

THE SYSTEMATIC REVIEW OF OPEN VERSUS LAPAROSCOPIC SURGERY IN THE MANAGEMENT OF PATIENTS WITH GALLBLADDER CANCER

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ABSTRACT

Background: Gallbladder cancer (GBC) is a rare highly aggressive disease with a global prevalence of 2/100000 people, with women being 2-3 times more likely than men. Management requires a multimodal strategy, with surgery being the gold standard for curative intent. Nowadays, treating common gastrointestinal cancers with laparoscopic techniques is commonly recognized. However, there is still debate on the laparoscopic method for treating GBC.

The aim: This study aims to show the differences between open and laparoscopic surgery for gallbladder cancer.

Methods: By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2014 and 2024 were taken into account. Several different online reference sources, like PubMed and ScienceDirect, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.

Results: In the PubMed database, the results of our search brought up 22 articles, whereas the results of our search on ScienceDirect brought up 85 articles. The results of the search conducted by title screening yielded a total 17 articles for PubMed and 12 articles for ScienceDirect. We compiled a total of 22 papers, 11 of which came from PubMed and 11 of which came from ScienceDirect. We excluded 3 review articles, 4 duplicate articles, 4 non-full text articles, 2 articles having ineligible subjects, and 1 article having insufficient outcomes. In the end, we included eight research that met the criteria.

Conclusion: The outcomes of laparoscopic and open surgery in the management of gallbladder cancer are comparable in terms of post-operative complications, recurrence rates, survival rates, and disease free survival rates. However, laparoscopic approach shows benefit on length of hospital stay.

Keywords: open surgery, laparoscopic, gallbladder cancer, comparison

INTRODUCTION

The gallbladder is a small, pear-shaped organ tucked under the liver. Among the biliary tracts, the gallbladder is the major cancer location that occurs most frequently.¹ Gallbladder cancer (GBC) is a highly aggressive disease that frequently invades nearby areas, spreads widely and quickly from nodes, and frequently metastasizes far away. It might be challenging to distinguish GBC from benign disease when the symptoms present similarly to biliary colic.²

GBC is an uncommon disease with a global prevalence of 2/100000 people. Women are 2-3 times more likely than men to get GBC.³ Globally, the death rate from gallbladder was 1.7 per 100,000 people. Cancer kills 1.5 and 1.6 men for every 100,000 people annually, and 1.4 and 2.0 women for every 100,000 people annually in both developed and developing countries. The five countries that had the highest death rates for gallbladder were Chile 7.8 per 100000, Bolivia with 7.5 per 100000, Korea, Republic with 4.8 per 100000, Lao PDR with 4.7 per 100000 and Nepal 4.1 per 100000.⁴ Female sex, advanced age, cholelithiasis or other benign GB pathology, chronic infection with *Helicobacter pylori* or *Salmonella* species, aberrant pancreatobiliary duct junction, porcelain GB, GB polyps, and obesity are the main risk factors for developing GBC.^{2,4}

GBC management necessitates a multimodal strategy. For curative intent, surgery is still the gold standard. When selecting surgical management for patients with GBC, a number of considerations must be made.³ If a patient is suspected of having GBC prior to surgery, it has long been advised that they have a laparotomy. If the histology T-stage is Tis or T1a, then simple cholecystectomy (SC) alone is regarded as definitive treatment according to the American Joint Committee on Cancer staging system.^{5,6} In GBC with the T stage of T1b or higher, more radical procedures are required.³ Treatment of gastrointestinal cancers with laparoscopic techniques is becoming more common. Nowadays, treating common gastrointestinal cancers with this treatment is commonly recognized. Laparoscopic surgery for GBC is still in its early stages of acceptance, though. Among hepatobiliary/pancreatic surgeons, there is still debate on the laparoscopic method for treating GBC.⁷ This study aims to show the differences between open and laparoscopic surgery for gallbladder cancer.

METHODS

Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

Criteria for Eligibility

For the purpose of this systematic review, we compare and contrast the effectiveness of open and laparoscopic surgery in the management of patients with gallbladder cancer. It is possible to accomplish this by researching or investigating the post-operative complications, hospital stays, recurrence rates, survival rates, and disease free survival rates. As the primary purpose of this piece of writing, demonstrating the relevance of the difficulties that have been identified will take place throughout its entirety.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English, and it should focus on determining the comparison of open and laparoscopic surgery in the management of patients with gallbladder cancer. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published within the last 10 years. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

Search Strategy

We used "open surgery"; "laparoscopic"; "gallbladder cancer"; and "comparison" as keywords. The search for studies to be included in the systematic review was carried out from January, 10th 2024 using the PubMed and ScienceDirect databases by inputting the words: "open"[All Fields] AND "surgery"[MeSH Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR "surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "general surgery"[MeSH Terms] OR "general"[All Fields] AND "surgery"[All Fields] OR "general surgery"[All Fields] OR "surgery s"[All Fields] OR "surgerys"[All Fields] OR "surgeries"[All Fields] AND "laparoscopes"[MeSH Terms] OR "laparoscopes"[All Fields] OR "laparoscope"[All Fields] OR "laparoscopical"[All Fields] OR "laparoscopically"[All Fields] OR "laparoscopies"[All Fields] OR "laparoscopy"[MeSH Terms] OR "laparoscopy"[All Fields] OR "laparoscopic"[All Fields] AND "gallbladder neoplasms"[MeSH Terms] OR "gallbladder"[All Fields] AND "neoplasms"[All Fields] OR "gallbladder neoplasms"[All Fields] OR "gallbladder"[All Fields] AND "cancer"[All Fields] OR "gallbladder cancer"[All Fields] AND "comparison"[All Fields] OR "comparisons"[All Fields] AND (y_10[Filter]) AND (english[Filter]) used in searching the literature.

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

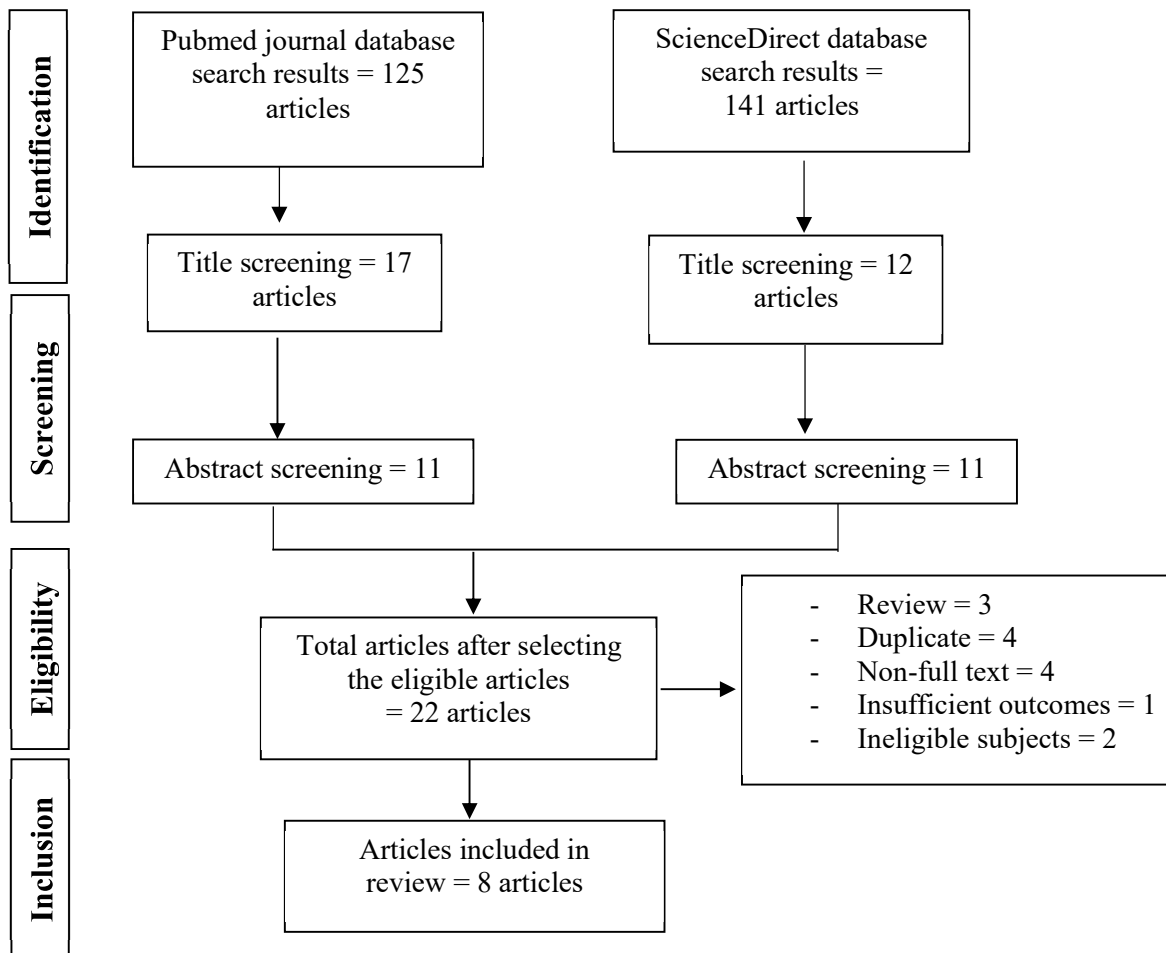


Figure 1. Article search flowchart

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

In the PubMed database, the results of our search brought up 22 articles, whereas the results of our search on ScienceDirect brought up 85 articles. The results of the search conducted by title screening yielded a total 17 articles for PubMed and 12 articles for ScienceDirect. We compiled a total of 22 papers, 11 of which came from PubMed and 11 of which came from ScienceDirect. We excluded 3 review articles, 4 duplicate articles, 4 non-full text articles, 2 articles having ineligible subjects, and 1 article having insufficient outcomes. In the end, we included eight research that met the criteria.

Table 1. The literature include in this study

Author	Origin	Method	Sample Size	Result
Agarwal, 2015 ⁸	India	Retrospective study	Laparoscopic 24; open 46	This findings suggested that laparoscopic radical cholecystectomy (LRC) was safe and feasible in selected patients with gall bladder cancer (GBC). The results of LRC were comparable to open radical cholecystectomy (ORC).
Cao, 2021 ⁹	China	Retrospective study	Laparoscopic 53; open 61	This result showed that laparoscopic approach was not inferior to open approach regarding perioperative outcomes, overall survival (OS), and disease-free survival (DFS) for T1b/T2 GBC patients. Less positive LNs and well-differentiated tumors were two independent predictors for better OS after laparoscopic approach, and less positive LNs were also identified for better OS after open surgery. Additionally, younger age, without gallbladder stone, smaller tumor size, and less positive LNs were potential risk factors for better DFS after open surgery.
Cho, 2022 ¹⁰	Korea	Retrospective study	Laparoscopic 37; open 44	This findings suggested that the effectiveness of laparoscopic surgery for T2 GBC was not inferior to that of open surgery in terms of perioperative outcomes and the three-year DFS and OS rates. Additionally, laparoscopic surgery offers significant functional advantages, such as a shorter operative time and length of hospital stay.

Dou, 2021 ¹¹	China	Retrospective study	Laparoscopic 56; open 43	The results showed that laparoscopic resection for GBC in T2 and T3 stages were comparable to open surgery regarding perioperative outcomes and long-term survival. Laparoscopic reduces the intraoperative bleeding and the duration of postoperative hospital stay.
Feng, 2019 ¹²	China	Retrospective study	Laparoscopic 41; open 61	The results showed the safety and effectiveness of laparoscopic approach. Laparoscopic approach does not increase the rate of incisional metastasis in GBC on the basis of the intact gallbladder wall. In addition, the survival rates of laparoscopic approach could achieve the same curative effect as open approach.
Jang, 2019 ¹³	Korea	Retrospective study	Laparoscopic 55; open 44	This finding suggested laparoscopic surgery for treatment of T2 GBC was technically feasible. Its perioperative outcomes and oncologic results were comparable to those of open surgery.
Kim, 2021 ¹⁴	Korea	Retrospective study	Laparoscopic 17; open 17	This result showed that laparoscopic extended cholecystectomy (LEC) had a significant advantage in terms of achieving a shorter postoperative hospital stay and similar results to those of open extended cholecystectomy (OEC) with respect to overall complications and pathological outcomes. The present results confirmed that laparoscopy can be considered a safe treatment for primary GBC in selected patients.

Nag, 2021 ¹⁵	India	Retrospective study	Laparoscopic 30; open 38	The findings suggested oncological outcome and survival rates after laparoscopic EC with bi-segmentectomy (LECB) in patients with resectable GBC is not inferior to that after open EC with bi-segmentectomy (OECB). Laparoscopic approach had a potential to improve perioperative outcome in patients with GBC.
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Post-operative Complications

All the identified studies showed there were no significant differences in complication rate in laparoscopic group and open group, the complications observed including Clavien-Dindo complications, bile leakage, wound infection, pleural effusion, dehiscence, post-operative pneumonia, and intraperitoneal complicated fluid collection.

Agarwal, et al. (2015)⁸ showed that there was no post-operative mortality in both groups. The post-operative morbidity included Grade A (International study group of liver surgery) bile leak (n = 5, laparoscopic group (LG) – 1 and open group (og) – 4), sub-hepatic collection requiring single time aspiration (n = 2, LG – 1, OG – 1), minor chyle leak which settled with conservative treatment (n = 1, LG), wound dehiscence requiring secondary suturing (n = 1, OG) and post-operative pneumonia (n = 2, OG).

Cho, et al. (2022)¹⁰ showed that there were no significant differences in complication rate in LG and OG (21.1% vs. 10.5%, p = 0.660). Postoperative complications occurred in four (21.1%) patients in LG, including wound infection (n = 3) and bile leakage (n = 1). In comparison, two (10.5%) patients in OG had postoperative complications, including symptomatic fluid collection in the gallbladder bed (n = 1) and wound infection (n = 1).

Dou, et al. (2021)¹¹ showed that laparoscopic and open surgery groups had comparable incidence of postoperative morbidities including bile leakage (LG 6/56, OG 3/43, P 0.521), postoperative bleeding (LG 3/56, OG 1/43, P 0.448), and abdominal abscess (LG 3/56, OG 3/43, P 0.738). The incidence of Clavien–Dindo¹² (C–D) grade III-IV was similar between groups (LG 6/56, OG 5/43, P 0.886).

Feng, et al. (2019) showed that there was no significant difference between the two groups (P 0.933). There were six cases (9.8%) of postoperative complications in the OG, including bile leakage, incision infection, and pleural effusion.

Jang, et al. (2019)¹³ showed that there were three Clavien–Dindo grade I and four grade IIIa complications in LG (paralytic ileus and intraperitoneal complicated fluid collection, respectively), and three grade II, three grade IIIa complications in OG (grade II: two urinary retention cases and one drain site infection, grade IIIa: wound dehiscence, hepaticojejunostomy site stricture, and bile leakage from liver resection site).

Kim, et al. (2021)¹⁴ showed that the overall surgical complication rate did not differ between the two groups. Postoperative morbidities with a Clavien–Dindo grade of > 3 were observed in three cases (17.6%) in OG and in two cases (11.8%) in the LG. Nag, et al. (2021)¹⁵ also showed that the difference of complication rate was not statistically significant between two groups, the complication rate was 16.6% in LG and 31.5% in OG (P = 0.259).

Hospital Stays

Six of seven identified studies showed that length of hospital stay in laparoscopic group was significantly shorter than open group. Cho, et al. (2022)¹⁰ reported the duration of hospital was 8.4 ± 5.9 in LG and 14.4 ± 6.0 days in OG, p = 0.004). Dou, et al. (2021)¹¹ reported the postoperative days of hospital stay was 10.32 ± 0.60 in LG and 14.74 ± 0.91 in OG, P < 0.01. Feng, et al. (2019)¹² reported the postoperative hospital discharge time (days) was 5± 3 in LG and 11 ± 5 in OG, P <0.001. Jang, et al. (2019)¹³ reported the post-operative hospital stay was significantly shorter in LG (5.8 ± 5.3 vs 9.5 ± 4.8, p < 0.001). Kim, et al. (2021)¹⁴ reported the post-operative hospital stay was 7 days in LG and 12 days in the OG (P = 0.009). Nag, et al. (2021)¹⁵ reported the mean hospital stay (LG vs OG) was 6.4 versus 9 days (P = 0.0001). However one study showed that the duration was similar in both groups. Agarwal, et al. (2015)⁸ showed that the length of hospital stay in days, median (range) were similar between laparoscopic group 5 (3–16) and open group 5 (3–17), p value 0.111.

Survival Rates

All identified studies in this review showed there were no statistically significant differences between the two groups in terms of overall survival rate and the 1-, 3- and 5-y survival rates. Cao, et al. (2021)⁹ showed that laparoscopic approach

compared with open approach demonstrated no significant benefit on OS (hazard ratio [HR], 1.572; 95% confidence interval [CI], 0.866–2.855; $p = 0.13$). Cho, et al. (2022)¹⁰ showed that the two groups (laparoscopic group vs open surgery group) showed no significant differences in the three-year OS rates (cancer-specific OS: 88.9% vs. 86.3%, $p = 0.660$). Dou, et al. (2021)¹¹ showed that the 1-, 2-, and 3-year overall survival rates were 61.2, 40.1, and 30.1%, respectively, in LG, and 53.3, 40.1, and 40.1%, respectively, in the OG ($p = 0.644$).

Feng, et al. (2019)¹² showed that there were no significant differences statistically in the 1-, 3-, and 5-y survival rates between LG and OG. The 1-, 3- and 5-y survival rates of LG were 97.1%, 69.4%, and 51.9%, respectively, and those of OG were 94.7%, 64.9%, and 55.7%, respectively ($P = 0.453$). Jang, et al. (2019)¹³ showed that there was no statistically significant difference between the two groups in terms of overall survival rate (at 5 year LS vs OS = 73.1% vs 65.7%; $p = 0.116$). There was also no significant difference between LS T2N0 and OS T2N0 group (at 5 year LS vs OS = 90.8% vs 79.1%; $p = 0.0941$), and LS T2N1 and OS T2N1 group (at 5 year LS vs OS = 54.4% vs 21.0%; $p = 0.579$). Nag, et al. (2021)¹⁵ showed overall survival of LG and OG was 51 months and 46 months, respectively ($P = 0.45$). The 1, 3 and 5-year survival was 96% versus 94%, 79% versus 72% and 79% versus 62% ($P = 0.45$).

Recurrence Rates

All the identified studies included in this review showed there was no statistically significant difference between the two groups in terms of recurrence rates. Agarwal, et al. (2015)⁸ reported that 23/24 patients in laparoscopic group and 43/46 patients in open group were alive without any evidence of recurrence after a median (range) follow-up of 18 months (6–34). One patient in LG with T3N0 (14 nodes resected) disease developed jaundice owing to nodal recurrence at 14 months follow up. No patient developed recurrence at a port site. Three patients in OG developed recurrence (nodal recurrence – 2, liver metastasis – 1) at 11, 13 and 16 months follow up, respectively. Of the 3 patients, 2 had T3N1 disease and 1 had T2N1 disease.

Feng, et al. (2019)¹² showed that there was no significant difference compared with the incisional metastasis rate, the incidence of postoperative incisional metastasis in the laparoscopy group was 4.9% (2/41) and (3.3%, 2/61) in the open group. Jang, et al. (2019)¹³ reported no case of port-site metastasis was observed from the patients of LG. Kim, et al. (2021)¹⁴ reported three cases (17.6%) of disease recurrence occurred in OG and two cases (11.8%) in LG ($P = 0.446$) during the follow-up. Nag, et al. (2021)¹⁵ reported the recurrence rate was 20% in LG versus 28.9% in OG ($P = 0.4$).

Disease Free Survival (DFS)

Four studies showed there were no significant differences in disease free survival (DFS) rate in laparoscopic group and open group. Cao, et al. (2021)⁹ showed that laparoscopic approach compared with OG demonstrated no significant benefit on DFS (HR, 1.225; 95% CI, 0.677–2.218; $p = 0.49$). Cho, et al. (2022)¹⁰ showed that laparoscopic group and open surgery group had no significant differences in the three-year DFS (DFS: 60.2% vs. 76.4%, $p = 0.448$). Kim, et al. (2021)¹⁴ reported the 1- and 3-year disease-free survival rates were 82.4% and 82.4% in OG and 94.2% and 71.5% in LG, respectively ($P = 0.94$). Nag, et al. (2021)¹⁵ reported the mean recurrence-free survival was 48 months in LG versus 44 months in OG ($P = 0.35$).

DISCUSSION

The purpose of this research was to review studies published after January of 2014 and up to January of 2024 that the differences between open and laparoscopic surgery for gallbladder cancer. Gallbladder cancer (GBC) is a rare malignancy but represents almost 50% of all biliary tract cancer. Biliary cancers are highly fatal malignancies with a 5-year survival rate of 17.6% (2007 to 2013). GBC is frequently discovered by accident during imaging tests or following surgery. Following a cholecystectomy and examination of the surgical pathology specimen, early-stage gallbladder cancer is frequently identified.¹⁶ For early-stage GBC, surgery is the first-line treatment. Radical resection is the only treatment available to GBC patients in order to ensure long-term survival, and preoperative confirmation of the clinical stage of GBC is a crucial prerequisite for the typical radical resection of GBC. At present, GBC is clinically staged mainly using the tumor-node-metastasis (TNM) staging system recommended by the American Joint Committee on Cancer (AJCC).¹⁷

For a considerable amount of time, laparoscopic surgery has been deemed inappropriate for GBC, mostly due to technical difficulties; additional reasons include the possibility of pneumoperitoneum spreading the disease and the increased risk of spreading in the event of bile leakage.¹⁸ In this review, the complications rate of laparoscopic surgery was similar with open surgery, including bile leakage and pneumoperitoneum. The morbidity (10.0%) and mortality (0.0%) rates in the laparoscopic group seemed to be acceptable and not inferior to those in the open group.¹⁸ More research has been done on laparoscopic surgery for GBC in the past several years. The use of laparoscopic surgery for GBC is supported by current research due to advancements in high-definition display technology, surgical equipment refinement, and surgeon progress.¹⁹ The progression of laparoscopic techniques has made it possible to adopt laparoscopic surgery for more advanced disease.

A study reported shorter hospital stays in laparoscopic group (3.5 ± 1.9 vs 5.6 ± 2.7 d) compared with open surgery. In addition, a study from China included 50 patients with GBC and found that laparoscopic surgery was associated with a shorter postoperative hospital stay (6.2 ± 2.4 vs 8.6 ± 2.3 d).¹⁹ Meta-analysis of data from eleven studies using a random-

effect model also showed that the patients in the laparoscopic group had a shorter length of postoperative hospital stay (WMD = -4.01; 95% CI -5.43 to -2.58; P < 0.00001) ($\chi^2 = 99.55$, P < 0.00001, I² = 91%). In this review, Six of seven identified studies showed that length of hospital stay in laparoscopic group was significantly shorter than open group.

Comparable survival rates and recurrence rates in patients with GBC for open and laparoscopic surgery have been observed in recent research, particularly in cases with early malignancies. According to the most recent statistics, patients with T1a tumors who had laparoscopic cholecystectomy had survival rates of more than 95%.²⁰ This is coherent with our findings.

Prior studies have reported as high as 66% disease recurrence in patients who had curative-intent resection at 2 years, with 28% of patients experiencing regional lymph node recurrences and 85% experiencing distant recurrences. In 2016, the US Extrahepatic Biliary Malignancy Consortium reported data on 217 individuals who received curative-intent surgical resection for GBC at ten academic institutions. The liver and peritoneum were the most frequently occurring recurrence locations, with a median recurrence-free survival of only 11.2 months for this sample.²¹

CONCLUSION

The outcomes of laparoscopic and open surgery in the management of gallbladder cancer are comparable in terms of post-operative complications, recurrence rates, survival rates, and disease free survival rates. However, laparoscopic approach shows benefit on length of hospital stay.

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