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OPINION REVIEW

Current status and progress in laparoscopic surgery for gallbladder carcinoma

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Abstract

Gallbladder carcinoma (GBC) is the most common biliary tract malignancy associated with a concealed onset, high invasiveness and poor prognosis. Radical surgery remains the only curative treatment for GBC, and the optimal extent of surgery depends on the tumor stage. Radical resection can be achieved by simple cholecystectomy for Tis and T1a GBC. However, whether simple cholecystectomy or extended cholecystectomy, including regional lymph node dissection and hepatectomy, is the standard surgical extent for T1b GBC remains controversial. Extended cholecystectomy should be performed for T2 and some T3 GBC without distant metastasis. Secondary radical surgery is essential for incidental gallbladder cancer diagnosed after cholecystectomy. For locally advanced GBC, hepatopancreatoduodenectomy may achieve R0 resection and improve long-term survival outcomes, but the extremely high risk of the surgery limits its implementation. Laparoscopic surgery has been widely used in the treatment of gastrointestinal malignancies. GBC was once regarded as a contraindication of laparoscopic surgery. However, with improvements in surgical instruments and skills, studies have shown that laparoscopic surgery will not result in a poorer prognosis for selected patients with GBC compared with open surgery. Moreover, laparoscopic surgery is associated with enhanced recovery after surgery since it is minimally invasive.

Key Words: Gallbladder carcinoma; Laparoscopic surgery; Simple cholecystectomy; Extended cholecystectomy; Hepatopancreatoduodenectomy; Incidental gallbladder cancer

Core Tip: Gallbladder carcinoma (GBC) is the most common biliary tract malignancy with a poor prognosis. Radical surgery is the mainstay of treatment, and the surgical extent depends on the tumor stage. Meanwhile, laparoscopic surgery has the advantage of enhanced recovery after surgery because it is minimally invasive, and has been widely used to treat gastrointestinal malignancies. Although GBC was once regarded as a contraindication for laparoscopic surgery, with improved surgical instruments and skills, recent studies have shown that laparoscopic surgery will not lead to a poorer prognosis compared with open surgery among selected patients with GBC in specialized centers.

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INTRODUCTION

Gallbladder carcinoma (GBC) has the highest incidence among malignant tumors of the biliary system, accounting for 80%-95% of all biliary tract cancers. GBC is more common in Chile, Japan and northern India[1]. Although GBC has a relatively low incidence of about 1.2% of all malignant tumors of the digestive system[2,3], its invasiveness is extremely high. The median survival time is six months, and the 5-year survival rate is less than 5%[4,5]. The prognosis is closely related to the tumor stage[5]. The high degree of malignancy of GBC is mainly due to the lack of submucosa and the relatively thin muscular layer of the gallbladder, and tumor cells are more likely to invade surrounding tissues and organs like the liver quickly[6]. Because of the frequent absence of typical symptoms, over 1/3 of patients are diagnosed with advanced GBC without the opportunity of radical operation. Only 15%-47% of patients with GBC diagnosed preoperatively will meet the indication for surgical resection. However, radical surgery remains the cornerstone of treatment because the effect of adjuvant therapy for GBC is very limited, and the surgical approach depends on the tumor stage (Table 1)[3]. With improvements in diagnostic and surgical techniques, the prognosis of patients with GBC who underwent radical surgery has been significantly improved in recent years[7].

Laparoscopic surgery has been widely used with the advent of "Enhanced Recovery After Surgery (ERAS)". With the advantages such as reducing the incision and magnifying the view, this surgical method can reduce intraoperative bleeding, alleviate postoperative pain, promote earlier oral intake, reduce complications like wound infection, and shorten the duration of hospitalization, achieving the goal of ERAS[8]. Since the rise of laparoscopic cholecystectomy in the early 1990s[9], laparoscopic surgery has been widely used to treat typical gastrointestinal malignant tumors. However, GBC was once regarded as a contraindication for laparoscopic surgery for the following main reasons[10,11]: (1) Bile spillage associated with intraoperative gallbladder perforation and repeated manipulation through the trocars could increase the incidence of peritoneal dissemination or port site metastasis (PSM); (2) The oncologic adequacy and safety of laparoscopic radical surgery for GBC still need to be verified by high-quality prospective studies; and (3) There were technical difficulties related to the procedure, such as lymph node dissection of hepatoduodenal ligament and around the hepatic artery, liver resection and bile duct resection in laparoscopic approaches. However, with the improvement of preoperative diagnosis of GBC, the progress of surgical skills and laparoscopic equipment, and the avoidance of bile spillage by careful manipulation and extensive implementation of retrieval bags, the incidence of peritoneal dissemination or PSM associated with laparoscopic surgery for GBC has been significantly reduced, with no significant difference in survival outcomes compared with open surgery in recent literature[10]. According to a systematic review by Berger-Richardson *et al*[12], the incidence of PSM after laparoscopic cholecystectomy for incidental GBC (IGBC) in the historic era (1991-1999) was about 18.6% and decreased to 10.3% in the modern era (2000-2014). Since the incidence of incision recurrence after open cholecystectomy is approximately 7%[12], the gap between the two approaches is gradually narrowing. Several studies have shown that there is no difference in the number of harvested lymph nodes by laparoscopy or laparotomy in radical resection of rectal cancer[13]. In addition, laparoscopy has been widely used in hepatectomy, which shows that the feasibility and safety of laparoscopic lymph node dissection and hepatectomy have been gradually proved by surgical experts[14]. Moreover, the development of laparoscopic suturing skills makes laparoscopic bile duct reconstruction possible[15]. The surgical extent of GBC varies greatly in different tumor stages. In order to ensure the safety and oncological adequacy of resection, surgeons should strictly select patients undergoing laparoscopic surgery for GBC[16]. This review will discuss the application of laparoscopic surgery in GBC according to the surgical approach and whether the cancer is IGBC.

Table 1 Summary of gallbladder carcinoma T staging according to the American Joint Committee on Cancer 8th edition and the corresponding surgical approach

	AJCC 8th T staging classification	Surgical approach
Tis	Carcinoma *in situ*	Simple cholecystectomy
T1a	Tumor invades the lamina propria	Simple cholecystectomy
T1b	Tumor invades the muscular layer	Extended cholecystectomy including cholecystectomy + lymphadenectomy ± hepatectomy (current consensus)/simple cholecystectomy (under debate)
T2a	Tumor invades the perimuscular connective tissue on the peritoneal side, without involvement of the serosa	Extended cholecystectomy including cholecystectomy + lymphadenectomy ± hepatectomy ± bile duct resection and reconstruction
T2b	Tumor invades the perimuscular connective tissue on the hepatic side, with no extension into the liver	Extended cholecystectomy including cholecystectomy + lymphadenectomy + hepatectomy ± bile duct resection and reconstruction
T3	Tumor perforates the serosa (visceral peritoneum) and/or directly invades the liver and/or one other adjacent organ or structure, such as the stomach, duodenum, colon, pancreas, omentum or extrahepatic bile ducts	Extended cholecystectomy including cholecystectomy + lymphadenectomy + hepatectomy ± bile duct resection and reconstruction (some T3 without distant metastasis)/hepatopancreatoduodenectomy (under debate)
T4	Tumor invades the main portal vein or hepatic artery or invades two or more extrahepatic organs or structures	No significant benefit from surgery

AJCC: American Joint Committee on Cancer.

SIMPLE CHOLECYSTECTOMY

For Tis and T1a GBC, R0 resection can be achieved through simple cholecystectomy, which meets the standard of oncological safety, and both laparoscopic and open surgery can reach the postoperative overall survival rate of 95%-100%[10]. However, it is controversial whether for T1b GBC, simple cholecystectomy or extended cholecystectomy, which includes lymph node dissection and hepatectomy, is oncologically safe[17], although the latter is recommended by the current guidelines[17]. A study of 536 T1b GBC subjects from Surveillance, Epidemiology, and End Results database showed that extended cholecystectomy could improve disease-specific and overall survival of those patients[18]. In addition, Butte *et al*[19] found that 35% of patients with T1b GBC had residual disease after simple cholecystectomy, which supports the necessity of extended cholecystectomy for patients with T1b GBC.

However, more studies in recent years have shown that simple cholecystectomy does not adversely affect the long-term prognosis of patients with T1b GBC[20-22], and the choice of surgical extent mainly depends on the experience of the surgeon[23]. In a meta-analysis in 2017, including 22 publications published in MEDLINE since 1994, Lee *et al*[17] compared the relationship between surgical extents *via* laparoscopic or open surgery and the prognosis of T1 GBC among patients with T1b GBC. They found that the risk difference between simple cholecystectomy and extended cholecystectomy was 0.03, while the risk ratio was 1.06, indicating no significant difference in overall survival outcomes between the two surgical extents. Recent studies have reported that long-term outcomes of patients with early GBC after laparoscopic cholecystectomy, which is now widely adopted, are comparable to laparotomy[24,25]. Therefore, the laparoscopic approach is safe and feasible for patients with early GBC undergoing simple cholecystectomy, and its minimally invasive characteristics can accelerate the postoperative rehabilitation process[26,27]. However, more large cohort studies are needed to confirm the long-term prognosis of this approach, given the low diagnostic rate and staging accuracy of T1 GBC. It should be taken into special consideration that gallbladder perforation caused by forceps during the operation will cause tumor dissemination. For suspected GBC, the resected gallbladder should be removed completely and extracted with a retrieval bag during laparoscopic cholecystectomy to avoid tumor dissemination caused by bile spillage into the abdominal cavity or port sites[24].

EXTENDED CHOLECYSTECTOMY

Extended cholecystectomy for GBC is now mainly recommended for T1b, T2 and some T3 patients without distant metastasis, which includes cholecystectomy + regional lymph node dissection ± adjacent hepatectomy ± bile duct resection and reconstruction[16]. A number of studies have shown that it is safe and effective to perform laparoscopic extended cholecystectomy for patients who meet criteria such as no surgical contraindications, no severe abdominal adhesion and tolerance of pneumoperitoneum. The postoperative recurrence and survival outcomes are comparable to and even better than those of laparotomy[28,29]. According to the single-center retrospective study of patients with T2 GBC treated from 2004 to 2017 by Jang *et al*[11], there was no significant difference between laparoscopic and open

extended cholecystectomy in terms of the number of retrieved lymph nodes and 5-year survival rate, and postoperative hospital stay was significantly shorter in the laparoscopic group. A recent meta-analysis including 14 studies comparing laparoscopic and open extended cholecystectomy for GBC published in several databases up to April 6, 2021, found that laparoscopic surgery had a lower risk of death than open surgery for T3 GBC, while there was no significant difference in death between the two methods for T1 and T2 GBC. In addition, the survival rate after laparoscopic surgery was higher than that after open surgery for the first two years for T2 and T3 GBC, but the three-year and five-year survival rates were similar between the two groups regardless of the tumor stage. Lastly, no significant difference in the overall recurrence was found between the two surgical approaches. The above results also confirm the feasibility and safety of laparoscopic extended cholecystectomy[30].

Lymph node dissection

Lymph node dissection during extended cholecystectomy for GBC is mainly used to stage the patient [31], but the optimal extent of regional lymphadenectomy is still under debate. In the published studies, the extent of lymph node dissection for GBC mainly includes lymph nodes around the hepatoduodenal ligament, and some centers also emphasize the necessity to dissect lymph nodes in the posterior superior pancreaticoduodenal area and along the common hepatic artery at the same time because of the high frequency of metastasis in this area and the possibly improved survival rate after complete resection[27,32,33]. More extensive dissection of the aorto-caval, celiac and superior mesenteric artery nodes has limited effect and insignificant survival benefit. However, some centers advocate aorto-caval node sampling at the beginning of the operation to estimate the presence of distant metastasis. Patients with positive lymph node biopsies in this area can hardly benefit from extended cholecystectomy for GBC[34]. Recent studies have shown that in selected patients with GBC, the extent of laparoscopic lymph node dissection and the number of retrieved lymph nodes are similar to open surgery with few intraoperative and postoperative complications[15,28,29,35,36]. A prospective cohort study by Yoon *et al* [36] showed that the median number of harvested lymph nodes was seven in the 32 patients with T1b-T2 GBC who underwent laparoscopic extended cholecystectomy in their center from 2004 to 2014, exceeding the minimum number of six recommended by the 8th AJCC[21,37], and there was no local recurrence within the extent of lymphadenectomy within 10 years after surgery[36], indicating the feasibility and oncological adequacy of laparoscopic lymph node dissection in patients with GBC. Vega *et al*[34] compared laparoscopic extended cholecystectomy with open surgery in 35 cases of GBC treated in their center, and found that the median number of lymph nodes harvested by the two methods was both six, and there was no significant difference in residual disease, recurrence rate, postoperative complications and 90-d mortality between the two surgical approaches.

Liver resection

Negative margins should be achieved in hepatectomy for patients with GBC in order to reduce tumor recurrence caused by liver micrometastasis. If the gallbladder is severely adherent to the liver, the attached thin layer of liver tissue is often removed in conjunction with the gallbladder to avoid bile spillage caused by gallbladder damage. The most common surgical extent is wedge resection for at least 2 cm of the liver bed, and IVb/V resection is also performed in some centers[16,34]. For some patients with T3 GBC, (extended) right hepatectomy can be performed to achieve R0 resection according to the patient's tolerance, but its clinical benefits need to be further confirmed as extensive hepatectomy will increase the rate of postoperative complications such as liver failure[1]. Current studies have reported the feasibility and safety of laparoscopic wedge resection or IVb/V resection[28,35,38], but there is no consensus on the best extent of hepatectomy, and no clinical data have confirmed the theoretical advantage of IVb/V resection over wedge resection[16]. A multicenter retrospective study by Lee *et al* [39] found that there was no significant difference in the 5-year survival rate or recurrence-free survival rate after wedge resection or IVb/V resection of the liver in patients with T2 GBC who underwent extended cholecystectomy, and some other researches also reported similar results[40,41].

It is worth noting that the hepatic-side and peritoneal-side GBC may have different prognoses. According to a multicenter retrospective study of patients with T2 GBC, the rates of nodal involvement, liver metastasis, postoperative intrahepatic recurrence and vascular and nerve invasion were higher in hepatic-side GBC, and the prognosis was worse than that of peritoneal-side GBC; however, there were no such differences in those with T1 and T3 GBC[42]. Some studies reported that the density of large vessels increased significantly in the deep layer of the gallbladder wall. The hepatic side of the gallbladder was drained by short veins directly connected to the intrahepatic portal veins, with the peritoneal side drained by 1 or 2 cystic veins terminating in the hepatic parenchyma or at the hepatic hilum[43]. The retrospective study suggested that the density of vessels and length of the drainage path caused the difference in the incidence of hepatic, vascular and lymphatic metastasis between hepatic-side and peritoneal-side GBC[42]. Another multicenter retrospective study showed that for patients with hepatic-side T2 GBC, the 5-year survival rate was higher in patients who underwent extended cholecystectomy, including both regional lymphadenectomy and hepatectomy, than in patients who underwent extended cholecystectomy without hepatectomy. In addition, the extent of hepatectomy did not affect the prognosis. Furthermore, for patients with peritoneal-side T2 GBC who underwent lymph node dissection, the 5-year survival rate was not affected by hepatectomy or the extent of lymphaden-

ectomy. Therefore, it is considered that extended cholecystectomy, including lymphadenectomy and R0 hepatectomy, is essential for patients with hepatic-side T2 GBC, while patients with peritoneal-side T2 GBC can only undergo cholecystectomy and lymph node dissection without hepatectomy[39].

Bile duct resection and reconstruction

Indications for bile duct resection in patients with GBC include a positive cystic duct margin, direct tumor invasion of the bile duct and inflammation or scarring around the hepatoduodenal ligament that compromise lymphadenectomy[16]. It is not recommended to perform routine bile duct resection for patients with GBC because it increases the risk of complications without improving the survival rate[44-47]. The present literature has proved the feasibility of laparoscopic bile duct resection in patients with GBC[48]. With the accumulation of experience in laparoscopic surgery in choledochal cysts and pancreatoduodenectomy, the need for bile duct resection and reconstruction is no longer a contraindication of laparoscopic extended cholecystectomy for GBC[16].

HEPATOPANCREATODUODENECTOMY

The gallbladder is adjacent to the liver, duodenum and colon. For patients with locally advanced GBC, it is feasible to achieve R0 resection with hepatopancreatoduodenectomy (HPD) and improve the long-term survival rate. However, only about 10% of the patients can meet the conditions for HPD[1], which include: Tumor at the body or bottom of the gallbladder (hepatic bed type); tumor invading the hepatic hilum (hilar type); massive mass (hepatic bed + hilar type); extensive regional lymph node metastasis (lymph node type); tumor invading the distal bile duct or duodenum; and lymph node metastasis around the head of the pancreas. The contraindications include chronic hepatic diseases, severe comorbidities, R2 resection, paraaortic lymph node metastasis, peritoneal dissemination and distant metastasis. Postoperative mortality and the risk of complications such as liver failure, pancreatic fistula and biliary leakage are extremely high[1]. It is reported that the in-hospital morbidity rate after HPD is more than 10%[49]. Less than 1000 cases of this surgical approach have been reported in the past 50 years[49,50]. Dr Kasumi of Japan performed the first HPD for a patient with GBC invading the duodenum in 1974[51,52]. Takasaki *et al*[53] performed HPD on five patients with GBC invading the duodenum and pancreatic head in 1980. The 30-d mortality was 60%, and the survival time of the other two patients was five months and 16 mo, respectively[1,53]. However, with the improvement in surgical and anesthetic techniques and perioperative management, the prognosis of HPD has been improved. It is reported that the 3-year and 5-year survival rates after HPD are 48% and 37% respectively[54], and more surgeons choose to try this procedure because it has a better prognosis than unresectable tumors [55].

Because of the technical difficulty and high risks of laparoscopic HPD, only four cases of locally advanced GBC or extrahepatic cholangiocarcinoma have been reported to undergo this surgical approach so far (Table 2)[56-59]. Despite the postoperative complications such as bile leakage and delayed gastric emptying[56], the successful implementation of laparoscopic HPD in the four cases has proven its safety and feasibility. This surgery should be performed in large volume centers[1], and the surgeons should have sufficient experience in laparoscopic pancreaticoduodenectomy and laparoscopic hepatectomy[60,61]. Patients who only need a small extent of hepatectomy should be selected as far as possible to reduce postoperative complications. If the patients need major hepatectomy, portal vein embolization should be performed before the operation to increase the remnant volume and avoid postoperative liver failure[49,62]. For patients with obstructive jaundice and cholangitis, bile drainage should be performed preoperatively to improve hepatic function and promote postoperative remnant liver regeneration[63]. The risk of pancreatic fistula after pancreatoduodenectomy in patients with GBC is usually greater than that in patients with adenocarcinoma of the pancreatic head attributed to the soft texture of the pancreatic gland and small pancreatic duct, which could be reduced by two-stage pancreatojejunostomy, external drainage of pancreatic fluid and wrapping omental flap[64].

INCIDENTAL GALLBLADDER CANCER

According to the literature, the incidence of IGBC after laparoscopic cholecystectomy ranges from 0.19% to 3.3% and has increased significantly with the widespread use of laparoscopic cholecystectomy[65]. About 47%-70% of GBC cases are incidentally found during or after cholecystectomy[34], and 45%-60% of patients with IGBC have residual disease after the initial cholecystectomy[45,66,67]. Patients with IGBC are usually at the early stage, and reresection can significantly improve oncological outcomes for patients with T1b-T3 GBC without distant metastasis[68-70]. For patients with bile spillage, positive margin, poorly differentiated tumor or high risks of tumor dissemination during the initial cholecystectomy, it is recommended to perform laparoscopy before secondary radical cholecystectomy to detect metastases that are difficult to be found by preoperative imaging and avoid ineffective reresection[71,72]. Inflammatory adhesion and fibrosis around the hepatoduodenal ligament and the

Table 2 Summary of the published cases of laparoscopic hepatopancreatoduodenectomy for locally advanced gallbladder carcinoma or extrahepatic cholangiocarcinoma

Ref.	Country	Age (yr)	Diagnosis	Operation	Operation duration (min)	Main complication	Hospital stay (d)
Zhang *et al*[57], 2014	China	61	ECC invading the duodenum	LPD + LRH	600	Bile leakage	16
Chong and Choi [58], 2019	South Korea	73	ECC	LPD + LLH	510	Cystitis	16
James *et al*[59], 2021	India	73	GBC infiltrating the CBD	LPD + segments IVb and V	610	Delayed gastric emptying	12
Yao[56], 2022	China	75	ECC + GBC	LPD + segments IVb and V	380	No	12

ECC: Extrahepatic cholangiocarcinoma; GBC: Gallbladder carcinoma; CBD: Common bile duct; LPD: Laparoscopic pancreatoduodenectomy; LRH: Laparoscopic right hemihepatectomy; LLH: Laparoscopic left hemihepatectomy.

gallbladder bed significantly increase the difficulty of radical reoperation for IGBC. However, a few studies have reported the feasibility of laparoscopic radical reresection for IGBC[15,28,73-75] and shown prognoses comparable to that of laparotomy in selected early GBC[70,76]. However, the effect of laparoscopic reresection in patients with IGBC after cholecystectomy for acute cholecystitis needs to be further studied[77-79]. The specimen of the previous operation should be assessed again by a specialized pathologist before reoperation for T stage[19,80], the tumor location (hepatic-side or peritoneal-side), a positive bile duct margin[42], peritoneal and lymphovascular invasion and the presence of Rokitansky-Aschoff sinuses[81], which will increase the rate of conversion to open surgery[34]. Although there is a risk of PSM after cholecystectomy for IGBC, routine port site resection is not recommended because it can't improve the oncological outcomes or reduce recurrence attributed to the high rate of combined peritoneal metastasis, and it can increase the risk of morbidities like incisional hernia[82].

DISCUSSION

Laparoscopic surgery has many advantages over open surgery. Firstly, for benign diseases, which can't be completely excluded from GBC before operation, such as xanthogranulomatous cholecystitis, laparoscopic surgery can retain the opportunity of minimally invasive treatment after frozen section analysis of the specimen is confirmed. Secondly, laparoscopy can provide a clearer surgical field, and laparoscopic exploration can detect liver or peritoneal metastases that are difficult to detect preoperatively, reducing the incidence of unnecessary laparotomy[10]. Thirdly, laparoscopic surgery can reduce postoperative complications such as ileus and infection by reducing contact between the viscera and external environment[83,84]. Finally, minimally invasive surgery can not only accelerate rehabilitation by reducing the incision, alleviating pain, reducing blood loss and promoting early mobilization and oral intake but also initiate postoperative adjuvant therapy earlier[85], which could improve quality of life and prolong long-time survival of the patients[86].

Recent studies have proven the short-term benefits of laparoscopic surgery compared to laparotomy for GBC. A single-center retrospective study by Dou *et al*[87], including 99 patients with T2 and T3 stage GBC who underwent radical resection, showed that compared with open surgery, the laparoscopic group had lower intraoperative bleeding volume (233.91 ± 26.35 mL *vs* 461.25 ± 53.15 mL, $P < 0.01$) and shorter postoperative hospital stay (10.32 ± 0.60 d *vs* 14.74 ± 0.91 d, $P < 0.01$); although it had longer operation time (292.35 ± 14.41 min *vs* 249.02 ± 13.30 min, $P = 0.033$). Lymph node yield (9.39 ± 0.68 *vs* 8.26 ± 0.52, $P = 0.208$) and incidence of postoperative morbidities, including bile leakage (0.11 *vs* 0.07, $P = 0.521$), postoperative bleeding (0.05 *vs* 0.02, $P = 0.448$) and abdominal abscess (0.05 *vs* 0.07, $P = 0.738$) were similar between the two groups[87]. Another retrospective analysis of 102 patients with GBC reported that the patients who underwent laparoscopic surgery experienced a shorter postoperative activity time (2 ± 1 d *vs* 4 ± 1 d, $P < 0.001$), eating time (2 ± 1 d *vs* 4 ± 2 d, $P < 0.001$) and drainage tube removal time (4 ± 3 d *vs* 6 ± 3 d, $P < 0.001$) compared with those who underwent open surgery[88]. Similarly, according to the 18 studies comparing laparoscopic and open radical cholecystectomy for GBC analyzed by Lv *et al*[89], the laparoscopic group had a significantly smaller volume of intraoperative blood loss, a shorter time of drainage tube extraction and diet recovery, a lower rate of postoperative complications such as pulmonary infection and thrombus formation (which was 10.1% compared with 15.8%) and a shorter length of postoperative hospital stay. The shorter hospital stay is theoretically because of reduced wound-related pain, early-period ambulation and earlier gastrointestinal peristalsis. Operative time, intraoperative gallbladder violation, R0 resection rate,

lymph node yield and overall recurrence rate were comparable in the two groups[89]. Predictive factors for conversion to open surgery may include a positive liver margin, massive intraoperative bleeding and an interval between surgeries of more than 60 d, which may cause severe abdominal adhesions[34]. In the prospective study of Cho *et al*[24], including 33 patients with early-stage GBC who underwent laparoscopic surgery, three patients with liver invasion noted by diagnostic laparoscopy had their procedure converted to laparotomy, and another conversion occurred owing to bleeding during locoregional laparoscopic lymphadenectomy. A retrospective study showed that 7 out of 30 patients undergoing laparoscopic extended cholecystectomy with bi-segmentectomy in their center required conversion to open surgery due to distortion of anatomical landmarks and suspected involvement of extrahepatic organs that caused technical difficulty[90]. The rate of conversion to open surgery decreases with the improvement of surgical experience and equipment.

Moreover, laparoscopic surgery will not worsen the survival outcomes compared with open surgery in selected early-stage GBC by experienced surgeons *via* improved diagnosis rate, staging accuracy and precision of operation to avoid bile spillage. A study by Yoon *et al*[36] showed that among the 45 patients with GBC who underwent laparoscopic extended cholecystectomy in their center, the 5-year survival rate of T1a and T1b GBC was 100%, and that of T2 GBC was more than 90%. Only four patients experienced recurrence postoperatively, which were all distant metastases. Itano *et al*[29] compared 16 patients with T2 GBC who underwent laparoscopic extended cholecystectomy with 14 patients who underwent open surgery and found no significant difference in disease-free or overall survival rate between the two groups. However, anatomical features such as thin gallbladder walls and the presence of Rokitansky-Aschoff sinuses make it difficult to evaluate the depth of tumor invasion, and the preoperative staging accuracy is only 40%[91]. Endoscopic or laparoscopic ultrasonography is superior to traditional abdominal ultrasonography and computed tomography in diagnosing T staging[92]. Only a few surgeons have rich experience in laparoscopic radical surgery for GBC, and no consensus has been reached on this operation. Steps such as laparoscopic lymph node dissection, hepatectomy and choledochojejunostomy demand high requirements on surgical instruments and techniques. For patients with a massive mass, duodenal or colonic invasion, jaundice or hilar involvement, more surgeons still prefer open surgery[34]. In addition, regarding the higher cost of laparoscopic surgery from the use of consumable materials and the possibility of conversion to laparotomy, some experts and patients still have concerns and disputes about laparoscopic surgery for GBC[10]. This surgical approach is still in the early stage of the adoption curve. More multicenter prospective studies are needed to confirm the safety and efficacy of laparoscopic surgery for GBC[16].

CONCLUSION

For strictly selected patients with early GBC, long-term survival outcomes of laparoscopic surgery are comparable to that of open surgery, and laparoscopic surgery has the advantage of accelerating rehabilitation because of its minimally invasive characteristics. However, as the progress of minimally invasive treatment for GBC is relatively slow, more studies are needed to further confirm its oncological safety and efficacy and improve the standardization of the procedures of laparoscopic surgery for GBC.

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