Review Article

Minimally invasive liver resection for gallbladder cancer

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Abstract: Gallbladder cancer (GBC) is a controversial subject in the field of minimal invasive hepatobiliary and pancreatic (HBP) surgery. The advent of minimal invasive surgery (MIS) in GBC has raised concerns ranging from port site recurrence, bile spillage causing cancer dissemination, to inadequate evidence of safety. Liver resection in GBC is performed with the aim of achieving negative margins as well as minimizing recurrence. With advancing experience in laparoscopic liver resection, these aims can be fulfilled with MIS. Increasing expertise in laparoscopic and robotic liver resection has enabled the indications of MIS in GBC to be expanded to those requiring liver resection. Wedge resection or IVb and V anatomical resection is recommended for T2 GBC. Similar outcomes have been achieved with both surgeries. Wedge resection is technically easier than anatomical IVb and V resection therefore making it easier to perform the resection by the MIS approach. At present, MIS can be recognized as a safe alternative to open surgery in GBC. Centers with expertise in both MIS and HBP surgery can extend their MIS indications in GBC to include liver resection. With increasing experience there may come a day when this minimal access approach will become the standard of care in patients with GBC.

Keywords: Laparoscopic radical cholecystectomy; robotic radical cholecystectomy (RRC); wedge resection; IVb and V resection

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Hepatobiliary and pancreatic (HBP) surgery is one of the most challenging aspects in the field of surgery. Introduction of laparoscopy has increased the technical difficulty further. Laparoscopic liver resection (LLR) with all its hurdles has gone a long way from small tumorectomy in the anterior-lateral area to major hepatectomy including donor hepatectomy.

With the advantages of 3D visibility, increased degrees of freedom, and reduced physiologic tremor, robotic surgery is gaining popularity. However, the high cost, loss of haptic feedback and few definite advantages over laparoscopic surgery have limited its use (1). Studies have shown that robotic liver resection (RLR) has acceptable conversion and complication rates and shows good overall safety with outcomes similar to laparoscopic and open surgery (2,3).

Gallbladder cancer (GBC) is a controversial subject in the field of minimal invasive HBP surgery. The advent of minimal invasive surgery (MIS) in GBC has started a dispute among hepato-biliary surgeons. Concerns ranging from port site recurrence, bile spillage causing cancer dissemination, to inadequate evidence of safety were prevalent among HBP surgeons. Not just the concern of oncological outcomes but the issue of patient safety associated with the technical difficulty in LLR has prevented the adoption of the minimal invasive approach for GBC. Another issue is the steep learning curve associated with safe lymph node dissection around the hepatoduodenal ligament (4). However, there have been increasing reports highlighting the advantages of MIS while maintaining patient safety. Reports on acceptable long-term oncological outcomes prompted a slow shift

towards MIS (5). MIS in GBC is gradually being adopted at a number of centers recently. There is still skeptism on MIS in GBC in patients requiring liver resection. With increasing expertise in LLR, high volume centers have begun extending indications of laparoscopic GBC. There is still very limited data on minimal invasive liver resection in GBC with most data including retrospective studies and cases reports. In GBC, the aim of liver resection is to achieve a negative hepatic parenchymal resection margin as well as minimize recurrence by removing microscopic metastases in the liver (6). With experience these aims can be fulfilled even with MIS.

LLR in GBC

The first prospective study on laparoscopic surgery for suspected early GBC was conducted from 2004 to 2007 by our team. 30 patients were selected based on a preoperative endoscopic ultrasound and intra-operative laparoscopic ultrasound done to rule out any liver invasion. The complication rate was 16.7% and no patient developed recurrence after a median follow up of 27 months (7).

A recent paper published by Jang *et al*. compared outcomes in T2 stage GBC between laparoscopic and open groups. Data of patients over 13 years was presented. Median follow up time was 35.2 months. There was no statistical difference between the 2 groups in terms of overall survival. Disease free survival was significantly higher in the laparoscopic group (at 5 years laparoscopic surgery *vs.* open surgery: 78% *vs.* 62.4%; P=0.0171). There was no case of port site recurrence reported in the laparoscopic surgery group (8). Agarwal *et al.* retrospectively compared outcomes of 24 cases of laparoscopic radical cholecystectomy and 46 cases of open radical cholecystectomy, showing no significant difference in terms of postoperative morbidity, mortality, number of lymph nodes collected, and recurrence rate (9). Itano *et al.* reviewed 19 laparoscopic and 14 open cases of suspected T2 GBC, and showed no significant difference in postoperative morbidity, mortality, number of lymph nodes collected, and recurrence rate (10).

The first prospective study did not include patients with LLR. The extent of liver resection has been a topic of debate. Still wedge resection or IVb and V resection is recommended for T2 GBC. There are reports that thin liver resection without wedge resection gives good results in T2 GBC (5). Lee *et al.* showed that there is no clear benefit of liver resection in selected patients with peritoneal side GBC (11).

There are several reports showing no difference in overall survival between wedge resection and IVb and V segmentectomy in GBC. Similar outcomes have been achieved with both surgeries (12,13). Wedge resection of the liver is technically easier than anatomical IV b and V resection therefore laparoscopic wedge resection can be easily performed.

In a recent consensus meeting involving 9 experts to discuss the role of laparoscopic surgery in GBC, the overall value of laparoscopic extended cholecystectomy for GBC was considered equivalent to open surgery (4).

Seven retrospective studies evaluating the outcomes of laparoscopic radical cholecystectomy including either wedge resection of the liver, segment IV b and V segmentectomy or major hepatic resections have been published (*Table 1*). All the reports show acceptable outcomes with laparoscopic surgery, some papers also showed results similar to those of open surgery.

The most recent retrospective study involving the largest cohort of patients was recently published online by Nag *et al.* They compared 30 patients of laparoscopic extended cholecystectomy with bi-segmentectomy, with 38 patients of open surgery. Mean blood loss (P=0.006) was significantly lower while mean hospital stay (P=0.0001) significantly shorter in the laparoscopic group. Median number of lymph nodes excised, post-operative complication rate, recurrence free and overall survival were similar in both groups. They concluded that laparoscopy can improve perioperative outcomes with similar oncological efficacy (20).

Robotic surgery in GBC

There are fewer published reports of robotic radical cholecystectomy (RRC) as compared to laparoscopic robotic cholecystectomy in GBC (*Table 2*). However, these reports on RRC show acceptable long term and short-term outcomes as well.

A study conducted in Italy evaluated the outcomes of completion cholecystectomy using both the robotic and laparoscopic approach. Three patients were present in each group. Segment IVb and V resection including lymphadenectomy was carried out with results similar to other studies and no recurrence after 32 months of follow-up. They thus concluded that radicalization of cholecystectomy can be achieved without compromising outcomes using MIS approach (24).

Table 1 Laparoscopic liver resection in gall bladder carcinoma

Authors	Total patients	Liver resection	Surgery time	EBL	LN	Complications >3a	Conversion	Hospital stay	OS
Agarwal *et al.* (9)	44	24	270	200	10	3	0	5	NA
Palanisamy *et al.* (14)	14	14	212.9	196.4	8	2	0	5.14	68.75%
Castro *et al.* (15)	18	18	490	125	6	1	1	NA	80.7%
Jang *et al.* (8)	55	16	231	225	7.6	4		5.8	73.1%
Piccolo *et al.* (16)	18	18	292	NA	1–3 (n=2); >4 (n=13)	1	3	8 (excluding those who developed complications)	NA
Nag *et al.* (17)	20	20	300	120	10	0	5	5.5	82.3%
Gumbs *et al.* (18)	15	15	220	160	4	0	1	–	NA
Walid *et al.* (19)	10	10	180	110	9	1	0	8	NA

NA, not applicable; EBL, estimated blood loss; LN, number of lymph nodes resected; OS, overall survival.

Table 2 Robotic liver resection in gall bladder carcinoma

Author	Liver resection	Surgery time	EBL	LN	Complications >3a	Conversion	Hospital Stay	3-year OS
Shen *et al.* (21)	5	200	170	9 (3 to 11)	0	0	7.4	NA
Sidrah *et al.* (22)	11	219	50	5	1	0	4	65%
Goel *et al.* (23)	27	295	200	10 (2 to 21)	1	4	4	NA

NA, not applicable; EBL, estimated blood loss; LN, number of lymph nodes resected; OS, overall survival.

Goel *et al.* studied the outcomes in 27 patients after RRC. All patients underwent IV b and V segmentectomy. Only one patient had complications post operatively clavien dindo 3b. After a median follow up of 9 months, 2 patients had a recurrence (23).

There have been reports evaluating outcomes of LLR and robotic liver resection in hepatobiliary malignancies including GBC (25,26).

Case reports on LLR and RLR

There are several case reports on both LLR and RLR in GBC (27-32). All these reports have shown encouraging results in the use of MIS in liver resection in GBC.

In conclusion, at present MIS can be recognized as a safe alternative to open surgery in GBC. Centers with expertise in both MIS surgery and hepatobiliary surgery can extend their MIS indications in GBC to include liver resection. With increasing experience there may come a day when this minimal access approach will become the standard of care in patients with GBC.

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Footnote

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aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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