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Radical resection of gallbladder cancer: could it be robotic?

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Abstract
Background The only potentially curative option for patients with gallbladder cancer is radical resection. This is the first report that describes the successful application of a minimally invasive, robot-assisted radical resection, including lymphadenectomy, in five gallbladder cancer patients.
Methods Medical records of patients who underwent radical resection of gallbladder cancer via the da Vinci robotic surgical system in the Hepato-Bilio-Pancreatic Surgical Department of the Shanghai Ruijin Hospital, China, between March 2010 and July 2011 were reviewed and analyzed.
Results Robot-assisted radical resection was successful in all five patients. The mean number of excised lymph nodes was 9 (range = 3–11), mean operative time was 200 min (range = 120–300 min), mean intraoperative blood loss was 210 ml (range = 50–400 ml), and mean length of hospital stay was 7.4 days (range = 7–8 days). All patients were discharged with no reported complications. Mean postoperative follow-up was 11 months (range = 1–17 months). One patient died due to tumor recurrence 10 months postsurgically, but there was no recurrence in the remaining four patients during the follow-up period.
Conclusions Robot-assisted radical resection for gallbladder cancer is both feasible and safe. Compared to laparoscopic surgery, the robotic surgery system is better suited for subtle dissection in a narrow, deep space. This is advantageous for both the removal of lymph nodes near the pancreas and hepatoduodenal ligament and the skeletonization of the hepatoduodenal ligament, the hepatic artery, and the celiac axis. The long-term outcome and direct comparisons to laparotomy in a larger patient cohort are needed to provide more clinical data supporting the superiority of this approach.

Keywords Radical resection · Gallbladder cancer · Robotic surgery · Robotic biliary surgery

Gallbladder cancer, although relatively uncommon, is the most common malignant tumor of the biliary system. This cancer can easily and directly invade the liver and can metastasize to the hilar lymph nodes. Radical resection is a viable treatment option for patients with gallbladder cancer to improve survival. There are a number of steps involved in radical resection procedures, including skeletonization of the hepatoduodenal ligament and hepatectomy, which are typically performed via an open procedure rather than laparoscopically, primarily because of the technical demands of the procedure and concerns about the risk of gallbladder rupture and the potential for intraperitoneal spread of malignant cells [1, 2]. As a result, radical resection of gallbladder cancer via laparoscopy has been reported on only rarely [3, 4].

The advent of the da Vinci robot system has essentially resolved the problems associated with traditional laparoscopes in terms of improved access to the operative field and flexibility of the instruments, prompting more surgeons to consider the feasibility of using robotic surgery in the treatment of gallbladder cancer. The purpose of this study was to describe the authors' experience with the da Vinci

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robotic surgical system for the radical resection of gallbladder cancer in five patients.

Patients and methods

Clinical data

Medical records of five gallbladder cancer patients treated via robot-assisted radical resection at the Hepato-Bilio-Pancreatic Surgical Department at the Ruijin Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai Institute of Digestive Surgery, Shanghai, China, between March 2010 and July 2011 were reviewed. Patient demographics, clinical data, surgery details (e.g., length of surgery and intraoperative blood loss), postsurgical recovery and complications, and follow-up information were extracted.

Case selection criteria

The following were the patient selection criteria: (1) a generally good condition without any serious cardiopulmonary complications and able to tolerate general anesthesia; (2) no imaging evidence of distant metastasis and local invasion and a preoperative suspicion of gallbladder cancer of stage $\leq$T3 (the new AJCC 7th staging edition); (3) no history of upper abdominal surgery; and (4) no special restrictions on age. It has been reported that the age factor alone is not a contraindication for robotic hepato-biliopancreatic surgery [5].

Surgical technique

Following routine preoperative patient (bowel) preparation and induction of anesthesia, patients were placed in left lateral recumbency with the head of the table tilted 30°. The position of the instrument ports were as shown in Fig. 1. The veress needle was through the intersection between the left midclavicular line and the inferior margin of the costal arch to establish carbon dioxide pneumoperitoneum at 15 mmHg. A trocar was inserted through the lens point to place the robot camera for exploring whether there were metastases and/or contraindications. The remaining trocars were placed according to the five-port method. All five operating arms of the da Vinci Surgical System (Intuitive Surgical Inc., Sunnyvale, CA, USA) were employed during the radical resection of gallbladder cancer. Operating arms 1 and 2 were the main operating arms while operating arm 3 was used to manipulate the liver. An auxiliary port was created between operating arm 1 and the lens port.

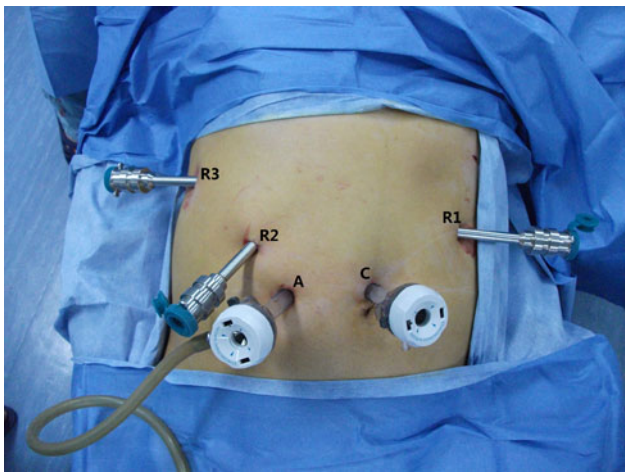

Fig. 1 Photograph showing the location of the trocars: *C* camera port (12 mm), *R1* operation port 1 (12 mm), *R2* operation port 2 (8 mm), *R3* operation port 3 (8 mm), *A* assistant port (12 mm)

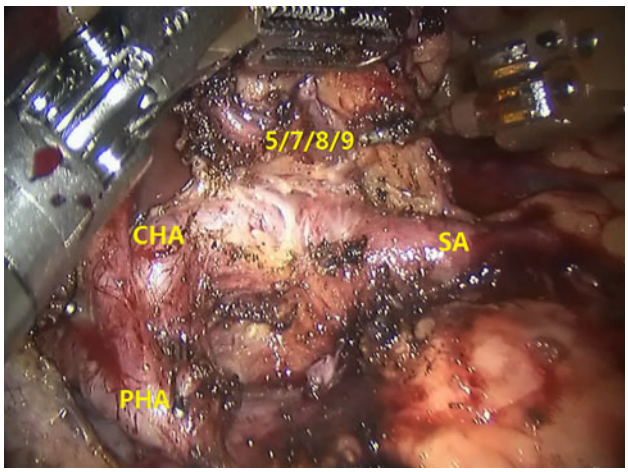

Fig. 2 The group of 5, 7, 8, 9 lymph nodes have been successfully dissected using the robotic surgical approach. *No. 5* suprapyloric lymph node, *No. 7* left gastric lymph nodes, *No. 8* hepatic artery lymph nodes, *No. 9* celiac artery lymph nodes, *PHA* proper hepatic artery, *CHA* common hepatic artery, *SA* splenic artery

The gallbladder was completely excised as well as all hepatic tissue within 2 cm of the gallbladder bed using an electric hook and ultrasonic scalpel. Electric coagulation was performed on the remnant surface wound of the liver.

The hepatoduodenal ligament and the hepatic artery were isolated and branch vessels were ligated. All lymph nodes of the group 5, 7, 8, 9, and 12 (12p included) were excised completely (Figs. 2, 3). Skeletonization of the portal vein, proper hepatic artery, hepatic artery, right and left hepatic arteries, and splenic artery was performed, and the gastroduodenal artery and left gastric artery were dissected. Lymph nodes around the hepatic artery were completely excised (Fig. 4).

A silicone drainage tube was placed in the hepatorenal recess in all five patients and drawn out through the

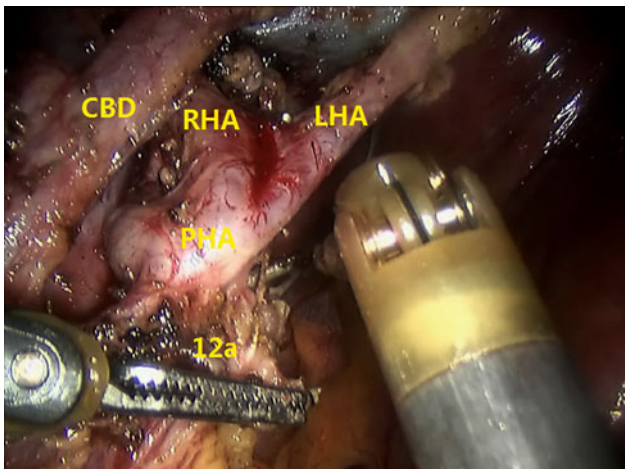

Fig. 3 The group of No. 12a lymph nodes has successfully been dissected using the robotic surgical approach. *No. 12a* hepatoduodenal ligament lymph nodes along the hepatic artery, *CBD* common bile duct, *PHA* proper hepatic artery, *LHA* left hepatic artery, *RHA* right hepatic artery

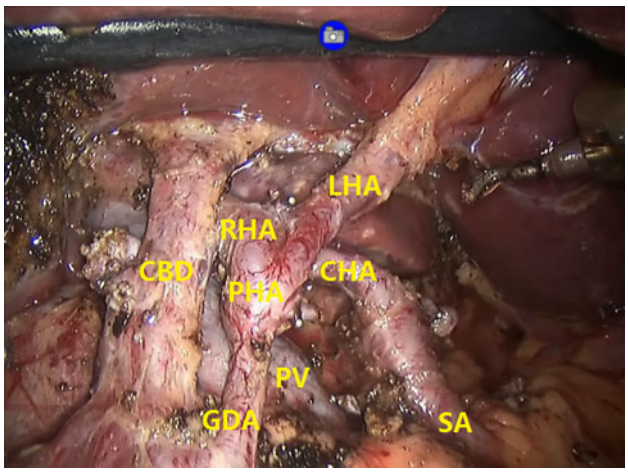

Fig. 4 Lymph nodes were successfully dissected using the robotic surgical approach. *CBD* common bile duct, *PHA* proper hepatic artery, *GDA* gastroduodenal artery, *PV* portal vein, *LHA* left hepatic artery, *RHA* right hepatic artery, *CHA* common hepatic artery, *SA* splenic artery

operating port. The robot-assisted surgery system was removed and the pneumoperitoneum was released. The auxiliary trocar port was extended and the specimen was placed inside a specimen bag and subsequently removed.

Results

In total, 44 patients underwent various types of robot-assisted hepatobiliary and pancreatic surgeries at our institution between March 2010 and July 2011. Of these, five gallbladder cancer patients (two males) underwent robot-assisted radical resection. As indicated in Table 1, mean patient age was 57.4 years (range = 46–63 years).

Patients 1 and 3 both reported upper abdominal pain for 3–6 months prior to diagnosis. In patients 2 and 5, gallbladder cancer was diagnosed following laparoscopic cholecystectomy via postoperative biopsy and the patients were referred for re-resection (Table 1). There was no specific clinical manifestation in patient 4; the gallbladder mass was found during a routine medical examination. Except for the patients who were diagnosed following laparoscopic cholecystectomy, preoperative imaging examinations of the remaining three patients revealed space-occupying lesions in the gallbladder (Fig. 5). Gallbladder wall thickening was identified in the bottom of the gallbladder in a preoperative PET/CT scan in case 3; this was associated with increased metabolism. There were no abnormal findings in preoperative tumor marker tests in any of the five patients.

Robot-assisted radical resection was successfully accomplished in all five patients. No conversion to laparotomy was required in any case. The mean surgical time was 200 min (range = 120–300 min) and the mean intraoperative blood loss was 210 ml (range = 50–400 ml). The mean length of postoperative hospital stay was 7.4 days (range = 7–8 days). All patients recovered postsurgically and were discharged from the hospital with no complications.

Postoperative pathological examinations showed that four patients had gallbladder adenocarcinoma and one had adenosquamous carcinoma. Three patients had tumor invasion to the liver. The mean number of lymph nodes excised from the five patients was 9 (range = 3–11).

The mean postoperative follow-up period was 11 months (range = 1–17 months). Patient 1 died 10 months after surgery due to tumor recurrence; however, no recurrence occurred in the remaining four patients during the follow-up period.

Discussion

Gallbladder cancer is the most common malignant tumor in the biliary system and is the fifth most common malignant tumor of the digestive system. Most patients in the early stage of gallbladder cancer have no specific clinical manifestation, and approximately 20 % of patients resected are diagnosed accidentally during routine cholecystectomy. Radical resection is the only potentially curative option for gallbladder cancer [6].

Clinical pathological staging determines the strategy for surgical treatment of gallbladder cancer. In 1976, Nevin et al. [7] proposed the Nevin staging system based on the depth of tumor invasion into the gallbladder wall and the

Table 1 Demographic and clinical data of the five patients described in this report

Case	Sex	Age (years)	Clinical manifestations	Surgical time (min)	Intraoperative blood loss (ml)	Tumor size (cm)	No. of positive lymph nodes	Liver invasion	Postoperative pathology	Nevin/AJCC classification	Postoperative length of stay (days)
1	F	63	Right upper abdominal pain for 3 months	300	100	3.0	3/3	Yes	Adenocarcinoma	V/III	8
2	F	55	Lesion was found after LC surgery	120	50	–	0/11	No	Adenocarcinoma	III/III	7
3	M	63	Upper abdominal pain for 6 months	270	300	2.0	0/11	Yes	Adenosquamous carcinoma	V/III	7
4	M	60	Lesion was found during routine medical examination	150	400	2.0	0/7	No	Adenocarcinoma	VI/II	8
5	F	46	Lesion was found after LC surgery	160	200	–	0/10	Yes	Adenocarcinoma	VI/II	7

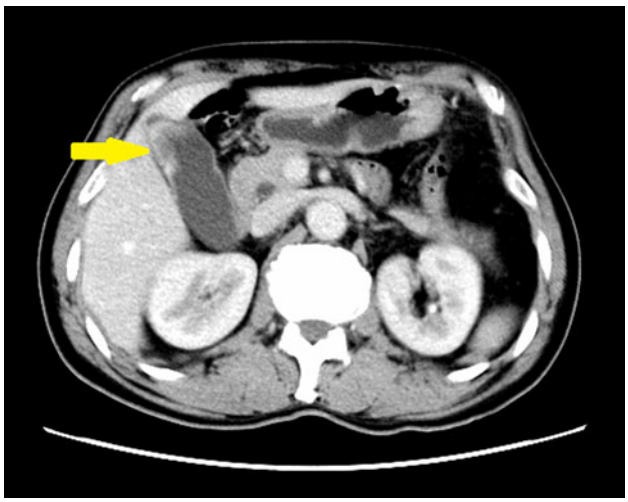

Fig. 5 CT scan in one case revealed thickening of the bottom of the gallbladder with obvious enhancement

range of tumor metastasis. The Nevin staging system focuses only on the degree of invasion by the tumor and does not take lymph node metastasis into account. In fact, the probability of lymph node metastasis increases significantly after gallbladder cancer invades the muscle layer (T2) because there is lymphatic drainage of the gallbladder between the muscle layer and the serous membrane. Therefore, lymph node metastasis is likely to occur after the tumor invades the muscle layer of the gallbladder [8]. In 1995, the UICC promoted the TNM staging of gallbladder cancer. In 2009, the American Joint Committee on Cancer (AJCC) and the National Comprehensive Cancer Network (NCCN) promoted the 7th edition of the TNM Classification of Malignant Tumors, which was considered a more reasonable classification system after comparative studies were performed [9]. The 7th edition of the TNM Classification of Malignant Tumors may better reflect the development of gallbladder tumors, which is essential for assisting surgeons in selecting a suitable treatment option and predict the patients' prognosis.

It is widely accepted that a simple cholecystectomy is suitable for early-stage gallbladder cancers (T0, T1), whereas T2 gallbladder cancer should be treated via radical resection. In addition to removing the gallbladder, wedge resection of hepatic tissues within 2 cm from the gallbladder bed should be performed as well as skeletonization resection of the hepatoduodenal ligament. For patients with >T3 gallbladder cancer, if radical curative resection R0 can be achieved, the patient's general condition is good, and the patient is a suitable surgical candidate, then extended radical resection of the gallbladder cancer can be considered. Additional extrahepatic bile duct resection and reconstruction and extended right liver resection can be performed if needed. In all surgeries, lymphadenectomy is advocated for lymph nodes located near the

hepatoduodenal ligament, hepatic port, and pancreatic head. If radical curative resection R0 cannot be achieved or the patient cannot tolerate the extended radical resection, palliative surgery is an option to relieve symptoms and improve the patient's quality of life [10].

Lymph node metastasis is the most common metastatic route of gallbladder cancer. The thoroughness of lymphadenectomy directly affects the prognosis of gallbladder cancer [11, 12]. Nonetheless, questions have been raised about the feasibility of achieving a successful lymphadenectomy via laparoscopic surgery. This concern has been a bottleneck to the advancement and development of laparoscopic radical resection of gallbladder cancer. At present, only a limited number of studies have been published that describe laparoscopic radical resection of gallbladder cancer. Moreover, most of those reports are limited to tumors $\leq$T2, and only a standard radical resection of gallbladder cancer was applied (Table 2) [3, 4, 13]. Only one case report about T3 gallbladder cancer treated with extended laparoscopic radical resection and a laparoscopic bilioenteric Roux-en-Y anastomosis has been published [3]. Because the hepatic portal structure is complicated and contains important vessels such as the hepatic artery and portal vein (among others), tumor resection or lymphadenectomy can potentially result in uncontrollable bleeding and/or injury to important peripheral structures such as the bile duct. Limitations in the design and flexibility of laparoscopic instruments can restrict the intricate and precise surgical procedure, and the laparoscopic procedure may result in intra-abdominal tumor spread.

Unlike laparoscopes, the da Vinci robotic surgical system can obtain clear 3D images. It has multiple functions such as seven degrees of freedom with the EndoWrist™ (Intuitive Surgical), which mimics the true wrist, eliminates hand vibration, has the ability to preset the motion ratio, and indexation of motion [13]. This robotic system permits surgeons to perform complicated surgical procedures such as digestive tract reconstruction, skeletonization of the hepatic artery and portal vein, and resection of lymph nodes deep in the abdominal cavity (e.g., retroperitoneal lymph nodes and para-aortic lymph nodes [14]), making this system a viable option for radical resection of gallbladder cancer. Key techniques such as lymphadenectomy for lymph nodes in the hepatoduodenal ligament, lymph nodes superior and posterior to the pancreaticoduodenum, lymph nodes around the superior mesenteric vessels, lymph nodes around the celiac axis, and bilioenteric anastomosis are therefore possible [15].

Table 2 Comparison between open and robotic radical resection of gallbladder cancer

	Open ($n = 18$)	Robot ($n = 5$)
Age (years)	60.85 ± 10.21	57.4 ± 7.16
Gender (male/female)	8/10	2/3
Symptoms (no/yes)	3/15	3/2
Surgical time (min)	206 ± 41.63	200 ± 79.69
Intraoperative blood loss (ml)	210 ± 143.18	170 ± 136.28
Tumor size (cm)	5.15 ± 3.4	2.33 ± 0.58
Number of positive lymph nodes	1.3 ± 1	1.28 ± 0.92
Liver invasion (no/yes)	12/6	2/3
AJCC classification (I/II/III/IV)	1/3/10/4	0/2/3/0
Complication rate (%)	72.22	0
Length of stay (days)	13.23 ± 7.8	7.4 ± 0.55

To the best of the authors' knowledge, this is the first report on robot-assisted resection of gallbladder cancer. Robot-assisted surgery has been performed in the Hepato-Bilio-Pancreatic Surgical Department of our institution between March 2010 and July 2011. In total, 44 patients have undergone various types of robot-assisted hepatobiliary and pancreatic surgeries. The authors have successfully performed 20 robot-assisted hepatobiliary and pancreatic surgeries prior to attempting the first and more complicated robot-assisted radical resection of gallbladder cancer. Despite the fact that only five patients were treated, the successful outcomes achieved in these patients suggest that robot-assisted radical resection of gallbladder cancer is both safe and feasible. Complete radical treatment can be achieved. For comparative analysis, we also reviewed the medical records of patients who underwent open surgery for gallbladder cancer during the same period. We compared the perioperative clinicopathological characteristics, including operative data, incidence of postoperative morbidity, and hospital stay, although the number of cases was limited and selection bias was involved in the comparative analysis. Our initial experience with robot-assisted radical resection of gallbladder cancer has shown very optimistic results: a small amount of intraoperative bleeding, a relatively shorter hospital stay, and no complications suggest the potential merits of minimally invasive robot-assisted surgery (Table 2). In addition, lymph nodes were successfully removed using this approach. The mean number of lymph nodes excised from the five patients was 9 (range = 3–11). These lymph nodes were located in and around the hepatoduodenal ligament, the hilar region, the celiac axis, and the aorta abdominalis. Thus, robot-assisted radical resection completely meets the requirements for standard and extended radical resection of gallbladder cancer.

In one of our five cases, postoperative biopsy results showed tumor invasion of the entire gallbladder wall as well as the liver, and N1 lymph node metastasis was also diagnosed. The patient survived 10 months after surgery, which it is consistent with postoperative survival previously reported [10].

In conclusion, five patients with gallbladder cancer were successfully treated by radical resection using a robotic surgical system. The outcome was reliable and the advantages of a minimally invasive procedure are well known. The robotic surgery system is well suited for subtle dissections in a deep and narrow space as evidenced by the fact that lymphadenectomy posterior to the head of the pancreas and the hepatoduodenal ligament can be performed successfully. Even more complicated procedures such as hepatolobectomy can be easily achieved using robot-assisted surgery systems, supporting the authors' contention that minimally invasive extended radical resection of gallbladder cancer is viable. Nonetheless, the long-term outcome and a direct comparison to studies of a large number of patients treated via laparotomy are needed to ultimately prove the value of this approach.

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