

Minireview on laparoscopic hepatobiliary and pancreatic surgery

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Abstract

The first laparoscopic cholecystectomy was performed in the mid-1980s. Since then, laparoscopic surgery has continued to gain prominence in numerous fields, and has, in some fields, replaced open surgery as the preferred operative technique. The role of laparoscopy in staging cancer is controversial, with regards to gallbladder carcinoma, pancreatic carcinoma, hepatocellular carcinoma and liver metastasis from colorectal carcinoma, laparoscopy in conjunction with intraoperative ultrasound has prevented nontherapeutic operations, and facilitated therapeutic operations. Laparoscopic cholecystectomy is the preferred option in the management of gallbladder disease. Meta-analyses comparing laparoscopic to open distal pancreatectomy show that laparoscopic pancreatectomy is safe and efficacious in the management of benign and malignant disease, and have better patient outcomes. A pancreaticoduodenectomy is a more complex operation and the laparoscopic technique is not feasible for this operation at this time. Robotic assisted pancreaticoduodenectomy has been tried with limited success at this time, but with con-

tinuing advancement in this field, this operation would eventually be feasible. Liver resection remains to be the best management for hepatocellular carcinoma, cholangiocarcinoma and colorectal liver metastases. Systematic reviews and meta-analyses have shown that laparoscopic liver resections result in patients with equal or less blood loss and shorter hospital stays, as compared to open surgery. With improving equipment and technique, and the incorporation of robotic surgery, minimally invasive liver resection operative times will improve and be more efficacious. With the incorporation of robotic surgery into hepatobiliary surgery, donor hepatectomies have also been completed with success. The management of benign and malignant disease with minimally invasive hepatobiliary and pancreatic surgery is safe and efficacious.

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Core tip: This minireview presents the importance of laparoscopy in facilitating laparoscopic hepatobiliary and pancreatic surgery, and the efficacy and safety of laparoscopic hepatobiliary and pancreatic surgery. Laparoscopic surgery is the preferred management of benign and malignant disease for selected patients. The advantages include confirmation of diagnosis, prevention of nontherapeutic operations, decreased hospital stay and better post-operative function and cosmetic outcome. Meta-analyses demonstrate that laparoscopic liver resections, pancreatectomies and cholecystectomies are efficacious. There is less blood loss; the hospital stays are shorter with laparoscopic surgeries. There is no compromise to the oncological resection margins when compared to open surgery. Laparoscopic surgery is safe and efficacious in the management of benign and malignant hepatobiliary and pancreatic diseases.

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LAPAROSCOPY

Pancreas

Pancreatic cancer carries a poor prognosis with a 5-year relative survival rate of 5.8% (SEER Stat Fact Sheets: Pancreas). At least 80% of patients with pancreatic cancer present with either locally advanced or metastatic disease and are not resectable at the time of diagnosis^[1]. Complete surgical resection is the only curative treatment with potential for long-term survival^[2]. Accurate staging is essential in treatment planning and in determining appropriate management of patients with pancreatic cancer by selecting patients who can benefit from surgery and identifying patients with non-resectable disease to avoid non-therapeutic laparotomies^[3].

Up to one third of patients with high-quality preoperative imaging will have radiographically occult distant metastatic or locally unresectable disease at the time of staging laparoscopy^[2]. In pancreatic adenocarcinoma, laparoscopic staging allows for the identification of sub-radiographic metastatic disease in 10%-15% of patients with radiographically resectable cancer, and in approximately 30% of patients with locally advanced disease^[2]. Staging laparoscopy is associated with decreased length of stay, reduced postoperative pain, and a higher likelihood of receiving systemic therapy compared to laparotomy without significantly increasing operative time^[2,4,5].

However, advances in imaging technology have decreased the yield of staging laparoscopy over time. Multiphase, multidetector thin-slice computed tomography (CT) scans produce high-resolution images providing details about local vascular involvement and distant metastatic disease^[6]. Endoscopic ultrasound (EUS) is also being increasingly used to image the tumor and its relationship to adjacent structures and to obtain biopsies of pancreatic lesions and regional lymph nodes^[6]. A study by White *et al*^[7] evaluated 1045 patients from a prospective database who underwent staging laparoscopy for radiographically resectable pancreatic and peripancreatic tumors over a 10 year period from 1995 to 2005 to examine the yield of staging laparoscopy. The study reports that the yield of laparoscopy has diminished over the 10 year period and exceeds 10% only for patients with pancreatic adenocarcinoma^[7].

The use of staging laparoscopy in pancreatic cancer remains controversial. Whether staging laparoscopy should be used routinely or only in selected cases is a matter of debate. Studies suggest that staging laparoscopy should be reserved for selected cases where the yield is likely to justify the additional procedural risk and cost. Studies recommend that patients with tumours larger

than three centimeters, tumours in the neck, body or tail, or patients with equivocal CT scan findings for metastatic disease, may benefit from laparoscopy^[8,9].

Gallbladder

Gallbladder carcinoma is a rare malignancy and the incidence of intra or post-operative diagnosis is between 0.2% to 2.8%. Due to an increase in laparoscopic cholecystectomies, incidental finding of gallbladder cancer has also increased^[10]. The best management for gallbladder carcinoma is surgical resection: a resection with malignancy negative margins (R0 resection). In a T3 to T4 gallbladder carcinoma, an R0 resection would result in a 26% 5-year survival rate, as compared to a 9% survival rate in a less than R0 resection^[11]. If gallbladder carcinoma is suspected on imaging, the role of laparoscopic staging for gallbladder carcinoma has been shown to be sensitive in detecting unresectable disease and diseased lesions. The evidence supports that staging laparoscopy does not impact on overall survival, and prevents patients with unresectable disease from a nontherapeutic laparotomy^[12]. The use of a laparoscopic ultrasound as an adjunct to laparoscopy further increases the accuracy and specificity of diagnosis and staging^[13]. A retrospective review completed by Ferrarese *et al*^[10], further re-enforces the role of meticulous peri-operative diagnosis, intraoperative staging and cholecystectomy in preventing unnecessary laparotomies, and identify the patients who will benefit from a resection.

Liver

This section discusses the importance of laparoscopy and the role of laparoscopic ultrasound in confirming the diagnosis and planning the liver resection or ablation.

Laparoscopy is particularly useful in cases when resectability is uncertain prior to surgery. Jarnagin *et al*^[4] examined the benefits of preoperative laparoscopy in patients with colorectal metastasis (CRM), and identified five factors that may predict the presence of occult intrahepatic or extrahepatic disease that may make patients unresectable. These factors are the presence of more than one liver tumor, positive node status of primary tumor, disease-free interval of less than 1 year, presence of liver tumor that is larger than 5 cm and carcinoembryonic antigen (CEA) level greater than 200 ng/mL. If any patient has more than 2 of these factors, 42% of the time would have occult disease rendering them unresectable.

Accurate staging of intrahepatic cholangiocarcinoma (IHC) is just as important, as complete resection offers the best long-term survival. Patients with large lesions, positive nodes or multifocal IHC do not benefit from resection^[14]. An adjunct to staging laparoscopy is the laparoscopic ultrasound. The laparoscopic ultrasound is sensitive in detecting parenchymal liver lesions^[15]. Because of this, the routine use of laparoscopy with concomitant laparoscopic ultrasound can save patients from unnecessary laparotomy^[4,14].

If a patient with hepatocellular carcinoma (HCC) is not eligible for liver resection, there are other multimodal

approaches to manage HCC primarily or in conjunction with liver resection or a bridge to transplantation: local ablation with alcohol or radio frequency, chemoembolization, and radioembolization^[16]. The laparoscopic ultrasound is useful in these cases as it allows precise examination of these lesions and the surrounding vessels, and facilitates ultrasound-guided ablation of HCC.

PANCREAS

This section will focus on the role of laparoscopic distal pancreatectomy and pancreaticoduodenectomy, and the alternatives to management of unresectable biliary and duodenal obstructive cancers.

Distal pancreatectomy

Report of the first laparoscopic distal pancreatectomy (LDP) was in 1996^[17,18]. Subsequent studies have demonstrated that laparoscopic distal pancreatectomy is as safe as open distal pancreatectomy^[19]. It is now increasingly performed as the better alternate approach for distal pancreatectomy in selected patients. Two meta-analyses further support that laparoscopic distal pancreatectomy is associated with a significantly lower blood loss and reduced length of stay as compared to open distal pancreatectomy (ODP)^[20,21]. In addition, the Meta-analysis completed by Venkat *et al*^[20] combined four retrospective studies to show that there is no difference in margin positivity between LDP and ODP, but there are more lymph nodes harvested in ODP than LDP. A retrospective study completed by Magge *et al*^[22] compared 62 consecutive patients undergoing ODP or minimally invasive distal pancreatectomy (MIDP), and found the medial lymph node clearance is similar (ODP 12 and MIDP 11) and demonstrate that the rate of pancreatic fistula (ODP 29% and MIDP 21%), and the overall survival after ODP or intended MIDP was equivalent after adjusting for comorbidity and year of surgery.

The rate of postoperative complications after LDP and ODP are similar or less in the LDP group. Nakamura and Nakashima demonstrate this in a meta-analysis. The overall morbidity is significantly lower in the LDP group, and there is no significant difference in mortality. The pancreatic fistula and wound infection rates are significantly lower in the LDP than in ODP groups [OR = 0.34/0.46, 95%CI: (0.20-0.57)/(0.23-0.91); $P < 0.0001/P = 0.03$]. A more recent retrospective American study also has similar findings^[23,24]. The estimated blood loss is less and the need for blood transfusion is less in the LDP group. Interestingly, the rates of grade B and C pancreatic fistulas are also less in the LDP group.

Despite all the current medical advancement, the incidence of pancreatic fistula associated with ODP and LDP can be as high as 30%. The following are some factors and techniques, which have been proposed to lower this rate. Meta-analysis comparing staple *vs* suture closure of pancreatic remnant after distal pancreatectomy demonstrated no difference^[25]. The use of fibrin glue adhe-

sive sealing may prevent postoperative pancreatic fistula formation^[26,27]. A single-blinded, randomized control trial, and subsequent meta-analysis and studies demonstrate that mesh re-enforcement (either with bovine pericardium, Seamguard or Peristrips Dry) decreases the rate of pancreatic fistula formation compared to bare metal staple lines^[28]. This has been challenged, as the use of Seamguard may increase leaks^[29]. In these studies, thick pancreases were excluded from these studies. Eguchi *et al*^[30] demonstrate that the thick pancreas is an independent risk factor for pancreatic fistula formation, and the stapler should be reserved for thin pancreas. The authors suggest that thick pancreases should be over sewn.

Konstantinidis *et al*^[31] reviewed 1705 patient from a clinic pathologic database for pancreatic cancer and identified that patients undergoing R1 resection still have an improved survival compared with patients with locally advanced unresectable pancreatic adenocarcinoma. R0 resections have an improved survival compared with R1 resections, but this survival benefit is lost when the tumor is within 1 mm of the resection margin. Meta-analysis and numerous study demonstrate that the oncological resection margin between LDP and ODP are similar, making LDP a suitable option for the management of pancreatic cancers of the body and tail in selected patients^[32].

The local recurrence of pancreatic cancer is 80% within 2 years after resection with curative intent. Encouraging results from Germany suggest that resection of locally recurring pancreatic cancer is feasible, safe and associated with an improved survival outcome. They evaluated 97 patients from 2001 to 2009, and found that patients with isolated local recurrence who underwent an R0 resection had a median survival of 30.5 mo^[33]. Perhaps the use of laparoscopic surgery may decrease the adhesion formation and facilitate re-do operations.

Controversy still remains over whether small PNET need to be excised or treated non-operatively^[32]. The management of PNET if it is larger than 2 cm, growing, functional or associated with the pancreatic duct, should be resected. A meta-analysis comparing 906 patients with PNET of who 22% underwent LPS and 78% underwent OPS, demonstrated that there is no difference in pancreatic fistula development, operative time or mortality. LPS for PNET is safe and associated with shorter length of stay than OPS^[34].

It was thought that LPD for the management of pancreatic malignancies should be managed in high-volume tertiary referral centers. A retrospective study demonstrates that LDP can be safely and effectively performed by any surgeon comfortable with laparoscopic techniques, and may not require specialized training or a special center, however, the authors also imply that further data are required to make more definitive conclusions^[35].

With the exception of the systemic review and meta-analysis completed by Jin *et al*^[21], most studies demonstrate that the operative time in LDP is significantly longer than in ODP. This is most likely due to a selection bias and an inherent learning curve associated with this

procedure. Interestingly, there is a clockwise technique developed by Asbun and Stauffer, which may be a superior technique with regards to, decreased operative time (182 min), relatively similar pancreatic fistula formation, larger lymph node harvest (14 nodes), and acceptable oncological (negative margins) resection quality. This series ($n = 28$) will need more surgeons to validate the reliable and safe five-step method^[36].

Robot-assisted minimally invasive distal pancreatectomy has been shown to be superior to laparoscopic distal pancreatectomy. It is equivalent to LDPs outcome and safety, and there is a significant reduction in conversion to open resection. As the result, the recovery time is faster. In addition, there is a reduced risk of excessive blood loss, improved lymph node yield, and higher rates of margin negative resections compared to LDP^[37,38]. This is most likely due to the larger field of view. With this in mind, perhaps robotic assisted surgery would be the better operative tool for malignant disease in the future.

Pancreaticoduodenectomy

Laparoscopic pancreaticoduodenectomy (LPD) was first reported in 1994^[18]. The cost analysis of an open pancreaticoduodenectomy (OPD) and LPD are equivalent. While operating time and supply costs are higher for LPD, this is balanced by decreased cost of the postoperative admission^[39].

There are several advantages robotic surgery has over laparoscopic surgery that make it more feasible to complete complex procedures. Although there is a learning curve, there is a larger surgical field than in laparoscopic surgery. A systematic review on robotic pancreaticoduodenectomy completed by an Italian group found that the rate of conversion was 14%, and the overall morbidity rate was reoperation rate was 7.3%^[40]. Data on cost analysis is lacking and further studies are needed to evaluate also the cost-effectiveness of the robotic approach.

Unresectable cancer causing obstruction

It is unclear as to the best management of patients with biliary and duodenal obstruction secondary to malignancy. Multiple systemic reviews have been completed to further determine the best options for these patients.

A meta-analysis of randomized trials comparing immediate stent placement to surgical bypass in the management of unresectable pancreatic and peripancreatic cancer in 379 patients conclude that nearly all patients would benefit from some procedure to manage biliary obstructions, but in patients with low surgical risk, they benefit more from surgery because the risk of recurrence and subsequent hospital utilization was lower than patients with stents^[41]. Although the initial postoperative stay is longer, patient with surgical bypass have significantly longer symptom free survival and fewer hospital readmissions^[42]. They recommend that patients with unresectable disease on exploratory laparotomy and those with no evidence of metastasis are candidates for operative bypass as they have a longer disease survival. Other groups have

not shown much difference between a gastrojejunostomy and stent^[43].

Duodenal and biliary stents are 90% successful with low morbidity, and compared to surgery, lower initial cost and better quality of life^[44]. With the use of expandable stents, the quality of life and hospital visits should improve. According to the SUSTENT study, when they compared the medical effects, quality of life and cost of surgical gastrojejunostomy or endoscopic stent placement for palliation, they demonstrate that despite slow initial symptom improvement, a gastrojejunostomy had better long-term results. Therefore, they also conclude that the surgical gastrojejunostomy is the better option for patients with life expectancy longer than 2 mo, and a stent is preferred for those patients with less than 2 mo life expectancy, as it has better short-term results^[45,46]. A group from China has reported laparoscopic roux-en-y cholangiojejunostomy in 103 patients with good outcomes. Patients with metastatic disease died from cancer, and not postoperative complications. Their complication rate was less than 5%^[47].

Endoscopic management of biliary and duodenal obstructions is an option for patients with unresectable malignant disease with short life expectancy, and an inability to tolerate an operation. Laparoscopic or open gastrojejunostomy and choledochojejunostomy are still effective options for selected patients. A randomized trial comparing laparoscopic bypass surgery to endoscopic procedure would give more information on the best outcome for these patients.

GALLBLADDER

The first laparoscopic cholecystectomy was in the mid 1980's. Doctors Muhe, Perissat, Berci, Cuschieri, Dubois, and Mouret all contributed to the development of this operation, and the beginning of a new era of laparoscopic abdominal surgery^[48,49]. This section will focus on the management of cholecystitis, choledocholithiasis and gallbladder cancer.

Laparoscopic cholecystectomy is the preferred care for cholecystitis, cholelithiasis and biliary colic. It is safe and effective in elective and emergency setting even in the elderly^[50]. Recent Cochrane reviews found that there is no significant difference between early and late laparoscopic cholecystectomy, for acute cholecystitis, in rate of bile duct injury, conversion rate, and operative time. However, the total hospital stay is shorter in the early group than the delayed group by four days. They also found that a laparoscopic cholecystectomy completed 24 h after diagnosis of biliary colic also decreased the morbidity, hospital stay and operating time during the waiting period of 4.2 mo^[51,52]. With regards to the management of choledocholithiasis, whether the stones are managed intraoperative setting or with endoscopic retrograde cholangiopancreatography (ERCP), there is no difference with the patient's final outcome^[53]. In addition, primary closure after laparoscopic common bile duct exploration

reduced hospital stay compared to T-tube drainage^[54]. Post cholecystectomy complications, such as a bile leak, is now frequently managed with ERCP first^[55]. Whether the cholecystectomy is completed *via* single-incision (SILC) or multiple-incisions (MILC), the long-term outcomes are the same. Recently reviewed by a Taiwanese group, they demonstrate that the SILC group had a faster recovery and shorter hospital stay than the MILC group by about one day^[56]. The patients with more challenging gallbladder disease had longer operative times, longer hospital stays and higher conversion rates as compared to the uncomplicated group. Although the SILC group has a better cosmetic outcome, there is a higher hernia rate^[57]. Patients with uncomplicated cholecystitis and choledocholithiasis benefit from laparoscopic cholecystectomy and common bile duct exploration when compared to an open operation. It is the complexity of the gallbladder pathology, which has more of an affect on operative time and hospital stay.

LIVER

In general, surgical resection is preferred to ablative procedures in the treatment of primary and secondary hepatic malignancy^[58,59]. The guiding principles of hepatic resection are the need to leave the patient with at least 30% of functional hepatic reserve and at least 1 cm of tumor-free resection margin for malignant tumors^[60,61]. Since its introduction by Gagner *et al*^[17] in the early 1990s, hepatobiliary and liver transplant surgeons have increasingly adopted laparoscopic liver resection. An international survey completed by a Japanese group revealed that 88% of the participating centers have now adopted the laparoscopic liver resection^[62]. The majority of these centers (76%) limited their indications to left lateral segmentectomy or limited resection of the peripheral parts of the liver. The other quarter of the institutions had applied laparoscopic approach to major hepatectomies or resection of tumors in the posterior part of the liver. Some institutions have also considered the laparoscopic approach to be feasible for donor hepatectomy^[62]. As supported by numerous publications, this is a feasible and safe option for well-selected cases^[62,64].

When planning a laparoscopic liver resection, lesion size, location, indication and surgical competency are all important. A Chinese study shows that laparoscopic liver resection is safe and feasible in patients with HCC with a tumor size of 5-10 cm^[65]. This group also shows that as seen by previous groups, the length of stay is shorter, and the estimated blood loss is similar, and there is a lower post op complication such as wound infection^[64,66,67]. In the past, laparoscopically accessible hepatic segments were in the peripheral segments of the liver (segments II, III, IVb, V, VI). The lesions in the non-laparoscopic segments were high and deep segments in the right side of the liver (segments VI, VII and VIII)^[62,68]. Many groups now report, that all segments of the liver can be approached with laparoscopic techniques^[68,69]. As in any laparoscopic

operation, the extraction wound is taken into consideration when planning the most efficient operation. Although better cosmetic results can be achieved with total laparoscopic method, this may not be feasible each time. Hand-assisted laparoscopic and laparoscopic assisted method are used by surgeons for unique resection such as with cirrhotic livers, laparoscopic resection of tumors in poor locations and living donor hepatectomies^[70]. This study noticed that patients with hand-assisted laparoscopic liver resections had better perioperative outcomes.

Laparoscopic liver resection is safe and appropriate in the management of benign and malignant disease. Parks *et al*^[68], 2013 completed a meta-analysis of long-term outcome comparing laparoscopic to open liver resections for the management of HCC and CRM in 1002 patients. They conclude there is no difference in survival up to a year. A systematic review by Rao *et al*^[64] also demonstrate that laparoscopic liver resection has reduced overall complications, fewer positive margins and less blood transfusion requirements. Intraoperative low blood loss and hemostasis can be successfully achieved with the use of a Pringle maneuver, identification of anatomy, and appropriate use of energy devices, staplers, topical hemostatic agents and pressure^[69]. In addition, Cheung *et al*^[67] demonstrate that not only do patients with laparoscopic liver resections for HCC and CRM have a shorter hospital stay and less blood loss, the operative times are not that much longer, and the patients have a longer disease free survival. This would facilitate future reoperations for recurrent disease^[66]. In the management of colorectal cancer, synchronous colorectal and liver resection has also been demonstrated to be feasible and safe as well^[71].

The management of carcinoid liver metastasis is multimodal. The management of liver metastasis includes medical, radiological and surgical modes. Kandil *et al*^[72] completed a retrospective analysis on 36 patients who had laparoscopic or open resections. The groups were similar in body mass index, tumor size, and incidence of carcinoid syndrome and extent of resection. Interestingly, the laparoscopic time was half that of open procedure time. There is less mean blood loss and shorter hospital stay. In addition, the three-year disease free survival of the laparoscopic group compared to the open group was better (73.3% *vs* 47.8%). These results support that laparoscopic liver resection is the preferred choice in the management of carcinoid liver metastasis^[72].

Hepatic cysts are treated nonoperatively, interventional radiology or with surgery. The management of symptomatic hepatic cysts is almost routinely excised or marsupialized laparoscopically. Bacterial infected cysts are usually treated non-operatively and can be drained percutaneously. Hydatid cysts traditionally have been treated medically and excised. The possibility of rupturing a hydatid cyst and disseminating echinococcus makes percutaneous drainage and laparoscopic resection of these cysts less attractive. However, with multimodal therapy and at specialized centers, laparoscopic resection of hydatid cyst has been successful^[73,74].

Overall, laparoscopic liver resection is feasible and has decreased blood loss and possibly better long term disease free survival when compared to an open operation, and when done by a surgeon skilled in hepatic laparoscopic surgery, in a supportive hospital.

CONCLUSION

Laparoscopic hepatobiliary and pancreas surgery for benign and malignant disease is just as safe and efficacious as open surgery. The benefit of this over open surgery includes smaller incisions, decreased wound infections, decreased blood loss and shorter hospital stay, as the result of a faster recovery rate. The increase in operative time in minimally invasive surgery may be due to the fact that there is a learning curve with each procedure. The use of hand assisted surgery or robotic surgery are useful in the extraction of large specimens and complex operations requiring the creation of multiple anastomoses. Minimally invasive surgery is safe and will be the preferred choice in the management of benign and malignant hepatobiliary and pancreatic disease in the future.

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