Role of Staging Laparoscopy in Gallbladder Cancer

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ABSTRACT

Background

Preoperative accurate staging of gallbladder cancer is still difficult. A number of patients with gallbladder cancer who undergo laparotomy for curative resection are ultimately found to have unresectable disease. The benifit of staging laparoscopy is its ability to find out the radilogical occult intraperitoneal metastasis and to spare from nontheraputic laparotomy. The role of staging laparoscopy has been extensively studied in hepatobiliary and pancreatic malignancies and found to be useful. But in recent time its utility in biliary cancers is sceptical probably because of the advent of positron emission tomography. However in gallbladder cancer it is still recommended.

Objective

To identify the utility of staging laparoscopy in gall bladder cancers.

Method

Hospital based study conducted at Nepalgunj Medical College, Nepal from October 2014 to June 2020. The patients with resectable gallbladder cancers on computed tomography were included. All patients underwent single stage staging laparoscopy. Staging laparoscopy was considered positive if the surface lesions (liver and/or peritoneal deposits) were detected. The surgery was terminated if positive. Patients with negative staging laparoscopy were proceeded with laparotomy.

Result

Staging laparoscopy was done in 47. The yield of staging laparoscopy was 14 (29.78%) and its accuracy was 58.33% (14/24). Out of 33 (70.21%) with negative staging laparoscopy, 10 (30.3%) had unresectable disease in laparotomy. The yield was higher in locally advanced in comparison to early disease (78.57% Vs 21.42%).

Conclusion

We recommend routine staging laparoscopy in gallbladder cancer, particularly when the disease is locally advanced.

KEY WORDS

Accuracy, Gallbladder cancer, Locally advanced disease, Staging laparoscopy, Yield

INTRODUCTION

Staging laparoscopy (SL) is a minimally invasive procedure to detect radiologically occult metastasis in different malignancies of gastrointestinal tract.[1,2] Its use may avoid nontheraputic laparotomies and therefore is associated with reduction in postoperative pain, hospital stay, surgical site infection. This improves the quality of life, reduces the cost and allows early start of systemic chemotherapy in patients with unresectable disease.[3-6]

SL can be done in one stage or in two stages. It can be done before a planned definitive surgery (one stage) or as a separate procedure (two stage). Two staged SL provides the ability to obtain final pathological evaluation of peritoneal washing and biopsy samples and allows better management of the valuable operating room time if unresectable disease is identified. For hepatobiliary cancers SL is performed as a one staged procedure.

Gallbladder cancer (GBC) is the most common malignancy of the biliary tract with a five year survival rate of 5%.[7] Many patients present with unresectable disease and/or with metastasis commonly to liver, peritoneum and nonregional lymphnodes.[8,9] The chance of detecting unresectable disease is significantly high during SL or laparotomies, even after an extensive preoperative imagings.[10,11] SL can prevent nontheraputic laparotomies in 38% to 68% of GBC.[12]

Complete resection is the only potential way to provide cure for patients with GBC. Preoperative computed tomography (CT) scan, magnetic resonance imaging (MRI) of the abdomen can assess the vascular involvement, involvement of the nonregional lymph nodes and distant liver deposits but small < 1 cm liver and/or specially the peritoneal deposits may be missed. Positron emission tomography (PET) scan can improve the detection of peritoneal deposits.[13] Its role is increasing with time as a modality with an ability to detect disseminated disease before surgery. Similarly high levels of preoperative tumor markers like carbohydrate antigen 19-9 (CA19-9) and carcinoembryonoc antigen (CEA) also have been found to predict the unresectable disease in cancers of biliary origins.[14]

Despite all these investigative modalities (CT scan and MRI) about 25 to 30% GBC have occult liver and/or peritoneal disease and SL can detect these lesions and help to avoid laparotomies.[10,15] In centres where the facilities like PET scan and assessment of tumour markers are lacking, SL may serve as a simple modality to detect the disseminated intraperitoneal lesions. This study was performed to define the role of SL in GBC.

METHODS

This was a hospital based study conducted at Nepalgunj Medical College Nepal in the department of surgery from 2014 October to June 2020. Ethical approval was obtained from the institutional review committee. Patients were counselled, explained about the procedure and informed written consent was taken before their enrolment. Detailed history and examination of the patients with clinical and radiological (mostly on Ultrasound abdomen) suspicion of GBC were performed. These patients underwent contrast enhanced CT abdomen and pelvis. The resectability was determined based upon the CT findings. Involvement of the hepatic artery, portal vein, enlarged nonregional aortocaval lymph nodes, presence of liver and obvious peritoneal or omental deposits were considered unresectable and excluded. Disease confined to the gallbladder, without any evidence of regional and nonregional lymphadenopathy was considered early and those involving the adjacent structures (liver, duodenum, stomach etc) and with significant regional lymphnodal enlargemet were considered as locally advanced disease. Patients with incidental GBC were also excluded. Patients considered resectable on CT scan were included.

Patients considered to have resectable disease underwent a single stage SL under general anaesthesia. Pneumoperitoneum was created by a closed technique through a 10mm supraumbilical port. Additional ports were placed under vision. The peritoneal cavity was explored with a 30 degree laparoscope. All peritoneal surfaces including the anterior and posterior surface of the liver, falciform ligament, porta hepatis, gastrohepatic omentum, transverse mesocolon, greater omentum, ligament of treitz, small bowel and the pelvic peritoneum were examined. Biopsy was taken in case of detection of any suspicious lesion and sent for histopathological examination. Frozen section was not done as this facility is not available at our institution. All with positive histopathology were sent for palliative chemotherapy. In case of negative histopathology patients were counselled for the need of definitive surgery within two weeks of SL. It took about 10-15 days for the histopathology report to available. However all patients who underwent SL had positive histopathology for malignancy. Further investigations were not planned in these type of patients. Laparoscopic dissection to find out the vascular and interaortocaval (IAC) lymph nodes were not done due to the lack of expertise of the authors. Laparoscopic ultrasound was also not done due to its unavailability. The liver and peritoneal deposits found on SL without any dissection were considered as surface lesions. SL was considered positive when these surface lesions were detected.

The main objective was to define the yield of SL and its accuracy in identification of surface lesions. The yield is defined as the ratio of patients with positive SL divided by the total number of patients undergoing SL. The accuracy is defined as the number of patients with unresectable disease identified during SL divided by the total number of patients with unresectable disease.The other objective was to identify the SL yield when early versus locally advanced diseases were compared.

The data were analysed using SPSS software. Comparison of variables like SL yield between early versus late diseases and between the detection of peritoneal versus liver deposits were done by using Chi-square test and statistical significance was established as $p < 0.05$. When the sample size was small t-test was used. The yield and accuracy of SL were calculated by using a formula mentioned in the methods.

RESULTS

There were total 131 diagnosed cases of GBC in the study period. Only 47 (35.87%) were operated. Eighty-four (64.12%) were not operated. There were 97 (74.04%) females and 34 (25.95%) males, the ratio being 2.85:1. The age ranged from 30-92 with a mean age of 61.41±12.18 years.

SL was done in all the 47 patients who were taken up for surgery with intention of R0 resection. Of the 47 patients 14 had surface lesions making the SL positive. Eight (57.12%) had peritoneal deposits, 3 (21.42%) had liver deposits and 3 (21.42%) had both peritoneal resection. Among them 10 (30.3%) had and liver deposits. The overall SL yield was 29.78%(14/47). In 33 (70.21%) with negative SL, laparotomy was performed for definitive unresectable disease in laparotomy (fig. 1). Unresctability was due to liver deposit (n=2), peritoneal deposit (n=1), interaortocaval nodal enlargement (n=3) and due to involvememt of the vascular structures like portal vein or hepatic artery and involvement of the biliary confluence (n=4) which were not evident on preoperative CT scan.
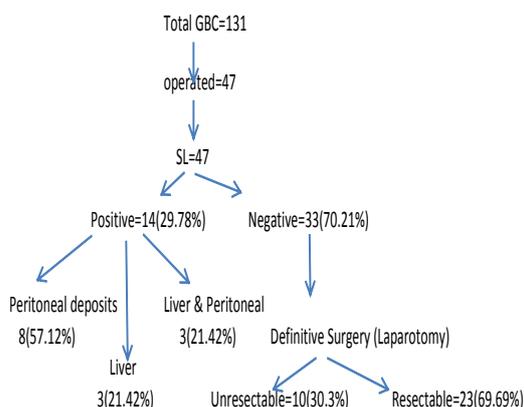

Figure 1. Operative details

Thirty six (76.59%) out of 47 had locally advanced disease and 11 (23.40%) had localized disease on preoperative imaging. Of the 14 patients with positive SL, 11 (78.57%) had locally advanced disease and only 3 (21.42%) had disease confined to the gallbladder. The SL yield was significantly higher in locally advanced in comparison to early localized disease i.e. 78.57% Vs 21.42% (p=0.003). The detection rate of peritoneal deposits was higher than liver deposits on SL i.e. 11 (78.57%) Vs 6 (42.87%) and when compared it was statistically significant (p=0.01). The accuracy of

SL in detecting surface lesion was 58.33% (14/24). There were no complications and death recorded in patients who underwent SL. Their mean hospital stay was 2±1.6.

DISCUSSION

In our study the SL yield was 29.78% and the accuracy to detect the surface lesions was 58.33%. Only 23 (48.93%) could finally undergo curative resection. We found that the SL yield was significantly higher in locally advanced disease (78.57% Vs. 21.42% respectively).

Although the use of SL in various gastrointestinal cancers including biliary cancers, especially GBC is common but its clinical benefit is variable. In a study by Weber et al. the yield of SL in GBC was 48% and in locally advanced hilar cholangio (HC) carcinoma it was 36%. The recommendation was SL should be used routinely in both types of biliary cancers. D'Angelica et al. showed a SL yield of about 50% for GBC and 20-25% for HC.[11] Similarly Vollmer et al. found the highest yield of SL in GBC comprising of 55% but for ampullary cancers it was nil (0%).[16] Goere et al. also reported a high SL yield in GBC (62%), intrahepatic cholangio carcinoma (36%) and 25% in extrahepatic cholangio carcinoma.[17] These studies showed highest yield of SL in GBC which subsequently avoided the nontheraputic laparotomy and suggested that the SL yield depends upon the anatomical location of the primary tumours.

Few studies from the near past have demonstrated the decreasing SL yield in biliary cancers. There was a study in 2011 which looked into a SL yield in HC carcinoma and found to be significantly declining from 41% to 14%. Forty one percent yield was reported by the same group in 2002.[18] The difference was explained by the improvement in the imaging techniques including CT, MRI and PET scan. PET combined with CT could effectively identify peritoneal and liver metastasis due to its ability to detect the tumour metabolic activity unlike in CT and MRI where the lesions < 1 cm can be missed.[13,19] A study in 2008 recommended that for GBC it is feasible to do PET/CT especially when tumour marker like CA 19-9 is elevated.[20] Studies focused on the use of PET imaging for the evaluation of primary GBC have reported sensitivities of 75-100% for the detection of disseminated disease.[21,22] In our cases we could not perform the PET/CT and CA 19-9 due to its unavailability.

One of the largest series of SL in GBC, SL identified unresectable disease in 23.2% out of 409 patients with radiologically resectable GBC. At laparotomy out of all SL negative patients 75 (23.8%) had unresectable disease most commonly due to nodal involvement. SL yield was significantly higher in locally advanced tumours compared with early (25.2% Vs 10.7% respectively). According to the author the improvement in SL was attributed to the use of laparoscopic ultrasound (LUS) for deep parenchymal liver lesions and/or laparoscopic sampling of IAC nodes.[10] SL yield and accuracy may be affected by the technique

of SL because the peritoneal and liver metastasis may be identified on SL but identification of IAC nodes, vascular invasion are more challenging and demand expertise.[16] Laparoscopic surface inspection without mobilization of structures, lymphnode sampling or LUS may reduce the yield and accuracy of SL compared with more extensive exploration.[10,23,24] In this study we only tried to find out the yield of SL and since we lack LUS and expertise to dissect the IAC nodes these manoeuvres were not done. However we did SL and explored all the peritoneal surfaces and liver surfaces as recommended for SL in hepatobiliary malignancy. Laparoscopic IAC lymphnode biopsy is a known procedure but it is argued that this procedures may cause tumour cell dissemination especially if cut through the positive nodes and the risk of this is higher when the nodes are significant in size and adherent to the surrounding structures Hence it is suggested a combination of PET/CT, SL and IAC lymphnode biopsy on laparotomy to identify unressectable disease.[25] A recent meta analysis comprising eight studies and 1062 patients undergoing SL for biliary cancers demonstrated the yield of 27.6% in GBC.[26] The accuracy of laparoscopic peritoneal metastasis is more than 90% when correlated with histopathology.[27]

Few studied have suggested certain preoperative characteristics that may predict an increased risk of metastasis disease, detectable on SL. These features are serum albumin level and CA 19-9.[28] Baseline CA 19-9 level may predict the tumour burden in GBC when above 20 units per mililitre and has been validated as a predictor for positive SL in pancreatic cancers.[29,30] Another study which looked into the role of CA 19-9, CEA and CA 125 as the predictor of resectability in GBC showed sensitivity of these markers to be 85%, 56.7%, 73.3% and specificity of 72.7%, 81.5% and 81.8% respectively. The positive predictive values of CA 19-9, CEA and CA 125 were 94%, 94.4%, 9.6% and negative predictive values were 25%, 25.7% and 36% respectively. They concluded that these tumour markers revealed a potentially good predictor for resectability.[31]

In our study the SL yield was significantly higher for peritoneal metastasis than the liver metastasis. This is probably because of the low sensitivity of CT scan in the detection of peritoneal metastasis, ranging from 42-47% when compared to detection of liver metastasis which ranges from 68-85%.[32,33] The role of SL in incidental GBC is debatable as most of the diseases are early. It may be considered in patients with T2 or greater tumors, positive surgical margin, poor tumor differentiation.[34] Incidental GBC were not include in our study due to its very small number.

Limitations are the smaller sample size, lack of PET scan, tumor marker like CA 19-9, and LUS. Larger sample size could have made findings more accurate but as GBC presents with an advanced disease it is not possible for many patients to undergo surgery. PET is still limited with its cost and unavailability. We assume with time these limitations will be eliinated. Tumour markers like CEA and CA 125 are done at our centre but unfortunately CA 19-9 is not done may be not being a dedicated cancer centre.

CONCLUSION

The SL yield and accuracy in our study was comparable with other studies. It was found that SL helped to avoid nontheraputic laparotomies thus reducing the postoperative complications, hospital stay and the expenditure. Hence SL is still necessary in countries where the use of facilities like PET scan and LUS may not be feasible for all. So we suggest for staging laparoscopy in all patients with GBC selected for curative resection with a strong recommendation for a locally advanced disease on preoperative imagings. Although some studies have suggested the role of CEA and CA 125 we think that these markers, especially CA 125 still needs further studies to be validated as a predictor of resectability in GBC.

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