

laparoscopic surgery for gallbladder cancer (GBC) is still in the early phase of the adoption curve. A laparoscopic approach for GBC is still controversial among hepatobiliary/pancreatic surgeons. Although this procedure has been contraindicated in patients with GBC for some time, many recent reports have shown that laparoscopic surgery does not adversely affect the perioperative and survival outcomes of patients with GBC [3–9]. One recent report showed that laparoscopic extended cholecystectomy for GBC achieved an outcome comparable with that of open surgery over long-term follow-up [10].

With this background, experts convened at a consensus meeting with the purpose of defining the current state of laparoscopic surgery for GBC and obtaining expert suggestions on the application of this procedure. Here, we report an expert panel statement for laparoscopic surgery for GBC compiled during the meeting.

Methods

An expert consensus meeting was held on September 10, 2016, during the 26th World Congress of the International Association of Surgeons, Gastroenterologists and Oncologists. International experts in GBC laparoscopic surgery were invited to participate in the meeting and to present specific issues regarding laparoscopic surgery for GBC, including oncologic concerns, selection criteria, surgical techniques, and future aspects of this procedure. Presentations were followed by panel discussions and open discussions with the audience. After the meeting, a first draft including summaries of the presentations and discussions was circulated to the panels, discussed, and edited. The present document, including expert consensus statements, was formulated and agreed on by all attending experts in this field.

Results

Concerns Regarding Laparoscopic Surgery for GBC

Laparoscopic surgery has been contraindicated for the treatment of GBC for the following reasons: (1) risk of port site recurrence or peritoneal metastasis due to bile leak associated with GB injury and (2) concerns regarding the oncologic adequacy and safety of laparoscopic radical surgery.

Port site recurrence or peritoneal dissemination was previously estimated to occur at a relatively high rate (10–18%) and to be associated with a poor prognosis in patients with GBC after laparoscopic cholecystectomy [11, 12]. However, these findings were based largely on older studies, in which bile leakage occurred mostly in patients with unsuspected GBC. With improved preoperative recognition of GBC and implementation of a plastic bag to

remove the resected GB, no significant differences in the occurrence of port site/wound or peritoneal metastases or in survival outcomes have been observed between laparoscopic and open surgeries. Nonetheless, bile spillage, if it occurs, remains a risk factor for tumor recurrence and reduced survival. Therefore, when GBC is suspected, careful manipulation is required to avoid bile spillage.

If GBC extends beyond the muscular layer, cancer cells may occur on the hepatic side of the GB, because dissection on the hepatic side is performed in the subserosal layer during standard cholecystectomy. Although an accurate preoperative/intraoperative diagnosis regarding the depth of mural invasion is very important to avoid this problem, the currently available diagnostic tools have limitations. Therefore, cholecystectomy inclusive of the cystic plate or a thin layer of liver parenchyma, even for early-stage GBC, and sometimes en-bloc liver resection of the GB bed, can serve as preventive measures to reduce the risks of microscopic residual cancer and GB perforation. With accumulation of experience, laparoscopic lymph node (LN) dissection, which is widely performed to treat colonic and gastric cancers, has become a safe and adequate procedure in oncologic contexts.

Consensus Statements

- Early concerns regarding port site/peritoneal metastasis after laparoscopic surgery for GBC have subsided with improved preoperative recognition of GBC and preventive measures such as using a plastic bag for removal of GB specimens.
- When GBC is suspected, perforation of the GB should be prevented by cautious and meticulous techniques.
- During cholecystectomy for early-stage GBC, cholecystectomy inclusive of the cystic plate or a thin layer of liver parenchyma is recommended to reduce the risks of GB perforation and residual cancer on the hepatic side.

Application of Laparoscopic Surgery for GBC

Open surgery has been recommended even for suspected early-stage GBC because of the abovementioned concerns regarding laparoscopic surgery. However, with the increasing incidental detection of GBC resulting from widespread application of laparoscopic cholecystectomy, many reports have shown that laparoscopic surgery does not adversely influence the prognosis of patients with early-stage GBC. When definitive oncologic resection is performed for GBC detected incidentally during surgery or that diagnosed postoperatively, survival was not adversely affected by laparoscopic surgery [13, 14].

Based on these results, laparoscopic cholecystectomy may be a feasible option for suspected GBC unless there is preoperative evidence of liver invasion. Cholecystectomy should be performed according to the abovementioned principles. However, the outcome of patients with GBC after laparoscopic surgery for acute cholecystitis is concerning [15–17]. Therefore, laparoscopic surgery may be better indicated for GBC that is not associated with acute cholecystitis.

Consensus Statements

- There is no evidence that laparoscopic surgery is associated with decreased survival compared with open surgery in patients with a suspicion of early-stage GBC if definite resection during/after laparoscopic cholecystectomy is performed.
- Laparoscopic surgery is not yet indicated for GBC associated with acute cholecystitis.

Laparoscopic Extended Cholecystectomy for GBC

Patient Selection

Patients with GBC have various clinical presentations requiring different surgical extents, from a small polypoid mass to a large mass invading the GB bed, hilum of the liver, or other adjacent organs. Among these, the appropriate patient group for GBC laparoscopic surgery should be carefully selected for oncologic safety during the initial period of adoption. In terms of depth of mural invasion, the indications for laparoscopic extended cholecystectomy (defined as cholecystectomy + dissection of regional LNs ± liver resection inclusive of the GB bed) in recent reports have been mostly stage T1 and T2 GBC; reports on this procedure for stage T3 GBC are limited.

Although the T stage (T1b or T2) at which extended cholecystectomy should be required is still controversial, decision-making on this should follow the same criteria for laparoscopic surgery as for open surgery. Accurate preoperative staging in terms of invasion depth is crucial, because this is used to determine the surgical approach and prognosis. Although conventional abdominal ultrasonography (US) and computed tomography are widely used for preoperative staging, these modalities are limited in their ability to predict the depth of invasion compared with endoscopic, high-resolution, or laparoscopic US, which have higher resolution and thus are better able to delineate the multiple layers of the GB wall [18, 19]. A recent intention-to-treat analysis of intended laparoscopic surgery showed favorable clinical and survival outcomes in patients with

GBC who were highly selected by multimodality imaging studies, including endoscopic and laparoscopic US [3, 10].

Technique

The technical concerns regarding laparoscopic radical surgery for GBC are adequate LN dissection, margin-free liver resection, and bile duct resection/reconstruction when needed. Despite limited experiences by experts, laparoscopic extended cholecystectomy has been shown to be safe and feasible in selected GBC patients, with similar results to those of open surgery [3, 5, 7–10, 18, 20–26]. According to published reports, the most commonly performed procedures are wedge liver resection and LN dissection. Laparoscopic bile duct resection may be performed in cases with positive cystic duct margins or involvement of the bile duct by tumor. Laparoscopic IVb/V segmentectomy has been performed in some centers [5, 9, 25].

LN Dissection

Laparoscopic LN dissection is now widely performed for colonic and gastric cancers, and its oncologic efficacy has been well established. Experience with these gastrointestinal cancers has provided a foundation for applying this procedure for GBC. There is no consensus on the optimal extent of LN dissection even for open extended cholecystectomy. The extent of LN dissection for GBC in all published reports includes removal of LNs around the hepatoduodenal ligament. Some centers additionally dissect LNs in the posterior superior pancreaticoduodenal area and along the common hepatic artery because of frequent LN metastasis in this area and improved patient survival if removed completely [27–29]. Recent reports have shown that LN dissection can be performed to the same extent in laparoscopic surgery as in the open procedure in selected GBC patients with few intraoperative and postoperative complications [3, 5, 7–10]. The number of retrieved LNs is comparable between laparoscopic and open surgeries.

The role of more extensive dissection of aorto-caval, celiac, superior mesenteric artery nodes seems limited, because no survival benefit is evident. However, aorto-caval LN sampling at the initiation of surgery is advocated in some centers because of frequent involvement of these LNs. This concept applies to laparoscopic surgery as well.

Liver Resection

The aims of liver resection in patients with GBC are to achieve a negative resection margin on the hepatic side and to minimize the likelihood of recurrence by removal

of microscopic metastases in the liver. There is no consensus on the optimal extent of liver resection between wedge resection and segment IVb/V resection even in open surgery. Theoretical advantages of segment IVb/V resection over wedge resection have not been demonstrated clinically. No significant difference in survival rate between the 2 procedures has been reported. Recent reports on laparoscopic extended cholecystectomy for GBC have demonstrated the technical feasibility and safety of laparoscopic wedge resection, and the feasibility of laparoscopic IVb/V resection for GBC has also been reported [5, 9, 25].

Bile Duct Resection

Routine resection of the bile duct for LN dissection is not recommended, because it increases morbidity with no evidence of improving survival [30–33]. Indications for this procedure include a positive cystic duct margin after cholecystectomy to obtain a negative margin, direct tumor invasion of the bile duct, and inflammation or scarring around the hepatoduodenal ligament compromising complete LN dissection. The feasibility of laparoscopic bile duct excision for GBC has been reported in the literature [23]. Considering the increasing reports on laparoscopic surgery for choledochal cysts and laparoscopic pancreatoduodenectomy, the necessity of bile duct resection is not a contraindication for GBC laparoscopic surgery.

Survival Outcomes

The reported survival outcomes of patients with GBC after laparoscopic extended cholecystectomy are encouraging. The recurrence and survival rates were found to be similar between laparoscopic and open surgery groups in comparative studies [5, 7]. Furthermore, the favorable long-term outcome of laparoscopic extended cholecystectomy was shown in a recent study, in which the survival rate of patients at 5 years postoperatively was over 90% [10]. However, considering the small numbers of included patients and the retrospective nature of those previous studies, further large-scale comparative studies are needed to confirm the oncologic safety of laparoscopic extended cholecystectomy for GBC.

Consensus Statement

- Experience with laparoscopic extended cholecystectomy for GBC has been limited to a few expert centers.
- The reports on laparoscopic extended cholecystectomy have shown acceptable postoperative outcomes compared with those of open surgery.

- For safe selection of indicated patients, accurate preoperative staging in terms of depth of invasion is important. Endoscopic or laparoscopic US may be more useful as a complementary procedure compared with conventional US and computed tomography for this purpose.
- The most common type of liver resection reported is wedge resection of the GB bed. Laparoscopic IVb/V segmentectomy is performed in some centers. As there are limited reports on the outcomes after laparoscopic surgery for GBC with liver invasion, more data are needed.
- Laparoscopic LN dissection for early GBC was shown to be a safe and adequate procedure from an oncologic point of view.
- Bile duct resection is not a contraindication for laparoscopic surgery for GBC.
- Although the evidence is limited, the survival outcomes of highly selected patients are similar between laparoscopic and open surgeries.

Laparoscopic Reoperation for Postoperatively Diagnosed GBC

The reported incidence of postoperatively diagnosed GBC after cholecystectomy is 0.19–3.3% [34]. Widespread adoption of laparoscopic cholecystectomy has resulted in an apparent increase in this rate. Radical reoperation after cholecystectomy is decided based on the postoperative pathology and is usually performed via open surgery. This procedure is considered technically challenging mainly because of inflammatory adhesions or fibrosis around the hepatoduodenal ligament and GB bed. There are a few recent reports on the technical feasibility of laparoscopic revisional surgery [5, 8, 21, 22, 26, 35]. Unlike initial laparoscopic surgery for GBC, laparoscopic reoperation is not associated with the risk of tumor seeding related to bile spillage, because cholecystectomy has already been performed. Despite very limited experience by experts, a laparoscopic approach for postoperatively diagnosed GBC seems to be feasible, with satisfactory clinical outcomes in terms of perioperative and mid-term oncologic results.

In patients with postoperatively diagnosed GBC, port site metastasis has been a concern during the early stage of laparoscopy. Although its incidence is rare, port site metastasis is associated with poor survival once it develops. However, routine port site resection is not recommended during definitive surgical treatment, because it has not been associated with improved survival or reduced recurrence [36].

Consensus Statement

- Laparoscopic reoperation for postoperatively diagnosed GBC is technically challenging, but its feasibility has been demonstrated by some expert teams.
- During this procedure, routine excision of the port site is not recommended, because there is no evidence of improved survival.

Conclusion

With preoperative recognition of GBC and careful manipulation to avoid bile spillage, laparoscopic surgery does not worsen the prognosis of patients with early-

stage GB if definitive resection during/after laparoscopic cholecystectomy is conducted. Although experience with laparoscopic extended cholecystectomy for GBC has been limited to a few experts, the postoperative and survival outcomes of highly selected patients were favorable. However, laparoscopic surgery for GBC is still in the early phase of the adoption curve, and more evidence is required before this procedure can be widely accepted.

Disclosure Statement

The authors have no conflicts of interest to declare.

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