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Laparoscopic Extended Cholecystectomy for Early Gall Bladder Cancer

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ABSTRACT

Background: Laparoscopic approach for early gall bladder cancer (T1b andT2) has been seen to have equal or better early outcomes and late outcomes in terms of overall survival rate and recurrence rate.

Methods: This is a prospective cross sectional observational study performed including all consecutive patients who were diagnosed with gall bladder cancer by a single surgical team from August 2018 to February 2020 at Kathmandu Medical College Teaching Hospital or referred from outside for completion extended cholecystectomy where laparoscopic cholecystectomy was done in some other centre.

Results: The mean age of the patients was 51.01±9.42 years in the laparoscopic extended cholecystectomy (N=10) group and 49.6±8.35 years in the open extended cholecystectomy (N=10) group (p value=0.711). Conversion rate was 20% in laparoscopic group. The operative time was longer in the laparoscopic group (287 +/-66.50 minutes, 120.0 to 446 minutes vs. 200+/-66.50 minutes, 100 to 405.0 minutes; p< 0.004.However, the laparoscopic extended cholecystectomy group showed faster time to oral intake and time to first passage of flatus and had shorter hospital stay by 2.2 days (4.8+/-0.78 days) than open approach 7+/-0.81 days.(p value=0.00).There were no significant differences between the groups in the tumour size (p=0.079) and number of harvested lymph nodes 9.3 (5 to 13) in laparoscopic group vs. 11.2 (8 to 15) in open extended cholecystectomy group (p=0.250).

Conclusions: Laparoscopic extended cholecystectomy is feasible in early gall bladder cancer along with achievement of oncological safety.

Keywords: Gall bladder cancer; laparoscopic extended cholecystectomy; open extended cholecystectomy

INTRODUCTION

With the wide use of laparoscopic approach in gall bladder stones, its use for cancer has been lately explored because of earlier studies questioning its implication due to high incidence of port site metastasis.[1-5] However, substantial number of studies showed its beneficial or equivocal advantage of laparoscopic extended cholecystectomy for early gall bladder cancer in terms of overall survival rate and recurrence rate.[6-9]

High incidence of gall bladder cancer have been reported in Chile (27.3/100000) followed by Indo-Gangetic belt (21.5/100000).[10, 11] In Nepal, the incidence of carcinoma gall bladder is 3.7% in males and 5.7% in females according to multi-institution hospital-based cancer data by Pradhananga et al.[12]

The purpose of this study was to evaluate the feasibility of laparoscopic extended cholecystectomy for early gall bladder cancer, compare lymph node yield between open and laparoscopic group; conversion rate and causes for conversion.

METHODS

This study was a prospective cross sectional observational study. All consecutive patients who were diagnosed as primary suspected early gall bladder cancer on CT scan /MRI or incidental gall bladder cancer (T1b and T2 on histopathology report) were included in blind envelope selection for laparoscopic or open group after detail explanation and with informed consent .Since this feasibility study incorporated only suspected early gall bladder cancer and incidental early gall bladder cancer, 10 in each group is suffice to see the feasibility of the study. Hence, study was conducted in total 20 cases, 10 on each arm to see the primary outcome in terms of operating time, blood loss, achievement of oncological safety as that of open extended cholecystectomy and

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lymph node yield .It was performed at Kathmandu Medical College Teaching Hospital by single surgical team from August 2018 to February 2020. Advanced gall bladder cancer (T3 and T4) were excluded from study. Approval from institutional ethical and review committee was taken.

Minimum standard oncological safety achievement for both group was described as:

Lymphatics clearance around hepatic artery up to origin of common hepatic artery and classifying according to Mitchel classification.[13]

Lymphatics clearance around the portal vein up to its bifurcation and classifying according to Nakamura classification.[14]

Lymphatic clearance around common bile duct up to its bifurcation.

Type of liver resection: Anatomical IVb/V or Non anatomical Wedge resection.

Cystic duct margin frozen section in all patient

Post-operative variables included were total hospital stay, pathological TNM staging, lymph node yield number and positive lymph node ratio and complications rate.

5-6 Laparoscopic ports were made. Kocherisation was done as a part of staging laparoscopy for sampling of aortocaval lymph nodes if present on CT scan and sent for frozen section. Hepato duodenal ligament clearance was done first, along with frozen section of cystic duct margin. Dissection was carried out identifying hepatic artery and circumferential lymphatic clearance along common hepatic artery to its origin from celiac trunk with routine dissection of posterior superior pancreatic lymph nodes including aortocaval lymph node sampling for frozen section if present in CT scan. Demonstration of bifurcation of portal vein with circumferential clearance was achieved. Then non-anatomical wedge resection of liver with 2 cm margin was done if the mass was towards peritoneal surface and anatomical segment 4b/5 resection was done whenever gall bladder mass was towards gall bladder bed. Photo and video documentation of each procedure was done (Figure 1).

For quantitative data, the results have been expressed as the mean ± standard deviation (SD). The median with interquartile range has been used for skewed quantitative data. For categorical data, the results have been expressed as the number and percentage of cases. Values have been expressed as the means and ranges, or percentages, when appropriate. The x2 test has been used to compare categorical variables and the independent t test has been used to compare continuous variables. All statistical analyses were performed using Statistical Package for the Social Sciences version 16.0 (SPSS Inc Chicago, IL).[15]

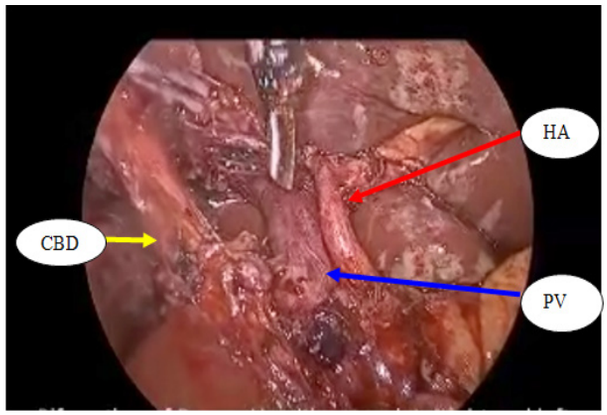

Figure 1. Laparoscopic lymphatic clearance of Hepatoduodenal ligament.

(Red arrow: Bifurcation of Hepatic artery (HA) proper into right and left; Blue arrow: Portal vein (PV); Yellow arrow: Common bile duct (CBD).

RESULTS

In total, 25 patients with early carcinoma of gall bladder (primary and incidental) underwent surgery for carcinoma of gall bladder from August 2018 to February 2020. Among them, ten patients underwent laparoscopic extended cholecystectomy and were compared with ten open extended cholecystectomy which were performed during the same period of time. Five patients denied giving consent for inclusion in the study.

Four patients had pre-operative diagnosis of carcinoma of gall bladder on CT scan abdomen (two in each group) and sixteen patients had incidental carcinoma of gall bladder post laparoscopic cholecystectomy for gall bladder polyp or gall bladder stone.

All patients had a median of 12 months of follow-up (range, 2 to 12 months). Demographics of the patients are shown in Table 1. The mean age of the patients was 51.01±9.42 years in the laparoscopic extended cholecystectomy group and 49.6±8.35 years in the open extended cholecystectomy group (p value=0.711).

In the laparoscopic group, two patients had to be converted to open; one because of bleeding from right gastric artery and another for frozen hepatoduodenal ligament leading to conversion rate of 20%.

The operative time was longer in the laparoscopic group (287 +/-66.50 minutes, 120.0 to 446 minutes vs. 200+/-66.50 minutes, 100 to 405.0 minutes; p< 0.004.). Moreover, open extended cholecystectomy have shown more blood loss than laparoscopic approach though not significant (p value=0.257), probably due to visual magnification of operative field in laparoscopic approach.

However, the laparoscopic extended cholecystectomy group showed faster time to oral intake and time to first passage of flatus and have shorter hospital stay by 2.2 days (4.8+/-0.78 days) than open approach 7+/-0.81 days (p value=0.00).

In the laparoscopic group, post-operative bile leak was observed in one patient who was managed with pigtail catheter insertion. However, two patients had bile leakage in open group, managed with pigtail catheter. Four patients in open group had pulmonary complications (Atelectesia-2, Hospital acquired pneumonia-2) prolonging hospital stay including two patients who had superficial surgical site infection which was treated with antibiotics.

There were no differences between groups in the tumour size (p value=0.079) and number of harvested lymph nodes 9.3 (5 to 13) in laparoscopic group vs. 11.2 (8 to 15) in open extended cholecystectomy group (p value=0.25).

Table 1. Patient characteristics.

	Laparoscopic extended cholecystectomy (N=10)	Open extended cholecystectomy (N=10)	p value
Age	51.01+/-9.42 years	49.6+/- 8.35 years	0.0711
Gender (M:F)	4:6	3:7	
Pre-operative staging	Primary carcinoma of gall bladder: 2 Incidental carcinoma of Gall bladder: 8	Primary carcinoma of gall bladder: 2 Incidental carcinoma of gall bladder: 8	
Hepatic artery classification	Mitchel type I: 6 Mitchel type II: 2 Mitchel type III: 2	Mitchel type I: 7 Mitchel type III: 2 Unclassified type: 1	
Portal vein classification	Nakamura type I: 4 Nakamura type II: 3 Nakamura type III: 3	Nakamura type I: 6 Nakamura type II: 4	
Liver resection	Non anatomical wedge resection: 8 Anatomical 4b/5 resection: 2	Non anatomical wedge resection: 2 Anatomical 4b/5 resection: 8	
Cystic duct margin on Frozen section	Negative: 10	Negative: 8 Positive: 2 (CBD excision with Hepaticojejunostomy)	
Pathological staging	$T_{1b}N_0$: 7 T_2N_0: 2 T_2N_1: 1	$T_{1b}N_0$: 6 T_2N_0: 3 T_2N_1: 1	
Conversion to open extended cholecystectomy (N=2)	1: Conversion due to frozen hepatoduodenal ligament. 2: Conversion due to bleeding from right gastric artery.		
Complication	Bile leakage: 1	Bile leakage: 2 Superficial wound infection: 2 Basal atelectasis: 2 Pneumonia: 4	

Table 2. Comparison between laparoscopic and open extended cholecystectomy.

	Laparoscopic extended cholecystectomy	Open extended cholecystectomy	p value
Mean operating time (minutes)	287 +/- 66.50	120 +/- 20	0.004
Estimated blood loss	348 +/- 85.60	405 +/- 127.91	0.257
Hospital stay (days)	4.8 +/- 0.78	7days +/- 0.81	0.000
Number of lymph nodes	9.3 +/- 4.39	11.2 +/- 3.86	0.250

DISCUSSION

This study shows the feasibility of laparoscopic approach for early gall bladder carcinoma without compromising early oncological outcomes in terms of lymphatic clearance or number of lymph yield in comparison to open method. Moreover, laparoscopic approach has lessened the post-operative hospital stay with early discharge though the operative time is longer.

Despite limited experiences by experts, laparoscopic extended cholecystectomy has been shown to be safe and feasible in selected gall bladder cancer patients with similar results to those of open surgery.[16,17] Ethun CG et al from a multi-institution analysis from the US Extra hepatic Biliary Malignancy Consortium have suggested that ideal timing for surgery is during time periods between 4 to 8 weeks of primary surgery as it has shown improved overall survival than those who have surgery done before 4 weeks and after 8 weeks (41.5 months vs 17.4 and 25.9 months, respectively; p=.04).[18] In our experience, early surgical intervention within 7 days after post laparoscopic cholecystectomy (n=8) was easier in terms of surgical plane of dissection than after 2 weeks (n=2) in laparoscopic group. However, our study sample is small and our patients are being referred from distant, therefore long term survival benefit of early intervention in our group is yet to be studied.

According to AJCC 8th edition TNM classification, at least six lymph nodes are necessary to label it as adequate lymphatic dissection of regional lymph.[19] In our study, mean lymph node yield was 9.3+/-4.39 in laparoscopic group and 11.2+/-3.86 which was comparable but not significant (p=0.25). However, one positive lymph node was present in both groups in patient with tumour dimension of T2. A study done by Leigh et al has shown that 80% of patients undergoing regional lymphadenectomy for ≥ pT1b gall bladder cancer had total lymph node count less than six and hence have recommended to include additional lymph node stations and incorporation of frozen section analysis.[20]

We performed routine dissection of posterior superior pancreatic lymph nodes and clearance along hepatic artery till coeliac axis including aortocaval lymph node sampling for frozen section which might have accounted for higher number of lymph node counts.

Beside regional lymph node, positive cystic duct margin are significantly more likely to have residual cancer at the common bile duct (42% vs. 4.3%) according to Pawlik et al.[21] Hence, we routinely perform frozen section of cystic duct margin in both the group and two of open extended cholecystectomy had positive cystic duct margin, who underwent common bile duct excision with Roux en Y hepaticojejunostomy.

Studies have shown that regardless of the type of liver resection (whether non-anatomical wedge resection or anatomical segmental resection approach), it does not have much difference in survival rate until R0 resection was achieved and moreover, anatomical resection of IVb/V segment have been linked with increased morbidity.[22-25] Majority of our patients in the laparoscopic group had undergone non-anatomical wedge resection with 2 cm of liver margin with achievement of R0 resection whereas open extended cholecystectomy has more of an anatomical segment IVb/V resection. This propensity may be due to the learning curve in laparoscopic approach than in open group. However, open extended cholecystectomy had more pulmonary complications like pneumonia and atelectasis probably due to wound related pain thus reinforcing the importance of laparoscopic approach.

Since presentation of primary early gall bladder cancer and incidental early gall bladder cancer itself are fewer than advance gall bladder cancer, major limitation of this study is small number of sample size limiting us to conduct multivariate analysis in subgroup, besides conducted by a single surgical team with short term follow up period.

Despite these limitations, this study shows the feasibility of laparoscopic extended cholecystectomy with adequate lymphadenectomy and has better early post-operative recovery in terms of post-operative hospital stay and morbidity. However, we recommend further large scale and randomized studies for use of laparoscopic approach for early as well as advanced gall bladder cancer in future to validate our conclusion.

CONCLUSIONS

Laparoscopic extended cholecystectomy is feasible in early gall bladder cancer along with achievement of early oncological safety in terms of adequate lymph node yield and has better early post-operative recovery in terms of post-operative hospital stay and morbidity.

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