

Survey Results of the Expert Meeting on Laparoscopic Surgery for Gallbladder Cancer and a Review of Relevant Literature

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Keywords

Laparoscopic surgery · Gallbladder cancer · Survey · Expert · Literature review

Abstract

Background: Favorable outcomes of laparoscopic surgery for gallbladder cancer (GBC) have been reported; yet consensus on the indications and surgical techniques for laparoscopic surgery for GBC is lacking. **Objective:** To evaluate the current status of laparoscopic surgery for GBC by analyzing the results of a survey of experts and by reviewing the relevant published literature. **Methods:** Before an expert meeting was held on September 10, 2016 in Seoul, Korea, an international survey was undertaken of expert surgeons in the field of GBC surgery. **Results:** The majority of surgeons who responded agreed that laparoscopic surgery has an acceptable role for suspicious or early GBC, and that laparoscopic extended cholecystectomy has a value comparable to that of open surgery in selected patients with GBC. However, the selection criteria for laparoscopic surgery for overt GBC

and the details of the surgical techniques varied among surgeons. **Conclusions:** This survey and literature review revealed that laparoscopic surgery for GBC is performed in highly selected cases. However, the favorable outcomes in the published reports and the positive view of experienced surgeons for this operative procedure suggest a high likelihood that laparoscopic surgery will be more frequently performed for GBC in the future.

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Introduction

The introduction of laparoscopic cholecystectomy ignited an explosion in the application of laparoscopic surgery not only to the treatment of biliary disease but also

This meeting was held during the 26th World Congress of the International Association of Surgeons, Gastroenterologists, and Oncologists (IASGO 2016) in Seoul, 2016.

to other gastrointestinal diseases. New developments in laparoscopic techniques and advances in laparoscopic devices have enabled the indications for laparoscopic surgery to be extended to gastrointestinal malignancy. However, initial reports regarding port-site recurrence following laparoscopic cholecystectomy, along with the rare incidence and poor prognosis of gallbladder cancer (GBC), have delayed the adoption of laparoscopic surgery for the treatment of GBC [1, 2]. As GBC is increasingly an incidental finding after laparoscopic cholecystectomy, several recent reports have demonstrated that an initial laparoscopic approach does not adversely influence the prognosis of patients when a definite oncologic resection is performed according to the postoperative pathologic results [3–5]. Further, some experienced surgeons began to report favorable outcomes of laparoscopic extended cholecystectomy, mostly for early-stage GBC [6–13]. However, controversy remains regarding the application of laparoscopic surgery to the treatment of GBC, and there is no consensus regarding the indications or surgical techniques for laparoscopic surgery for GBC.

Against the background of very limited evidence in this procedure, the first expert panel statement on laparoscopic surgery for GBC was prepared during the 26th World Congress of the International Association of Surgeons, Gastroenterologists and Oncologists (IASGO 2016) in Seoul, 2016. Before the meeting was convened, a questionnaire was circulated among experienced surgeons worldwide to collect information about the current status of laparoscopic surgery for GBC, and details of the indications and surgical technique. In this report, we describe the results of the survey and the current status of laparoscopic surgery for GBC based on a literature review.

Methods

An online survey was conducted among 9 expert hepato-pancreato-biliary surgeons in 5 countries between July 2016 and August 2016. The surgeons were selected based on their professional recognition and proven experience in the field of surgery for GBC. The survey questions are provided in the online supplemental material (see www.karger.com/doi/10.1159/000486208). The survey comprised 34 questions. The first 6 questions related to the country of origin, hospital type, and details of surgical experience (general surgery, cholecystectomy, surgery for GBC). The next 2 questions addressed opinions on the current role of laparoscopic surgery for GBC. The subsequent 26 questions concerned the diagnostic work-up for GBC, indications, operative strategies, and techniques for the laparoscopic approach for GBC in various clinical settings, including the laparoscopic approach for suspicious and overt GBC, laparoscopic extended cholecystectomy, and laparoscopic reoperation for postoperatively diagnosed GBC.

Results

Characteristics of Participating Surgeons

All the 9 surgeons from 5 countries who were asked to participate in the survey responded. Their median surgical experience was 19 years (range 10–36) after completion of a residency program. Seven of the nine surgeons practiced at an academic center. Regarding the surgeons' institutions, the number of cholecystectomies performed annually was <500 at 4 centers, 501–1,000 at 2 centers, and >1,000 cholecystectomies at 3 centers. The number of surgical resections for GBC was 11–50 in the majority of centers ($n = 6$), 51–100 in 2 centers, and <10 at one center. Of the 9 responding surgeons, 8 reported performing laparoscopic surgery for overt GBC.

Opinions on Laparoscopic Surgery for GBC

With regard to the current role of laparoscopic surgery for GBC, staging laparoscopy was the most frequently adopted strategy by the responders ($n = 8$), followed by initial laparoscopic approach for suspicious GBC ($n = 7$), extended cholecystectomy for early GBC confined to the GB (T1 or T2; $n = 7$), and extended cholecystectomy for T3 GBC ($n = 3$). The current overall value of laparoscopic extended cholecystectomy for GBC was considered equivalent to that of open surgery by 6 of the 9 surgeons, whereas it was considered inferior to open surgery by 2 surgeons, and superior by one surgeon.

Diagnostic Work-Up for GBC

The preferred radiologic imaging technique for preoperative evaluation of GBC was abdominal computed tomography ($n = 9$), followed by conventional ultrasonography ($n = 7$), endoscopic ultrasonography ($n = 7$), positron emission tomography ($n = 6$), and endoscopic retrograde cholangiopancreatography or magnetic resonance cholangiopancreatography ($n = 4$). Most of the surgeons reported performing frozen biopsy during surgery for suspicious GBC to confirm the diagnosis of malignancy, depth of tumor invasion, and involvement of the cystic duct margin. The depth of invasion of GBC was intraoperatively evaluated by frozen biopsy ($n = 7$), gross morphology ($n = 6$), and laparoscopic ultrasound ($n = 5$).

Laparoscopic Approach for Suspicious GBC

All 9 surgeons reported performing laparoscopic surgery when GBC was suspected, and selectively performed open conversion when malignancy was confirmed intraoperatively. The most frequently mentioned reason for open conversion was involvement of the cystic duct mar-

gin ($n = 6$), followed by tumor invasion beyond the muscle layer ($n = 3$), liver invasion ($n = 2$), and LN metastasis ($n = 1$). One surgeon stated that he would convert to open surgery only if technically necessary.

Laparoscopic Approach for Overt GBC

Eight of the nine surgeons reported performing laparoscopic surgery in selected patients with overt GBC. The most common indication for open surgery for overt GBC was cystic duct/CBD involvement ($n = 6$), followed by association with acute cholecystitis ($n = 4$), large-sized tumor ($n = 3$), tumor invasion beyond the muscle layer ($n = 2$), liver invasion ($n = 2$), LN metastasis ($n = 1$), and adjacent visceral organ invasion ($n = 1$).

Laparoscopic Extended Cholecystectomy for GBC

Seven out of the nine surgeons reported having performed laparoscopic extended cholecystectomy for GBC. Four surgeons had performed >50 procedures, one had performed 20–30 procedures, and 2 had performed 10–20 procedures. The most frequently mentioned technical concern regarding this procedure was perforation during dissection of the GB ($n = 7$), followed by ability to achieve a complete, margin-free resection ($n = 3$), risk of intraoperative bleeding ($n = 3$); and difficulty of achieving adequate LN dissection ($n = 1$) and liver resection ($n = 1$). The surgeons considered the following contraindications for laparoscopic extended surgery for GBC: invasion of other visceral organs ($n = 6$), cystic duct/CBD involvement ($n = 3$), large-sized tumor ($n = 3$), association with acute cholecystitis ($n = 3$), and prior upper abdominal surgery ($n = 1$).

The trigger criterion for performing liver resection was reported as tumor stage of T1b ($n = 3$), T2 ($n = 3$), and T3 ($n = 3$). Five surgeons stated that the decision regarding liver invasion is affected by whether the tumor is located near the liver or at the peritoneal side. Regarding the type of liver resection, wedge resection was performed by the majority of surgeons ($n = 5$). All 7 of the surgeons who performed laparoscopic extended cholecystectomy stated that they always performed LN dissection for GBC at stage T1b or higher. The extent of laparoscopic LN dissection was as follows: LNs around the hepatoduodenal ligament ($n = 7$), posterosuperior pancreaticoduodenal LNs ($n = 7$), common hepatic artery LNs ($n = 5$), and celiac axis LNs ($n = 2$). Two surgeons reported performing dissection or sampling of para-aortic LNs. None of the surgeons mentioned routinely resecting the common bile duct unless the GBC involved the cystic duct or the CBD.

Laparoscopic Reoperation for Postoperatively Diagnosed GBC

For GBC diagnosed postoperatively, reoperation was performed with curative intent either when the pathological stage of GBC was T1b or more advanced ($n = 5$) or when the stage of GBC was T2 or more advanced ($n = 4$). In terms of the timing of reoperation, reoperation was performed either as soon as possible ($n = 7$) or more than one month after the initial operation ($n = 2$). Five out of the nine surgeons had performed laparoscopic redo surgery for postoperatively diagnosed GBC. During reoperation, 2 surgeons reported excising the port sites at the reoperation and 2 reported resecting the CBD for complete removal of LNs.

Discussion and Literature Review

The results of this survey suggest that laparoscopic surgery is not contraindicated in patients with GBC, provided it is performed by experts. Most of the responding surgeons agreed that laparoscopic surgery has an acceptable role for treating suspicious or early GBC, and that laparoscopic extended cholecystectomy has a value comparable to that of open surgery in selected patients with GBC. However, there was variation with regard to the selection criteria for laparoscopic surgery for overt GBC. Cystic duct/bile duct involvement, visceral organ invasion, associated acute inflammation, and large-sized tumor were the factors of concern for safe oncologic resection, to various levels among the surgeons; these factors were potential indicators of whether initial open surgery or open conversion was performed.

The literature review shows that experience with laparoscopic surgery for GBC with curative intent is in the initial stage. The indications for laparoscopic surgery for GBC in published reports have been mostly early-stage GBC (T1 and T2), although some experts have extended the indication to GBC with liver invasion. The surgical extent in laparoscopic surgery was the same as that in open surgery. The survey and previous reports of laparoscopic extended cholecystectomy for GBC revealed that the most common procedure was liver wedge resection and LN dissection including the LNs around the hepatoduodenal ligament, the common hepatic artery, and the superior portion of the pancreas. With the accumulation of experience, some experts reported more advanced laparoscopic surgeries such as IVb + V segmentectomy, bile duct resection, and para-aortic LN sampling, although the advantages of these procedures remain controversial,

Table 1. Perioperative outcomes of published case series in which more than 5 patients with GBC underwent laparoscopic extended cholecystectomy

Publication	Number of GBC patients	Indication	Open conversion (reason)	Operative time, min	Blood loss, mL	Complication, n (%)	Hospital stay, days
Cho et al. [7]	18	Primary	1 (portal vein injury)	190*	50*	3 (16.7)	4*
de Aretxabala et al. [8]	7	Completion	2 (LN metastasis, bile duct injury)	NA	NA	0	3
Gumbs et al. [9]	15	Primary (10), Completion (5)	1 (CBD resection)	220	160	0	4
Agarwal et al. [6]	24	Primary (20), Completion (4)	0	270*	200*	3 (12.5)	5*
Itano et al. [10]	16	Primary (16)	0	360	152	1 (5.2)	9
Shirobe et al. [12]	11	Primary (4), Completion (7)	1 (CBD resection)	196	92	1 (9.1)	6
Yoon et al. [13]	30	Primary	1 (portal vein injury)	205*	100*	6 (18.8)	4*
Palanisamy et al. [11]	1	Primary	0	213	196	4 (28.6)	5

* Median.

even in open surgery [6, 11, 14, 15]. Laparoscopic bile duct resection was performed when the tumor involved the bile duct, but not for complete LN dissection. In addition, there have been a few reports of laparoscopic completion surgery for postoperatively diagnosed GBC after laparoscopic cholecystectomy [6, 8, 9, 12, 16]. This operative procedure has been considered technically demanding because of the risk of postoperative inflammatory adhesions or fibrosis around the hepatoduodenal ligament and gallbladder bed. In the first report on this operative procedure by de Aretxabala et al. [8], more than half of the patients undergoing laparoscopy underwent conversion to open surgery owing to dense adhesions rendering a complete exploration or lymphadenectomy. Acceptable immediate postoperative and oncologic outcomes of laparoscopic completion surgery compared with open surgery have recently been reported [6, 9, 12].

Laparoscopic extended surgery for GBC has acceptable clinical outcomes as reported previously (Tables 1, 2) [6–13]. Few patients required conversion to open surgery owing to bile duct or portal vein injury, or required bile duct resection. These patients had minimal intraoperative blood loss and the rate of postoperative complications was less than 20%. In comparative studies between open and laparoscopic surgery for GBC, intraoperative blood loss was significantly less in laparoscopic surgery

than in open surgery, and the postoperative hospital stay was similar or shorter after laparoscopic surgery [6, 10]. However, the operative time for laparoscopic surgery was similar to or longer than that required for open surgery. The number of retrieved LNs was similar between laparoscopic and open surgery. Curative resection was possible in all patients except 2 patients who had a positive margin at the cut end of the bile duct after bile duct resection. Tumor recurrence occurred in a few patients, with systemic recurrence being more frequent incidence of systemic recurrence. The survival outcomes after laparoscopic surgery were similar to or better than those after open surgery [11–13]. Yoon et al. [13] reported favorable long-term outcomes after laparoscopic surgery for GBC, with a 5-year actual survival rate of more than 90%.

This study has some limitations. The results of this survey may not reflect the current clinical practice because only a few experienced surgeons were involved and their experiences were quite limited in the early stage. Literature review of this operative procedure revealed that only about 110 patients have been included in a few case series (Table 1). Therefore, the accumulation of more experience and high-quality evidence is required to evaluate the role of laparoscopic surgery in the treatment of patients with GBC. However, this study enables the evaluation of the current status of laparoscopic surgery for GBC

Table 2. Oncologic outcomes of published case series that included more than 5 patients with GBC who underwent laparoscopic extended cholecystectomy

Publication	7th AJCC stage	Curative resection, %	No of retrieved LNs	Recurrence (local/systemic)	Survival
Cho et al. [7]	I (6), II (8), IIIB (2)	100	8*	0	NA
de Aretxabala et al. [8]	NA	NA	6	1 (systemic)	NA
Gumbs et al. [9]	I (4), II (8), IIIB (3)	100	4	2 (local, systemic)	NA
Agarwal et al. [6]	I (3), II (10), IIIA (6), IIIB (5)	100	10*	1 (local)	NA
Itano et al. [10]	I (3), II (13)	100	13	0	NA
Shirobe et al. [12]	I (3), II (6), IIIB (2)	82	13	2 (local + systemic, local)	5-Year survival rate: 100% for T1b 83.3% for T2
Yoon et al. [13]	I (8), II (17), IIIB (5)	100	7*	4 (systemic)	5-Year survival rate: 94.2%
Palanisamy et al. [11]	II (8), IIIA (1), IIIB (3)	100	8*	2 (systemic)	5-Year survival rate: 68.75%

* Median.

based on the clinical experiences of experienced surgeons at a time when there is no consensus on the indications or surgical techniques for this procedure.

Conclusions

Our survey results reveal that laparoscopic surgery for GBC is currently being performed in highly selected cases, and that the indications and details of the surgical techniques vary among experienced surgeons. Nonethe-

less, the favorable outcomes in the published reports and the positive view of experienced surgeons regarding the value of laparoscopic surgery compared with that of open surgery suggest a high likelihood that laparoscopic surgery will be performed more frequently for GBC in the future.

Disclosure Statement

The authors have no conflicts of interest to declare.

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