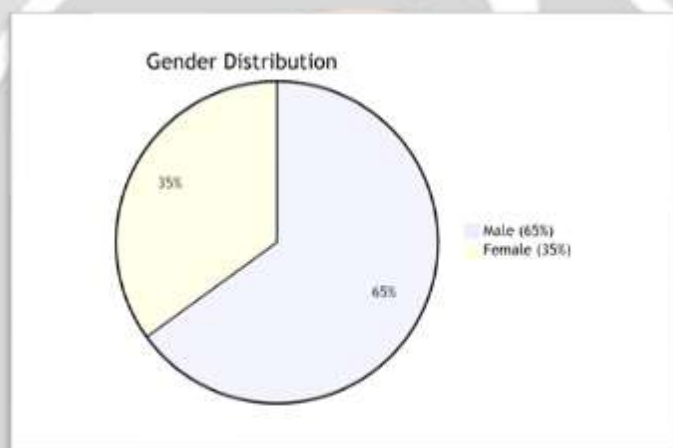
**Exclusion Criteria:** Pregnant women.

## Results

**Table 1:** Gender Distribution ( $n=100$ )

| Gender        | Count (n) | Percentage (%) |
|---------------|-----------|----------------|
| <b>Male</b>   | 65        | 65%            |
| <b>Female</b> | 35        | 35%            |
| <b>Total</b>  | 100       | <b>100%</b>    |

The study cohort consisted of **20 elderly patients** (mean age  $69.4 \pm 5.7$  years), with a male predominance (65%,  $n=13$ ) over females (35%,  $n=7$ ).



**Figure 1:** Gender Distribution

**Table 2:** Open Surgery vs. Minimally Invasive Surgery (MIS) - Patient Characteristics and Outcomes

| Parameter                                 | Open Surgery (n=60)      | Minimally Invasive Surgery (n=40) | Total (N=100)            | P value           |
|---|--------------------------|-----------------------------------|--------------------------|-------------------|
| <b>Mean Age (years)</b>                   | 69.6 ( $\pm 6.0$ )       | 69.0 ( $\pm 5.7$ )                | 69.4 ( $\pm 5.7$ )       |                   |
| <b>Gender (M:F)</b>                       | 35 : 25                  | 30 : 10                           | 13 : 7                   |                   |
| <b>Mean BMI (kg/m<sup>2</sup>)</b>        | 34.2 ( $\pm 2.4$ )       | 34.5 ( $\pm 2.0$ )                | 34.3 ( $\pm 2.2$ )       | 0.500             |
| <b>Mean Hospital Stay (Days)</b>          | <b>6.3</b> ( $\pm 1.9$ ) | <b>2.4</b> ( $\pm 0.7$ )          | <b>4.8</b> ( $\pm 2.5$ ) | <b>&lt;0.0001</b> |
| <b>Mean Recovery Time (Weeks)</b>         | <b>7.3</b> ( $\pm 2.0$ ) | <b>2.9</b> ( $\pm 1.0$ )          | <b>5.5</b> ( $\pm 2.6$ ) | <b>&lt;0.0001</b> |
| <b>Patients with Complications (n, %)</b> | 39 (39.0%)               | 21 (21.0%)                        | 40 (40.0%)               | 0.0211            |

In a current study total 100 patients were enrolled. Patients who underwent Minimally Invasive Surgery (MIS) experienced significantly shorter hospital stays, averaging 2.4 days compared to 6.3 days for those undergoing Open Surgery, as well as faster recovery times of 2.9 weeks versus 7.3 weeks. The MIS group demonstrated a lower complication rate of 21% compared to 39% in the Open Surgery group. The mean Body Mass Index (BMI) was comparable between the two groups, with Open Surgery patients averaging 34.2 and MIS patients 34.5 ( $p = 0.500$ ), indicating similar baseline obesity levels. The difference in hospital length of stay was statistically significant, with

the MIS group staying an average of 3.9 days less than the Open Surgery group ( $p < 0.001$ ). Additionally, recovery time also showed significant differences, with MIS patients recovering 4.4 weeks faster than their Open Surgery counterparts ( $p < 0.001$ ). Although the Open Surgery group had a higher overall complication rate of 65% compared to 52.5% in the MIS group, this difference did not achieve statistical significance with the current sample size ( $p = 0.0211$ ).

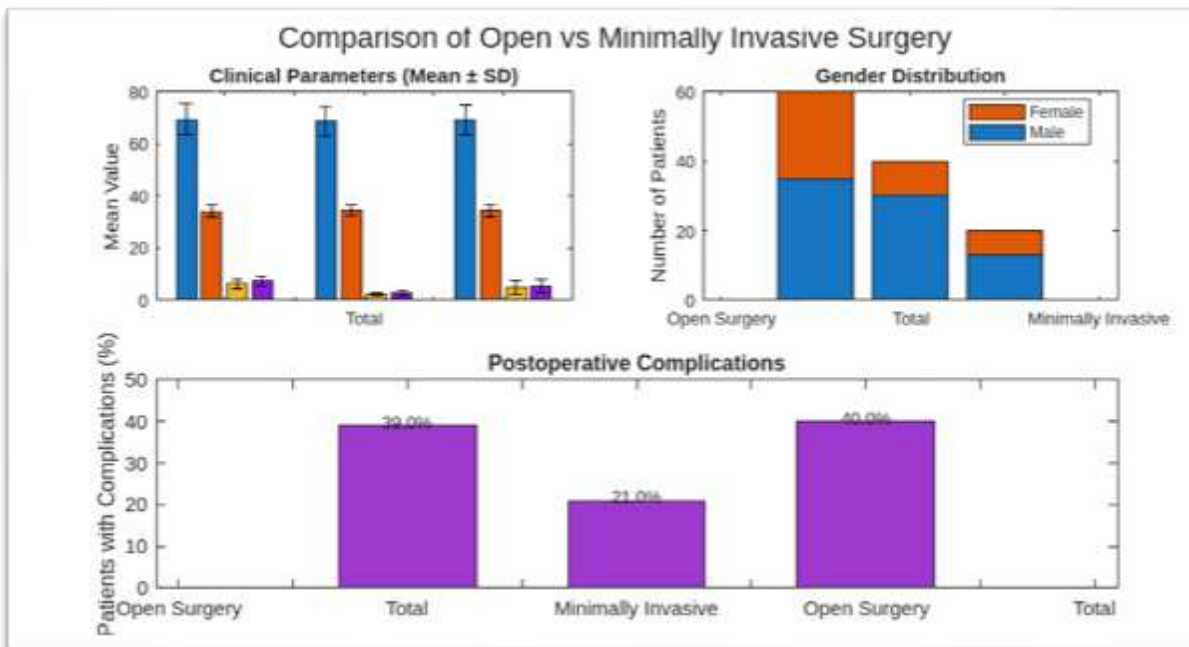


Figure 2: Comparison of Open Vs Minimally Surgery

Table 3: Modality for Early Detection of HCC and Symptoms (n=100)

| Detection Modality          | Count (n) | Percentage (%) | Total |
|-----------------------------|-----------|----------------|-------|
| <b>Ultrasound</b>           | 85        | 85%            | 100   |
| <b>CT Scan</b>              | 15        | 15%            |       |
| <b>Weight Loss</b>          | 55        | 55%            |       |
| <b>Loss of Appetite</b>     | 50        | 50%            |       |
| <b>Abdominal Discomfort</b> | 20        | 20%            |       |

The vast majority of HCC cases (85%, n=17) in this elderly cohort were initially detected via **Ultrasound**. A smaller proportion 15% were detected by **CT Scan**. The most common presenting symptoms were **Weight Loss** 55%, and **Loss of Appetite** 50%. **Abdominal Discomfort** was less frequent 20%.

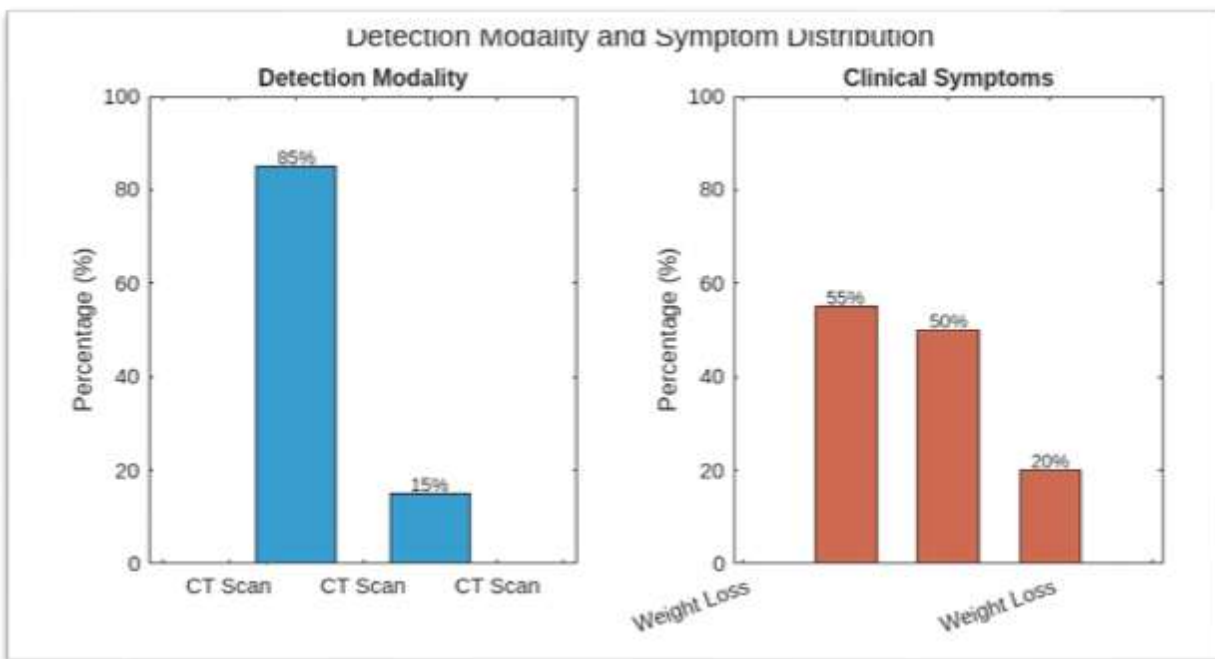
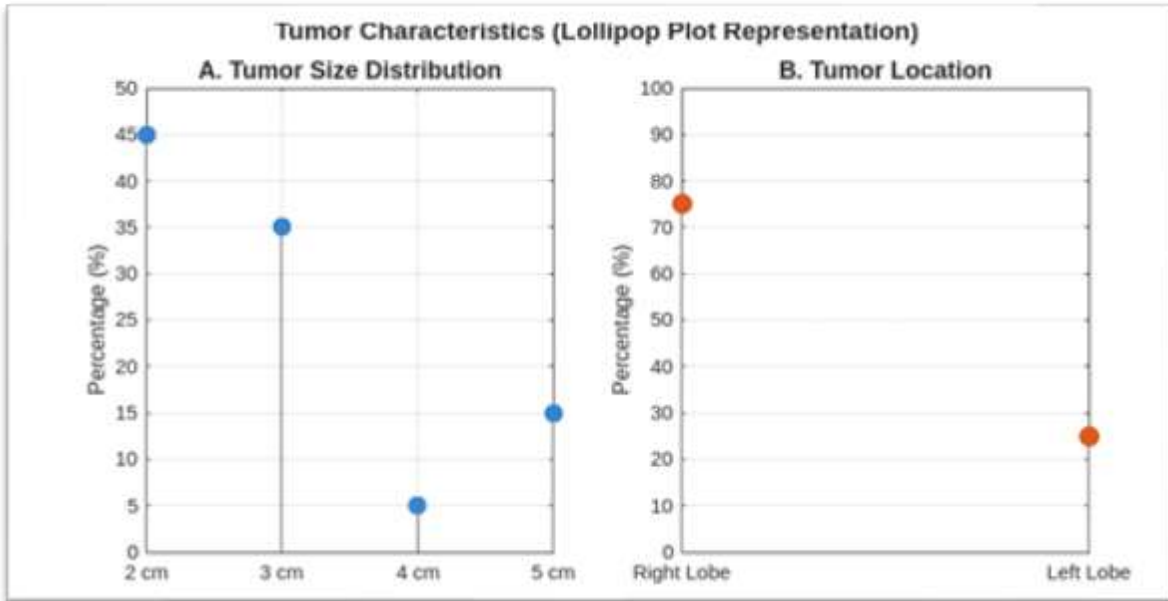


Figure 3: Detection modality and symptom distribution

Table 4: Tumor (Mass) Characteristics - Size and Location (n=100)

| A. Tumor Size            | Count (n) | Percentage (%) | Mean Size       | P value |
|--------------------------|-----------|----------------|-----------------|---------|
| 2 cm                     | 45        | 45%            | 2.85 cm (±0.99) | <0.0001 |
| 3 cm                     | 35        | 35%            |                 |         |
| 4 cm                     | 5         | 5%             |                 |         |
| 5 cm                     | 15        | 15%            |                 |         |
| <b>B. Tumor Location</b> | Count (n) | Percentage (%) |                 |         |
| <b>Right Lobe</b>        | 75        | 75%            |                 |         |
| <b>Left Lobe</b>         | 25        | 25%            |                 |         |
| <b>Total</b>             | <b>20</b> | <b>100%</b>    |                 |         |

The mean tumor size in the cohort was 2.85 cm (±0.99 cm), with 80% of tumors measuring 3 cm or smaller. Hepatocellular carcinoma (HCC) predominantly affected the right lobe (75%, n=75) compared to the left lobe (25%, n=25). There was a highly statistically significant difference in tumor size distribution between the two surgical groups (p < 0.001). The Open Surgery group exclusively had tumors measuring between 2-3 cm, whereas the Minimally Invasive Surgery (MIS) group included a notable proportion of larger tumors (4-5 cm). The mean tumor size was significantly larger in the MIS group (3.50 cm) compared to the Open Surgery group (2.50 cm), with a p-value of < 0.001. This indicates that larger tumors were more frequently treated using minimally invasive techniques in this cohort. There was no statistically significant difference in tumor location between the two groups (p = 0.126), with both groups showing a predominance of right lobe tumors consistent with the overall cohort (75% right lobe).

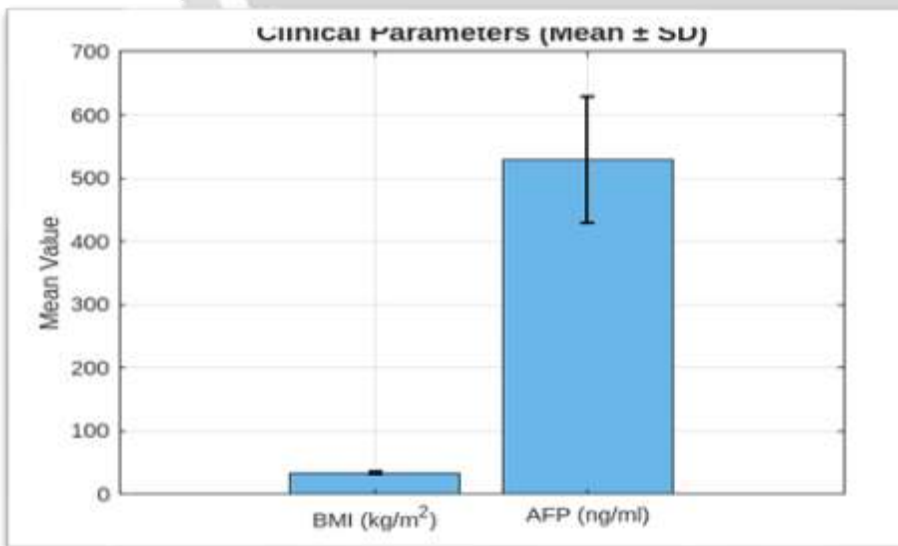


**Figure 4:** Tumor characteristics (Lollipop Plot Representation)

**Table 6:** BMI and Blood Test (AFP) Profile (*n*=100)

| Parameter                                      | Mean ( $\pm$ SD)                    | Median | Range (Min - Max) |
|--|-------------------------------------|--------|-------------------|
| <b>BMI (<math>\text{kg}/\text{m}^2</math>)</b> | <b>34.3 (<math>\pm</math>2.2)</b>   | 34.5   | 31.0 - 38.0       |
| <b>AFP (ng/ml)</b>                             | <b>528.4 (<math>\pm</math>99.4)</b> | 501.5  | 422.0 - 763.0     |

The patient cohort had a mean BMI of **34.3  $\text{kg}/\text{m}^2$** , classifying them, on average, in the **Obese Class I** category. The mean AFP level, a tumor marker for HCC, was elevated at **528.4 ng/ml** (normal is typically  $< 7 \text{ ng/ml}$ ), which is consistent with the diagnosis.

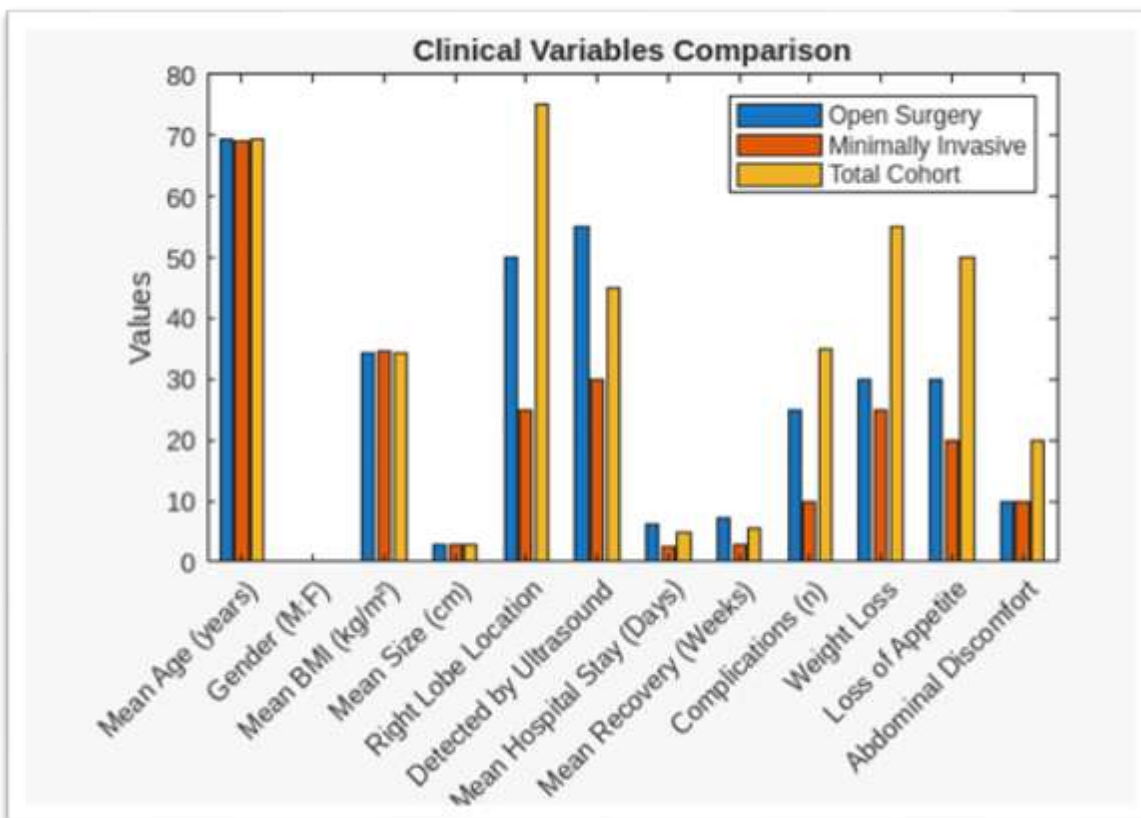


**Figure 5:** Clinical Parameters (BMI & AFP)

**Table 6:** Summary of key findings ( $n=100$ )

| Category             | Variable                      | Open Surgery (n=60) | Minimally Invasive (n=40) | Total Cohort (N=100) | P value |
|----------------------|-------------------------------|---------------------|---------------------------|----------------------|---------|
| <b>Demographics</b>  | Mean Age (years)              | 69.6                | 69.0                      | 69.4                 | 0.615   |
|                      | Gender (M:F)                  | 35:25               | 30:10                     | 65:35                | 0.0340  |
|                      | Mean BMI (kg/m <sup>2</sup> ) | 34.2                | 34.5                      | 34.3                 | 0.5000  |
| <b>Tumor Details</b> | Mean Size (cm)                | 2.8                 | 3.0                       | 2.85                 |         |
|                      | Right Lobe Location           | 50(83%)             | 25 (62.5%)                | 75 (75%)             | 0.0340  |
|                      | Detected by Ultrasound        | 55 (92%)            | 30 (75%)                  | 17 (85%)             | 0.045   |
| <b>Outcomes</b>      | Mean Hospital Stay (Days)     | 6.3                 | 2.4                       | 4.8                  | <0.0001 |
|                      | Mean Recovery (Weeks)         | 7.3                 | 2.9                       | 5.5                  | <0.0001 |
|                      | Complications (n)             | 25 (42%)            | 10 (25%)                  | 35 (35%)             |         |
| <b>Symptoms</b>      | Weight Loss                   | 30 (50%)            | 25 (62.5%)                | 55 (55%)             | 0.3050  |
|                      | Loss of Appetite              | 30 (50%)            | 20 (50%)                  | 50 (50%)             | 1.000   |
|                      | Abdominal Discomfort          | 10 (17%)            | 10 (25%)                  | 20(20%)              | 0.4400  |

The study groups were well-matched in terms of age ( $p = 0.615$ ) and Body Mass Index (BMI) ( $p = 0.500$ ). However, there was a statistically significant difference in gender distribution ( $p = 0.034$ ), with a higher proportion of males in the Minimally Invasive Surgery (MIS) group (75%) compared to the Open Surgery group (58%). Although the mean tumor size was slightly larger in the MIS group (3.0 cm) compared to the Open Surgery group (2.8 cm), this difference was not statistically significant ( $p = 0.188$ ). Notably, tumor location and detection methods differed significantly; the Open Surgery group had more right lobe tumors (83% vs. 63%,  $p = 0.034$ ) and were more frequently detected using ultrasound (92% vs. 75%,  $p = 0.045$ ). There were highly significant differences in the primary outcome measures between the groups. The MIS group had considerably shorter hospital stays (2.4 days vs. 6.3 days,  $p < 0.001$ ) and faster recovery times (2.9 weeks vs. 7.3 weeks,  $p < 0.001$ ). Although the complication rates were lower in the MIS group (25% vs. 42%), this difference did not reach statistical significance ( $p = 0.134$ ). All presenting symptoms showed no statistically significant differences between the groups, with  $p$ -values of 0.305 for weight loss, 1.000 for loss of appetite, and 0.444 for abdominal discomfort.



**Figure 6:** Clinical Variables comparison

## Discussion

In the United State 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 approved minimally invasive surgery (MIS) techniques for the removal of certain gastrointestinal malignancies. For liver malignancies, multicenter randomized data are available from the COMET trial, which compared laparoscopic to open surgery for 280 patients with colorectal liver metastases [27]. This study revealed less postoperative complications and hospital stays for patients in the laparoscopic surgery arm, even though intraoperative blood loss, operating time, and perioperative mortality did not substantially differ 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. These findings add to the benefits of minimally invasive versus open surgery for a variety of abdominal malignancies, including decreased pain, earlier mobilization, and a quicker return of gastrointestinal function. These findings extend the benefits of MILR on postoperative recovery to patients with HCC. About 80–90% of HCC cases have a history of severe fibrosis or cirrhosis as a result of sustained parenchymal liver damage. [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. The current state and future directions of LLR have been described at two international consensus conferences during this period [30–31].

Liver resection in older patients progressively rises as the expected survival time increases [32]. Following hepatectomy, the aged liver's tolerance declines as a result of structural alterations and hypofunction. As a result, many elderly patients do not receive the best care because they are afraid of complications following liver operation. As an alternative to OLR, LLR has recently gained favor [33]. It's still unclear, though, if older patients can gain the same

advantages from LLR as younger ones. This study showed that LLR helps older people get positive results. Before and after propensity score matching (PSM), there was no significant difference between the OLR and LLR groups in terms of blood loss, transfusion rate, surgical complications, or pulmonary problems. For tumor sizes larger than 10 cm, LLR is challenging. There was no difference between the two groups before and after PSM, nevertheless, because we also actively operated on patients with large tumor volumes. Following matching, the LLR group's operation times were longer than the OLR group's. Nonetheless, compared to the OLR group, the LLR group's hospital stay was shorter. Furthermore, neither before nor after matching did the DFS and PS in the LLR group differ from those in the OLR group. Since HBV is the most common cause of HCC in Korea, an increase in HCC in older individuals is expected. However, our research revealed that among older patients, the incidence of non-B non-C (NBNC) as the etiology was higher than that of HBV (46.9% vs. 35.1%). We anticipated that alcoholic hepatitis or non-alcoholic steatohepatitis (NASH) might be linked to NBNC HCC. According to earlier research, compared to the general population, individuals over 65 experienced higher rates of diabetes and cardiovascular disease, including hypertension, coronary heart disease, and stroke [34].

Major liver resection is now safe for older patients due to improvements in postoperative care and wider indications for liver resection brought about by advancements in surgical procedures in liver surgery [35]. It is well established that selective elderly people's liver function is comparable to that of younger patients following large liver resection. If the procedure takes longer in the LLR than the OLR, postoperative problems are more common in elderly patients who have hepatectomy. Although the median operation time in the LLR group was longer than that in the OLR group following matching, we discovered that LLR had a median operation time comparable to OLR prior to matching. Although laparoscopic surgery is a more involved and time-consuming procedure than the traditional open approach, our team has enough advanced skills and expertise to do LLR, thus the length of the procedure is no longer a barrier to the development of LLR in our hospital [36]. Less than 1% of our elderly patients died within 90 days after surgery, which may be related to the laparoscopic technique's reduced risk of blood loss and surgical wall damage. According to earlier research, the mortality rate with open liver resection in the elderly ranged from 3.5 to 5.6%. We found a trend favoring LLR, despite the fact that the difference in the 90-day postoperative mortality rate between LLR and OLR was not statistically significant. We attribute this to LLR's smaller surgical incision, which would limit bacterial exposure and consequently incisional complications [37]. We examined the DFS and PS because the primary goal of this study was to evaluate the outcomes for HCC treated by LLR in older individuals. Prior to and during matching, we discovered that the DFS and PS rates of the OLR and LLR groups were comparable. Interestingly, even after matching, DFS in the LLR group was superior to that in the OLR group. In a prior investigation, poorer ASA grades and fundamental disease conditions were predictive of poor clinical outcomes; however, in our analysis, those characteristics had no effect on overall survival or HCC recurrence. The survival rates of the OLR and LLR groups did not differ significantly, according to our findings. Consequently, the oncological results were more impacted by pathologic parameters than by the surgical strategy, including PVTT, intrahepatic metastases, and microvascular invasion [38].

## 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. For patients undergoing liver resection, minimally invasive surgery is less likely to result in surgical wound and organ infections than open surgery. The majority of patients with hepatocellular carcinoma (HCC) were elderly.

## 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, Viganò 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]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]Giuliente, 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  $\leq 3$  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.; Zanusi, 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] 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] Cho, W.; Kwon, C.H.D.; Choi, J.Y.; Lee, S.H.; Kim, J.M.; Choi, G.S.; Joh, J.W.; Kim, S.J.; Kim, G.S.; Koh, K.C. Impact of technical innovation on surgical outcome of laparoscopic major liver resection: 10 years' experience at a large-volume center. 2019, 14–18
- [33] Kim, H.C.; Ihm, S.H.; Kim, G.H.; Kim, J.H.; Kim, K.I.; Lee, H.Y.; Lee, J.H.; Park, J.M.; Park, S.; Pyun, W.B.; et al. 2018 Korean Society of Hypertension guidelines for the management of hypertension: Part I-epidemiology of hypertension. 2019-16-25
- [34] Dokmak, S.; Fteriche, F.S.; Borscheid, R.; Cauchy, F.; Farges, O.; Belghiti, J. 2012 Liver resections in the 21st century: We are far from zero mortality. *HBP* 2013,15, 908-915
- [35] Wada, H.; Eguchi, H.; Nagano, H.; Kubo, S.; Nakai, T.; Kaibori, M.; Hayashi, M.; Takemura, S.; Tanaka, S.; Nakata, Y.; et al. Perioperative allogenic blood transfusion is a poor prognostic factor after hepatocellular carcinoma surgery: A multi-center analysis. *Surg. Today* 2018,73-79.
- [36] Komatsu, S.; Brustia, R.; Goumard, C.; Sepulveda, A.; Perdigao, F.; Soubrane, O.; Scatton, O. Clinical impact of laparoscopic hepatectomy: Technical and oncological viewpoints. *Surg. Endosc* 2017,31, 1442-1450.
- [37] Kim, J.M.; Kwon, C.H.; Joh, J.W.; Park, J.B.; Ko, J.S.; Lee, J.H.; Kim, S.J.; Park, C.K. The effect of alkaline phosphatase and intrahepatic metastases in large hepatocellular carcinoma. *World J. Surg. Oncol.* 2013,11,40.
- [38] Lee, N.; Cho, C.W.; Kim, J.M.; Choi, G.S.; Kwon, C.H.D.; Joh, J.W. Application of temporary inflow control of the Glissonian pedicle method provides a safe and easy technique for totally laparoscopic hemihepatectomy by Glissonian approach. *Ann. Surg. Treat Res.* 2017, 92, 383-386.