Preliminary Experience of Laparoscopic Cholecystectomy with Gallbladder Bed Dissection for Suspected Gallbladder Cancer

Hisashi Kasugai*, Kenta Nakahara, Yusuke Takehara, Shumpei Mukai and Shin-ei Kudo

Abstract: Selecting the appropriate operation for gallbladder cancer depends on the depth of cancer invasion, which remains difficult to determine preoperatively, especially with respect to the subserosal layer (pT2). We devised a laparoscopic cholecystectomy with gallbladder bed dissection (LC with GBD) as a new total biopsy method for suspected gallbladder cancer. We retrospectively reviewed the medical records of 19 patients who underwent LC with GBD to assess the usefulness of this procedure and the pathological findings. No severe morbidity or recurrence was encountered. LC with GBD could be performed easily and safely, and the patients’ postoperative course was almost equal to that of patients treated by conventional LC. Histologically, gallbladder cancer was diagnosed in five cases (pT1a, 3; pT2, 2). We believe that LC with GBD could play an important role in the potential treatment strategy for pT2 gallbladder cancer.

Key words: suspected gallbladder cancer, laparoscopic surgery, gallbladder bed dissection, total biopsy, pT2 gallbladder cancer

Introduction

A definitive diagnosis of gallbladder cancer remains difficult to attain preoperatively. Thus, cholecystectomy is sometimes needed to attain a total biopsy for making a definitive diagnosis1-3). Nevertheless, although an extended operation should be performed for patients with gallbladder cancer at pT2 or a more advanced stage, the exact depth of the cancer invasion, especially for pT2, is difficult to determine using imaging modalities alone. In fact, in the past 8 years at our institute we correctly estimated the depth of invasion preoperatively in only 9 (45%) of 20 resected pT2 gallbladder cancer cases.

We consider that cholecystectomy as a total biopsy thus remains necessary to obtain two important pieces of information: the qualitative diagnosis and the vertical invasion of the malignant lesion. Although the diagnostic procedure should be as noninvasive as possible, a few advanced cancers may be included among the lesions subjected to total biopsy. It is thus necessary to carefully consider not only low invasiveness, but also the risk of exposing cancer cells during surgery. To be consistent in both intentions, lower invasiveness and oncological...
safety, we performed laparoscopic cholecystectomy with gallbladder bed dissection (LC with GBD) for 19 clinically suspected early gallbladder cancer patients. In this paper, the short- and mid-term results of LC with GBD are reported, and the feasibility and significance of LC with GBD are discussed.

Patients and Methods

The medical records of 19 patients who underwent LC with GBD for suspected early gallbladder cancer from November 2008 to December 2011 were retrospectively reviewed. The mean age was 56.4 years old (34~88 years), and there were 13 men and 6 women. Imaging modalities were used preoperatively at the following frequencies: abdominal ultrasonography (AUS) 100% (19/19), multidetector computed tomography (MD-CT) 100% (19/19), endoscopic ultrasonography (EUS) 84.2% (16/19), magnetic resonance imaging (MRI) 52.6% (10/19), endoscopic retrograde cholangio-pancreatography (ERCP) 5% (1/19), and positron emission tomography-CT (PET-CT) 26.3% (5/19). The lesions eligible for LC with GBD were: 1. elevated lesions over 10 mm in diameter; 2. elevated lesions with dense enhancement, despite their size; 3. diffuse wall-thickness lesions mimicking cancer [for example, adenomyomatosis (ADM) or xanthogranulomatous cholecystitis (XGC)]; and 4. gallbladder lesions associated with pancreatobiliary maljunction. Lesions with suspected invasion of the liver or surrounding tissue were excluded. The preoperative diagnoses of the 19 patients who underwent LC with GBD were: gallbladder polyp in 11, gallbladder cancer in 6, and 1 case each of congenital biliary dilatation and XGC. The short-term results of the operation, the final pathological diagnoses, and the mid-term outcomes of these 19 patients were analyzed retrospectively.

Operative procedure

In all cases, we performed 4-port LC with GBD as well as conventional LC. Each GB lesion was first evaluated by intraoperative US. Then, after confirming the absence of liver invasion by the lesion, the serosa of the triangle of Calot including the sentinel lymph node (LN; No.12c) was cut. The cystic duct and cystic artery were identified in the space of the triangle of Calot and exposed in the usual manner. Intraoperative cholangiography was not performed, to prevent bile spillage. Both the cystic duct and the cystic artery were divided after clipping, and then the gallbladder bed, 1 cm in width, was dissected using a soft coagulation device (EndoSH2.0™, TissueLink Medical Inc., Dover, NH, USA) without the Pringle maneuver (Fig. 1a). It was rarely necessary to clip the vessels during dissection of the gallbladder bed, although if a branch of the middle hepatic vein was encountered (Fig. 1b) that was larger than 3 mm in diameter, it was usually clipped. The resected specimen was taken out in a vinyl bag. Pathological diagnosis was carried out on a paraffin section, cut out strips 5 mm in width, after formaldehyde fixation. Representative histological findings of a case of pT2 gallbladder cancer that underwent LC with GBD are shown in Fig. 2. No cancerous lesions were exposed at the excisional margin in this study.

The constituted Ethics Committee of our institution approved the operative procedure for this
research and informed consent was obtained from all patients.

**Results**

Table 1 summarizes the results of the 19 cases in which LC with GBD was performed. The mean operation length was 138.5 (79~203) min, and mean blood loss was 7.0 (0~50) ml. The mean postoperative hospital stay was 4 (3~7) days. No severe postoperative complications occurred. There were two cases of emphysema that were discharged on the 4th and 7th postoperative day [Clavien-Dindo classification\(^4\) Grade I ]. Table 2 details the patients’
clinicopathological characteristics. Among the 19 cases, there were 10 (52.6%) neoplastic lesions and 5 (26.3%) cancer lesions, including 2 (10.5%) advanced cancer cases (pT2). The final pathological diagnoses of the lesions diagnosed preoperatively as gallbladder cancer were adenoma, pT1a cancer, and pT2 cancer (two cases each). One of the pT2 cases had lymph node metastasis (pN1), although since both patients declined an extended operation because of their age (88 and 78 years), no additional resection was performed. The lesions that received a preoperative histological diagnosis of gallbladder polyp were definitively diagnosed as gallbladder cancer (pT1a) in one, adenoma in three, hyperplastic polyp in two, cholesterol polyp in four, and ADM in one. Classification of the polypoid lesions morphologically revealed 11 cases of type Ip and 6 cases of type Is or Isp. Of the 11 cases of type Ip, there were 2 gallbladder cancer (pT1a) cases, 3 adenoma cases, 2 hyperplastic polyp cases, 4 cholesterol polyp cases, and no invasive cancer cases (pT2). On the other hand, of the 6 cases of type Is or Isp, there were 3 gallbladder cancer cases, including 2 invasive cases (pT2), one adenoma, one adenoma + ADM, and 1 ADM case. All gallbladder cancer cases, including the patients with pT2, received no further treatment. At a median follow-up of 29 (10～45) months, all cases were alive without recurrence.

**Discussion**

It continues to be difficult to make an exact preoperative diagnosis of gallbladder cancer, especially for small lesions or diffuse wall-thickness lesions, despite the recent progress in diagnostic modalities\(^1\)\(^-\)\(^3\). As a less-invasive means of obtaining a definitive diagnosis of gallbladder cancer, cytological analysis of bile through transpapillary gallbladder drainage\(^5\) or EUS-FNA\(^6\),\(^7\) have returned good, accurate diagnoses. However, both procedures are technically difficult, and the reported results are mainly for rough and advanced lesions, with no reports of efficacy for small lesions. Since both the choice of appropriate operation and the prognosis of gallbladder cancer depend on the depth of cancer invasion, it is also very important to clarify that depth, and in particular to determine whether the subserosal layer (pT2) has been reached\(^9\). Fujita *et al*\(^9\) and Sadamoto *et al*\(^10\) reported the efficacy of EUS to determine the depth of invasion of gallbladder cancer, and indicated that EUS could be the best modality for
observing detail in the gallbladder. However, Fujita et al.\textsuperscript{11} later reported that it was almost impossible to detect shallow subserosal layer invasion even when using EUS, because the inner hypoechoic layer of EUS findings reflected not only the mucosa and muscle layer, but also a part of the shallow subserosal layer. Even today, since it is difficult to determine the exact depth of gallbladder cancer invasion with various imaging examinations, various lesions (benign lesions, pT1a and pT1b gallbladder cancers, and also some pT2 gallbladder cancers) can be included among the lesions suspected preoperatively as being early gallbladder cancer. The gold standard for definitive diagnosis, including for depth of cancer invasion, may still be the surgical

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (y)</th>
<th>Sex</th>
<th>Preoperative diagnosis</th>
<th>Macroscopic type</th>
<th>Size (mm)</th>
<th>Location</th>
<th>Pathological diagnosis</th>
<th>Complications</th>
<th>Outcome (months)</th>
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<td>Ip</td>
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<td>Gn</td>
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<td>(−)</td>
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<td>(−)</td>
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<td>Ip</td>
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<td>(−)</td>
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<td>Is</td>
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<td>Gfbn</td>
<td>Cancer (pT2)</td>
<td>(−)</td>
<td>No recurrence, alive (37)</td>
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<td>(−)</td>
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<td>(−)</td>
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<td>Isp</td>
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<td>Gn</td>
<td>Hyperplastic polyp</td>
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<td>Isp</td>
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<td>Hyperplastic polyp</td>
<td>Grade I</td>
<td>Alive (12)</td>
</tr>
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<td>male</td>
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<td>Isp</td>
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<td>Gb</td>
<td>Cancer (pT1a)</td>
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<td>Gf</td>
<td>Adenomyomatosis</td>
<td>(−)</td>
<td>Alive (9)</td>
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CBD, congenital biliary dilatation; XGC, xanthogranulomatous cholecystitis

Table 2. Clinicopathological features of the 19 patients who underwent LC with GBD
approach, because it is best to choose the appropriate operation based on an exact diagnosis. Moreover, we think that it is most important to recognize invasion of the subserosal layer (pT2) because of the substantial difference remaining for both the recommended operation and the expected prognosis.

Whether the laparoscopic approach is acceptable for suspected gallbladder cancer remains controversial. Some papers reported that laparoscopic surgery should not be performed for suspected gallbladder cancer because of an increased incidence of port-site recurrence or peritoneal dissemination. On the other hand, Ouchi et al. analyzed the results of a large number of gallbladder cancer cases treated by LC in Japan, and found no association between LC and a worse prognosis for gallbladder cancer. Some other recent reports also reached the same conclusions. Furthermore, papers in which laparoscopic surgery was intentionally used in cases of gallbladder cancer have gradually increased. Despite the pros and cons of LC, surgeons on both sides of the debate have reported that, in cases with perforation of the gallbladder during operation, port-site recurrence was significantly increased and prognosis was poor. Furthermore, wound recurrence following open surgery for gallbladder cancer has also been reported, with Lundberg and Kristoffersson reporting a 6.5% incidence of wound recurrence following open surgery for gallbladder cancer and concluding that wound recurrence was not rare following open surgery. Ricardo et al. also reported a high rate of wound recurrence following open surgery for gallbladder cancer at 31%, while that for portal-site recurrence after laparoscopic surgery was 29%; thus, there was no significant difference between open surgery and laparoscopic surgery. Based on these reports, it appears that the implantation of cancer cells at the port site or the wound site is more strongly related to the spillage of cancer cells due to perforation of the gallbladder or exposure of the cancer during the operation than to the choosing a laparoscopic approach. Therefore, for cases of suspected gallbladder cancer, all care should be taken during surgery to avoid cancer cell spillage due to perforation of the gallbladder or exposure of the cancer, and we consider that laparoscopic surgery could be acceptable for cases of suspected gallbladder cancer.

In the present study, 2 cases of pT2 (10.5%) were included among the cases of suspected early gallbladder cancer. Since it seems impossible to completely exclude even a small number of pT2 cases among cases of suspected early gallbladder cancer in which total biopsy is indicated, LC with GBD was considered useful as a safe total biopsy procedure to prevent cancer exposure. However, although the present two cases of pT2 chose to decline further surgery due to their advanced age, additional extended excision (gallbladder bed dissection, LN dissection, etc) should be performed according to the stage if pT2 lesions or more advanced invasion are found.

With respect to the indications for LC with GBD, it may not be appropriate for benign or pT1 lesions. In the present 19 cases, 47.4% (9/19) of the lesions on pathological examination were non-neoplastic, and, moreover, about 90% (17/19) of the lesions were benign or early cancer. Fujita et al. reported the EUS classification of gallbladder cancer, noting that all lesions that showed Ip (their EUS classification, Type A) were pT1a early cancers. In the
present study, all nine lesions that showed Ip were pT1a cancers or benign lesions; thus, lesions that were morphologically recognized as Ip (Type A) by preoperative imaging examinations or intraoperative US could be acceptably treated with simple LC alone, as long as care is taken during the procedure to avoid perforation of the gallbladder. Given the above discussion, broad-based protruding lesions or wall-thickness lesions (Fujita’s classification Type B) are the most suitable for LC with GBD.

LC with GBD could be performed easily and safely, and the postoperative course was almost equal to that for conventional LC. We believe that LC with GBD is a feasible method of total biopsy for suspected early gallbladder cancer and may form an important part of the treatment strategy for pT2 gallbladder cancer.

Conflict of interest

The authors declare no conflicts of interest.

References


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