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Laparoscopic radical cholecystectomy for early gall bladder cancer: The way forward

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Abstract
Gall bladder cancer (GBC) is the most frequent and aggressive malignancy of the biliary tract with very poor prognosis. Radical resection remains the main potential curative treatment for operable injuries. Despite the fact that laparoscopic approach is presently considered as standard of care for some gastrointestinal malignancies, surgical community is still hesitant to utilize this approach for GBC probably because of fear of tumor dissemination, deficient lymphadenectomy and in general agnostic approach. Aim of this study was to share our initial experience of laparoscopic radical cholecystectomy (LRC) for suspected early GBC. From Dec 2015 to June 2016, six patients were included in this study. 2 were incidental, diagnosed in histopathology after laparoscopic cholecystectomy in our center. We selected the patient for lap radical cholecystectomy who are in early stage cancer and not much of liver parenchymal invasion. There were 3 male and 3female patients in study group and mean age was 54years (Range 35-74yrs). Majority of the patient presented with pain abdomen and one patient presented with cholangitis because of obstructed CBD stone. Mean operative time was 332 minutes (Range 240-480minutes) and average blood loss was 232ml (Range 180-300ml). The average post op hospital stay was 5.6 days (Range3-13days) and all other details are represented here below. Laparoscopic radical cholecystectomy with lymphadenectomy can be a reasonable option for the management of early GBC as far as specialized practicality and oncological freedom along with offering the conventional advantages of minimal access approach.

Keywords: Radical cholecystectomy, GBC, gastrointestinal malignancies, CBD stone

Introduction
Gall bladder cancer (GBC) is the most common biliary tract cancer [S1]. The incidence of GBC varies worldwide depending upon geographic and ethnicity variables. The high incidence of GBC has been found to be in Chili, Indian subcontinent, Japan and Korea [2]. The high incidence has been someway corelates with high incidence of subclinical *Salmonella Typhi* and Paratyphi infection [3, 4]. GBC is one of the aggressive cancer which carries very poor prognosis. Because of nonspecific symptoms, most of the patients present in very late stage of the disease. TShe survival and prognosis solely depends upon early diagnosis and radical surgical intervention.

Staging Laparoscopy has been an integral part of the GBC operation for which diagnostic yield has been very high. In almost 30-40 percent cases peritoneal and liver metastasis has been detected in different studies which prevent non therapeutic laparotomy in those patients. But there has been very pessimistic attitude among surgeons regarding use of laparoscopy for radical resection of GBC. The commonly stated reasons are fear of dissemination of malignant cells, bile spillage and complexity of the surgery which includes liver resection and lympahadenectomy. In view of advancement in the field of hepato biliary surgery and laparoscopic surgery many surgeons have attempted laparoscopic radical cholecystectomy for early GBC. There has been case reports and retrospective series of such successful attempts of completion of the radical surgery with patient safety without compromising oncologic principle of the GBC Surgery [5, 10]. We are presenting our initial experience of managing such cases by laparoscopic method in early stage GBC, incidentally detected GBC and preoperative suspicion of GBC in imaging.

Materials and Methods

This is a retrospective analysis of prospectively maintained data base of all incidental or suspected case of Ca GB which were managed with laparoscopic method between December 2015 to June 2016. We selected the patient for lap radical cholecystectomy who is in early stage cancer and not much of liver parenchymal invasion. The surgical technique is being described in detail below. We avoided the patients for laparoscopic surgery who were having multi organ involvement. After surgery, patients were evaluated for anesthesia recovery and if it was satisfactory, the patients were directly shifted to ward with transient stay in post op recovery ward. All patients started on oral diet 6 hours after surgery except the patient who had hepaticojejunostomy. The patients were discharged when they were fully ambulant and on normal diet without any fever or any other symptoms. All the operated specimens were sent for histopathological examination. The patients were followed up for any symptoms or any clinical evidence of recurrence.

Surgical Technique

The patient under general anesthesia in semi lithotomy reverse trendelenburg position, the surgeon stands between the legs of patient. The camera surgeon stands left of primary surgeon and another assistant stands at left shoulder patient. After pneumoperitoneum was created with open technique, camera port at umbilicus, right and left working port at left and right mid clavicular line above umbilicus were inserted. Additional trocars (5mm) are introduced at epigastric and left anterior axillary line if required (Figure No.01). The pneumoperitoneum was kept around 10-12mm Hg to prevent CO_2 embolism during parenchymal resection. As first step we did staging laparoscopy in all of our cases to rule out metastatic disease. Then we proceed with 2 to 3cms of liver wedge resection around gall bladder bed after taking stay sutures at the intended edge of liver parenchymal resection (Figure No 02) We usually kept the CVP (Central Venous Pressure) around 4-5mm Hg to prevent excess blood loss during liver wedge resection. Initially planned resected area was marked with diathermy and then with the help of harmonic shear parenchyma was transected. At deeper level the major segmental vessels and bileduct were isolated, clipped and divided. At the end of resection, hemostasis was achieved. At no point of time GB was not handled directly to prevent GB rupture and bile spillage. Then we proceed for regional lymphadenectomy which includes periportal, hepatic artery, pericholedochal, retropancreatic and inter aortocaval lymphnode groups (Figure No. 03). We usually take cystic duct stump margin for biopsy. If tumor is located at neck of GB causing obstructive jaundice we plan for common bile duct (CBD) resection and roux-en y hepatico jejunostomy otherwise routine CBD excision protocol was not followed in all of our cases. After thorough checking of biliostasis and hemostasis at the resected margin site 24Fr abdominal drain was placed in Morison's pouch. The resected specimen was kept in a plastic bag and extracted through umbilical port site. We did only epigastric port site excision in incidental cases where it was used for GB specimen removal in previous surgery. All CBD stone the specimen removed sent for final histopathological examination (Figure No.04).

Fig. 1: Port Sites of the patient

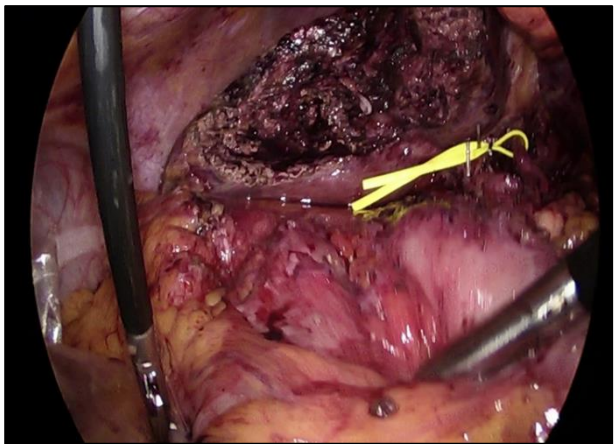

Fig 2: Liver Wedge Resection

Results

We operated 6 patients of incidental or suspected Ca GB in laparoscopic method between December 2015 to June 2016. Out of six patients 2 were incidental, diagnosed in histopathology after laparoscopic cholecystectomy in our center. Other four patients were having pre-operative suspicion of gall bladder carcinoma in ultrasound and CT imaging feature. There were 3 male and 3female patients in study group and mean age was 54years (Range 35-74yrs). Majority of the patient presented with pain abdomen and one patient presented with cholangitis because of obstructed CBD stone. Both the cases of incidental Ca GB was operated in our center for symptomatic cholelithiasis. During follow up visit after obtaining biopsy report both the patient were planned for completion radical cholecystectomy within 3weeks of primary surgery. The tumor was located in GB fundal region in 3 cases, body 2 and neck region in one case.

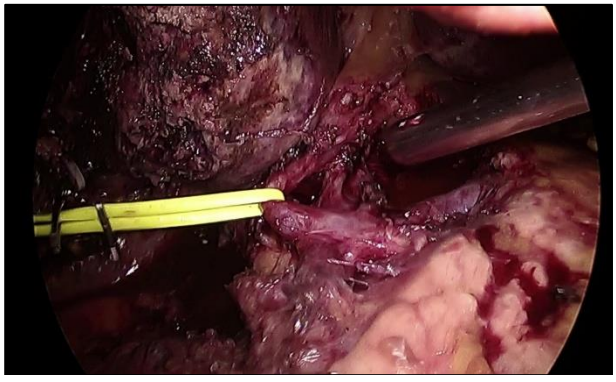

Fig 3: Lymphadenectomy

Fig 4: Excised Specimen

The patient who had GB neck cancer underwent CBD excision along with radical cholecystectomy and hepatico jejunostomy (HJ) was performed completely by laparoscopy method.All the patient underwent 2 to 3cms of parenchymal wedge resection around GB bed. The patient who presented with cholangitis because of CBD stone planned for ERCP (Endoscopic Retrograde Cholangio Pancreatography) CBD stone extraction and stenting then taken for lap radical cholecystectomy. Mean operative time was 332minutes (Range 240-480minutes) and average blood loss was 232ml (Range 180-300ml). The average post op hospital stay was 5.6 days(Range3-13days).Only one patient who had HJ had minor bile leak which was managed conservatively and he had prolonged hospital day. Otherwise rest of the patient had uneventful post op recovery without any complications. All patients were started on oral liquid diet 6 hrs after surgery on same day except patient who had additional HJ. Out of four patients who had pre op suspicion of Ca GB in two patients it turned out to be Xanthogranulomatous cholecystitis in final biopsy specimen. Average LN yield was 9 (Range: 8-10). All resection margins were free. Mean follow up of all patients was 8.5months and all are doing well without any evidence of clinical recurrence (Table 1).

Discussion

There has been paradigm shift in the management of GBC by minimal invasive surgery (MIS) with advent of new technology, experience in both liver surgery and advance laparoscopic surgery. The new enthusiasm to apply laparoscopy method in GBC surgery is to provide all the benefits of MIS (e.g. Less pain, less analgesic requirement, shorter hospital stay, better cosmesis, low incidence of surgical site infection and early return to work) without compromising oncological principle of the radical surgery. However it requires extensive experience in both open GBC surgery and advance laparoscopy skill.

There has been few issues regarding laparoscopy in liver resection part of radical cholecystectomy. One of the concern is fear of CO_2 embolism because of pneumoperitoneum and open venous channel during parenchymal resection. However in practically there is very minimal chance of such incidence if pneumoperitoneum is kept around 10-12mm Hg. WE in all our cases kept the pneumoperitoneum pressure below 12mm Hg and did not experience either operative difficulty because of low pressure or CO2 embolism. One should be very careful enough not to handle the GB directly with any instrument to prevent inadvertent injury to GB and bile spillage. We always put stay sutures in either side of parenchymal resection line to manipulate during wedge resection.

Table 1: Demographic and clinical surgery details of patient

Sl No.	Age Sex	Clinical presentation	Time of Diagnosis of Ca GB	Tumor Location	Surgery	Duration of surgery	Blood Loss	Morbidity	Hospital stay	Histopathology	Follow up
1	74 M	Pain abdomen	Pre op	Fundus	Lap Wedge resection of Liver	240min	200ml	Nil	3 days	Adeno Carcinoma Ro Margin 1/9LN positive	12 months
2	61 F	Pain abdomen	Incidental	Body	Lap Wedge resection of Liver	280min	250ml	Nil	6 days	Adeno carcinoma Ro Margin T1b NMx 1/8LN positive	10 months
3	65 F	Cholangitis	Preop	Fundus	Lap Wedge resection of Liver + ERCP CBD stone extraction	300mins	300ml	Nil	4 days	Xanthogranulomatous cholecystitis	6 months
4	50 M	Pain abdomen	Incidental	Neck	Lap Wedge resection of Liver + RYHJ	480mins	260ml	Bile leak	13 days	Adenocarcinoma, Liver and CBD margin free1/9LN positive	9 months
5	35 M	Pain abdomen	Pre op	Fundus	Lap Wedge resection	420mins	200ml	Nil	4 days	Xanthogranulomatous cholecystitis	16 months
6	40 F	Pain abdomen	Pre op	Body	Lap Wedge resection	270mins	180ml	Nil	3 days	Adenocarcinoma, Margin free. 2/10LNs positive	8months

Regarding patient positioning we prefer semi lithotomy and reverse Trendelenburg position which makes us feel more comfortable and adequate space for the assistant and the camera person to stand. Pallanivellu *et al* use normal supine position like simple lap cholecystectomy procedure [11]. We use 4 trocar technique where-as few other authors used 5 trocars. One additional trocar may facilitate proper exposure during hepatico jejunostomy if required at all.

We do not use specialized instrument like Cavitron Ultrasoonic Aspirator (CUSA) during parenchymal resection. Harmonic scalpel and bipolar diathermy is good enough to carry out the wedge resection. For proper hemostasis normal gauge pressure and bipolar diathermy is helpful.

Among all our cases there were 2 cases of xanthogranulomatous cholecystitis in final biopsy specimen.It is really difficult it to differentiate it from GBC in imaging, clinically and intra operative findings.It is better to go for safety side rather than feel sorry for making one

operable case to non-operable one and upstaging the disease process by violating the oncological safety plane.

There has been debate regarding wedge resection and formal segment 4b and 5 resection [12]. But studies have shown that there is no survival or oncological clearance benefit if there is not so much liver parenchymal invasion. In all our patients GBC was confined to GB only and no macroscopic liver parenchymal invasion.

In special circumstances like GBC with jaundice one should rule out other common cause of jaundice like associate common bile duct (CBD) stone which was found in one of our case. It was initially managed by endoscopic method. If jaundice because of GB neck cancer infiltrating to common hepatic duct causing obstructive jaundice one can attempt excision of bile duct and intracorporeal anastomosis of hepaticojejunostomy which has been done in one of our case. But it requires high degree of skill to complete the procedure in total laparoscopic method. There has been few reports of successful completion of the procedure in pure laparoscopic approach [12].

Our average lymph node retrieval was 9 which is comparable to any other study with laparoscopic method. We do not send inter aorto caval LN for frozen biopsy routinely which is done by few authors before formal radical surgern [12]. It is considered as metastatic disease with poor prognosis. However there are authors who do not follow this protocol [13]

One of the limitation of our study is very small duration follow up to draw any conclusion regarding long term outcome regarding recurrence, disease free survival and overall survival. However in this study we intended to show the technical feasibility of laparoscopic radical cholecystectomy without compromising oncologic principle GBC surgery [14].

Conclusion

Laparoscopic Radical cholecystectomy is the way forward in managing incidental GBC and early GBC with all benefits of MIS without compromising patient and oncological safety. However it requires extensive experience in open liver surgery and advance laparoscopic surgery and should be attempted in high volume center.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

All authors critically reviewed the article and read and approved the contents.

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