

Laparoscopic pancreatoduodenectomy: How far have we come and where are we headed?

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Abstract

Minimally invasive pancreatoduodenectomy is currently a feasible option in selected patients at high volume centers with available expertise. Although the procedure has

been described two decades ago, laparoscopic surgeons have been reluctant to perform it since it is technically demanding. Currently there is no standardized training process for minimally invasive pancreatoduodenectomy and this is required to ensure the safety of the procedure. Even the open pancreatoduodenectomy can be a challenging procedure where the outcome depends much upon the patient volume and surgeon's experience. In the minimally invasive setting, all the current evidence comes from retrospective data with inherent selection bias. Although the proposed benefits have been reported in many series, a randomized trial comparing with the open approach is highly unlikely to happen, given the complexity of pancreatic cancer and patient selection for complex surgery. Rather, in a disease for which cure is an utopian statement, perhaps the ultimate aim of minimally invasive pancreatoduodenectomy can be the improvement in the quality of life. Also further studies are needed to assess the immunologic role affecting the oncologic outcomes in patients undergoing minimally invasive pancreatoduodenectomy. The robotic platforms have got easily accepted since they can overcome some of the limitations of the laparoscopic platforms such as limited range of motion, two dimensional visualization and poor ergonomics. The main limitations of robotic procedures are related to the high costs associated with the system and disposable equipment. Currently evidence is lacking regarding the cost effectiveness of the procedure and also the push from the industry is on rise. All these minimally invasive techniques have a long learning curve and prior extensive experience in hepatopancreatobiliary surgery is mandatory for surgeons embarking on these endeavours.

Key words: Laparoscopic pancreatoduodenectomy; Robotic pancreatoduodenectomy; Minimally invasive pancreatoduodenectomy

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Core tip: This editorial while discussing the evidence and controversies surrounding minimally invasive pancreatoduodenectomy, aims to update the reader about the highest level of evidence accumulated over the past few years. Pancreatoduodenectomy remains a demanding procedure even in the open approach and only few surgeons in high volume centres have published the outcomes following minimally invasive pancreatoduodenectomy. All these reports are retrospective data with inherent problems related to bias. To settle this issue, any randomized trial is unlikely to happen given the complexity of the cancer and patient selection for surgery in a resectable cancer. All these issues have been addressed in this editorial so that the pros and cons of minimally invasive pancreatoduodenectomy have been well conveyed and the reader takes home a balanced message.

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HISTORY OF LAPAROSCOPIC PANCREATODUODENECTOMY

Ever since the first description of laparoscopic pancreatoduodenectomy (LPD) in 1994 by Gagner and Pomp^[1], the procedure has remained a technically challenging one due to many reasons such as difficult access in laparoscopy, daunting task of controlling hemorrhage laparoscopically due to major vascular injury, demanding skills for biliary and pancreatic reconstruction and also the need to maintain oncologic principles. All these aspects require a high level of surgical expertise. While the safety and feasibility of the technique has been established somewhat, only few published series comprise more than 50 patients^[2]. This procedure has been proposed to decrease blood loss, shorten hospital stay, expedite recovery and also shorten time to initiate adjuvant treatment. The ultimate aim of performing minimally invasive pancreatoduodenectomy (PD) should be to perform a better PD with lesser complications and with proven oncologic advantages^[3]. Till date, majority of the reports which have shown comparable outcomes with laparoscopic approach are retrospective and they are inherently prone to selection and publication bias.

LPD: FEASIBILITY TO REFINEMENT

In an early experience, Palanivelu *et al*^[4] reported the safety of this procedure in a series comprising of 42 patients and safe tumour free margins could be obtained in all patients (Table 1). In another series from Mayo clinic^[5], 65 patients underwent LPD with comparable

median operative time, blood loss and morbidity. They have shown that LPD has the same advantages which are seen with other minimally invasive procedures. In another review by Gumbs *et al*^[6] comprising 285 cases of LPD, the rate of conversion to the open approach was 9% with a morbidity and mortality rate of 48% and 2%, respectively. They concluded that laparoscopic pancreatic head resections were feasible with low mortality rates and acceptable morbidity rates. During these early experiences, there was lack of long term follow-up data and also most were small series retrospectively comparing minimally invasive techniques with open techniques. As more and more experience has been gained in these complex procedures, there are reports where even major venous resections have been performed during LPD. In a cohort of 129 patients undergoing LPD, Kendrick *et al*^[7] reported 11 major venous resections with a median operative time of 413 min and 500 mL blood loss without any perioperative mortality.

LPD VS OPEN PD: IS IT COMPARABLE OBJECTIVELY?

With increasing number of surgeons rapidly gaining experience in complex laparoscopic pancreatic techniques, a number of comparative studies have been recently published. In a retrospective series involving 51 consecutive patients who underwent either an open or LPD, Kuroki *et al*^[8] found decreased blood loss in the laparoscopic assisted PD group compared with the open PD group without any significant difference in the postoperative complications. In another series by Asbun *et al*^[3], 215 and 53 patients underwent open PD and LPD respectively. There were significant differences favouring LPD with respect to intraoperative blood loss, length of ICU stay and length of hospital stay (12.4 d vs 8 d). They also observed that the operative time was significantly longer in LPD group (608 min vs 401 min). However no significant differences were observed with respect to pancreatic fistula rate and delayed gastric emptying. Even though the complication rates were similar, the discrepancy in the length of hospital stay could not be explained and this raises the possibility of bias in outcome measurement commonly observed in retrospective studies. With respect to oncologic clearance, there was no difference in resection margin status. Lymph nodal clearance has been shown to be better with the LPD group (23.4 vs 16.8) as well as lower lymph node ratio (0.159 vs 0.241). In a retrospective series involving 905 patients undergoing PD, long term survival was better in patients with decreased lymph node ratio^[9]. The better vision and magnification offered by the laparoscopy might aid in the better nodal clearance and aggressive lymphadenectomy. However further studies are needed to reach firm conclusions. The time to initiation of adjuvant chemotherapy was not affected by the minimally invasive technique and also

Table 1 Retrospective series showing outcomes following Laparoscopic Pancreatoduodenectomy

Ref.	No. of cases	RO rate (%)	Mean operative time (min)	Mean node retrieval	Mean blood loss (mL)	Pancreatic fistula rate (%)	Overall morbidity (%)	Mortality (%)	Mean length of stay (d)
Asbun <i>et al</i> ^[3]	53	95	541	23	195	16.7	24	5.7	8
Kendrick <i>et al</i> ^[5]	62	89	368	15	240	18	42	1.6	7
Palanivelu <i>et al</i> ^[4]	42	100	370	13	65	7	NR	2	10
Croome <i>et al</i> ^[10]	108	78	379	21	492	11	5.6	1	6

NR: Near.

there were no reports of port site metastases. The main contraindications for minimally invasive PD included either major vascular involvement or patients with previous abdominal surgeries. The minimal blood loss associated with LPD could be explained by the precise dissection that could be possible due to the better clarity and magnification offered by the state of the art minimally invasive technology. In addition, human instinct is such that laparoscopic surgeons tend to be inherently extra careful with bleeding since any bleeding can greatly obscure telescopic vision. The conversion to open procedure was usually due to failure to progress or difficulty to control a hemorrhage^[2].

ONCOLOGIC OUTCOMES: ANY BETTER?

In a retrospective series comprising 108 patients undergoing LPD and 214 patients undergoing open PD, Croome *et al*^[10] reported the oncologic advantages over the open approaches. There was no significant difference in the incidence of pancreatic fistula in the LPD vs open group (11% vs 12%). The median time to initiate adjuvant therapy was 48 d in the laparoscopic group and 59 d in the open group. The authors also observed that a significant proportion (12%) of patients in the open PD group had a significant delay in the initiation of adjuvant chemotherapy when compared to the LPD group (5%). Again this observation is surprising given the fact that tumor size and pancreatic fistula rates between both groups were comparable. The overall survival among the two groups was not significantly different. However the progression free survival was in favour of the LPD group. On univariate analysis, significant predictors of survival included tumour size, positive margins, positive nodal status and those patients having delayed initiation of chemotherapy or no chemotherapy at all. Pertinently, with respect to chemotherapy, the recent ESPAC-3 study has shown that overall survival was better determined by the completion of all cycles of chemotherapy rather than the time of initiation as long as it was started within 12 wk^[11].

EVOLUTION OF ROBOTIC PD—HAVE THINGS TRULY PROGRESSED FURTHER?

The well known and accepted advantages of robotic systems with improved 3-dimensional imaging, enhanced

dexterity, better visualization with magnification and improved ergonomics fare better than the conventional laparoscopic platform in minimal access approaches^[12]. There are a lot of interesting observations from the initial experience of using robotics for PD. Giulianotti *et al*^[13] reported in 2010 the first series of 50 patients who underwent robotic assisted PD and showed the operative feasibility of this approach. Few investigators have compared robotic assisted PD with open PD. In the retrospective series reported by Chalikonda *et al*^[14] comparing robotic assisted PD with open PD, the duration of surgery was significantly longer in the robotic group but the overall blood loss and the duration of hospital stay (9.79 d vs 13.26 d) were lower. Similar results were reported by Zhou *et al*^[15] on a cohort of 16 patients, though the number was smaller. Based on these data, the robotic approach has been shown to be associated with faster recovery times but longer operative times. With regards to the oncologic outcomes, Zeh *et al*^[16] have reported on 50 consecutive patients who underwent robotic assisted PD where the mean lymph node retrieval was 17 and the overall margin negative resection rate was 89%. Another Italian study has reported on 34 patients who underwent robotic PD without any conversion despite three patients requiring vascular reconstruction^[17]. There were no reports of bile leaks and this has been attributed to the precision of robotic suturing in this retrospective study. Although the earlier series of robot assisted PD had documented conversion rates of upto 37%, this rate has decreased with increasing experience^[18]. The associated decreased blood loss can have an impact in terms of cancer recurrence^[19]. In a recent report by Wada *et al*^[20], the use of surgical microscope during reconstruction has shown to decrease the incidence of pancreatic fistula. The precise fine movement in multiple axes as offered by the robotic technology along with its magnified 3-D visual has been claimed to reduce the incidence of fistulas following pancreatic reconstruction in robotic PD. In the Italian cohort^[17], there were no clinically significant pancreatic fistulas even though the majority had soft pancreas and small ducts. Quite a significant amount of extra time gets utilized in instrument traffic (upto 1 h in the Italian series) and this necessitates the need for further technical improvisation in order to improve the effective utilization of operative room time. In another major series of 132 patients undergoing robotic PD, Zureikat

et al.^[21] have found the median operative time to be 527 ± 103 min and mortality rate of 1.5%. The conversion rate is equivalent or lower than the conversion rates observed in early series of LPD. They concluded that safety and feasibility metrics including the low incidence of conversion support the robustness of this platform with no extra risks apart from inherent risks of this new technology.

CHALLENGES FACING MINIMALLY INVASIVE PD

The minimally invasive approach has been propagated mainly for the advantage of lesser morbidity and reduced hospital stay thereby decreasing cost of treatment. Due to certain inherent disadvantages with LPD such as prolonged operating times, high cost and technical complexity as well as the low quality of evidences for its advantages, currently it may not be possible to recommend it as the standard of care^[3]. While well conducted randomized trials have proven the advantages of laparoscopic resections in colonic cancer, the low prevalence of resectable pancreatic cancer, coupled with the complexity of the procedure and the challenges it faces, is likely to ensure that a adequately powered randomized trial is unlikely to happen in the near future^[10]. Further, laparoscopic major venous resections can be endeavoured only with extensive laparoscopic experience in pancreatic resections and this demands a long learning curve in a high volume centre. The excess mean operative cost of robotic PD was up to 6193 Euros which is likely to be questioned in the current era^[17]. In addition to various challenges mentioned above, cost is also expected to remain a major challenge for minimally invasive PD.

CONCLUSION

Minimally invasive PD is currently a feasible option in selected patients at high volume centers with available expertise. Although the procedure has been described two decades ago, laparoscopic surgeons have been reluctant to perform it since it is technically demanding. Currently there is no standardized training process for minimally invasive PD and this is needed to ensure the safety of the procedure. Even the open PD can be a challenging procedure where the outcome depends much upon the patient volume and surgeon's experience. Even for the open approach, the learning curve extends till the first 60 cases for improvement in measured outcomes^[22]. Standardization and service reconfiguration has been shown to improve outcomes following open PD^[23]. In the minimally invasive setting, all the current evidence unfortunately comes from retrospective data with obvious selection bias. Rather, in a disease for which cure is an utopian statement, perhaps the ultimate aim of minimally invasive PD can be the improvement in the quality of life. Further

studies are needed to define its role concerning quality of life. The robotic platforms have got easily accepted since they can overcome some of the limitations of the laparoscopic platforms such as limited range of motion, two dimensional visualization and poor ergonomics. The main limitations of robotic procedures are related to the high costs associated with the system and disposable equipment. Currently evidence is lacking regarding the cost effectiveness of the procedure and also the push from the industry is on rise. Clearly, with increasing data in this era of information explosion, the surgical fraternity needs to evolve a consensus about minimally invasive PD.

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