Robotic pancreaticoduodenectomy versus laparoscopic pancreaticoduodenectomy

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Abstract: Robotic and laparoscopic pancreaticoduodenectomy have both been shown to have similar outcomes compared to the open technique, however, few large trials have compared the efficacy and outcomes of RPD and LPD. As an oncological operation, the key considerations for minimally invasive pancreaticoduodenectomy are peri-operative outcomes, oncologic outcomes, and feasibility. The optimal approach should offer non-inferior mortality, morbidity, and oncologic outcomes compared to the open approach. The new approach should also be technically feasible. RPD has been shown in the literature to be as safe, with comparable morbidity and mortality, as OPD and with no significant difference compared to LPD. RPD is less likely than LPD to convert to open, reducing potential operative times and complications. High volume centers have begun to demonstrate shorter operative times with RPD than LPD, a trend that is expected to progress as the technology and technique is more widely adopted. Similar high volume centers have also experienced less transfusion requirements with RPD than LPD and significantly less estimated blood loss with either MIPD compared with OPD. Oncologic outcomes such as R0 resection rates and lymph node harvest are similar between RPD and OPD both in the largest multi-center trial by Zureikat *et al.* and in database analyses. Robotic surgery in general has advantages of magnification, greater degrees of freedom, and high fidelity training modules compared to laparoscopy. LPD has been hindered in part by its technical difficulty with most studies including less than 50 patients each. Both RPD and LPD have been shown to be safe and effective alternatives to OPD. There is limited high level evidence comparing RPD and LPD but RPD offers several advantages. We expect that RPD will become increasingly widespread as more data emerges and the technology continues to mature.

Keywords: Whipple; pancreaticoduodenectomy; robotic pancreaticoduodenectomy; laparoscopic pancreaticoduodenectomy (LPD); outcomes

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Introduction

Since the first description of the laparoscopic pancreaticoduodenectomy (LPD) for chronic pancreatitis by Gagner and Pomp in 1994, there has been a wave of advances in the field of minimally invasive hepato-pancreatico-biliary (HPB) operations (1). The first robotic distal pancreatectomy (RDP) was performed by Melvin *et al.* in 2003. The same year, an Italian group led by Giulianotti described a 13-patient series of oncological pancreatic resections including two entirely robotic pancreaticoduodenectomies (RPD) (2,3). As robotic surgical systems have continued to develop and evolve in the past decade, it has been applied more frequently to previously laparoscopic operations with great strides in the fields of colorectal, urological, gynecological, and bariatric surgery.

The same momentum has not translated as quickly in the field of pancreatic resection nor in HPB operations generally. Very few large multi-center trials have been performed in comparing the efficacy and outcomes of LPD, RPD, and open pancreaticoduodenectomy (OPD); no randomized controlled trials assessing all three are described in the literature (4). This review will explore the perioperative outcomes, oncologic outcomes, and feasibility of RPD compared to LPD.

Perioperative outcomes

Mortality and overall morbidity

LPD and RPD have comparable overall morbidity and mortality rates with OPD (5-9). A 2019 retrospective review of 2014–2016 American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP), a comprehensive national surgical database, found a decreased 30-day overall morbidity of minimally invasive pancreaticoduodenectomy (MIPD), including both laparoscopic and robotic data, as compared with OPD, the gold standard. After risk adjustment, the 30-day mortality for MIPD was 1.8% compared with 2.1% with OPD (CI: 0.21–1.81, P=0.38). Overall 30 day morbidity was 51.1% with MIPD and 56.9% with OPD (CI: 0.51–0.87, P<0.01); severe postoperative morbidity including sepsis, surgical site infection, hemorrhage requiring transfusion, and pancreatic fistula was also significantly lower in the MIPD group by 7.2% (CI: 0.44–0.77, P<0.01), largely because OPD required more transfusion (5). The non-inferiority of RPD to OPD has been best described in a large multi-center retrospective analysis from the University of Pittsburgh with Zureikat *et al*. finding reductions in major complications (CI: 0.47–0.85, P=0.003) with RPD. On univariate analysis, operative technique was not associated with 90-day mortality (RPD OR 0.67, P=0.23, OPD OR 0.70, P=0.27) (4). Nassour *et al*. reviewed the 2014–2015 pancreas-targeted ACS-NSQIP database and identified 235 LPD and 193 RPD in this period. Within this cohort, the 30-day mortality for LPD was 2.6% and 1.0% for RPD (P=0.303), overall complication (LPD 48.9%, RPD 54.9%, P=0.218) and major complication (LPD 40.9%, RPD 42.0%, P=0.815) were also not significantly different. These results have been confirmed in several other studies (6-8). RPD is non-inferior to the gold standard approach in terms of overall morbidity including major complication and in short-term overall mortality, affirming the safety of the robotic approach. RPD has also been demonstrated to have no statistically significant major morbidity or mortality difference with LPD.

Conversions

Unplanned conversion to open is one potential surrogate marker for feasibility and successful MIPD. Across a variety of gastrointestinal operations, laparoscopic and robotic approaches have a lower incidence of surgical site complication compared to an open approach (10-12). Unplanned conversion to open from a minimally invasive approach is liable to negate the potential benefits of a totally minimally invasive approach. In a 2017 retrospective review of 2014–2015 ACS-NSQIP data, Zimmerman *et al*. and Zureikat *et al*. separately demonstrated a significant increase in unplanned conversion to open (UCO) with a LPD compared to RPD; UCO incidence was as high as 31.9% with LPD and nearer to 15% with RPD (6,13). A systematic review in 2016 by Wright *et al*. confirmed these results and found that UCO was especially lower in RPD for pancreatic adenocarcinoma (14). Multivisceral resection, dyspnea, vascular resection and laparoscopic approach were all independent predictors for UCO in a multivariate analysis (8). In fact, with MIPD, conversion to open resulted in a significant increase in LOS (7 days purely MIS versus 9 days with conversion to open, OR 3.4, P=0.04) and discharge to a non-home destination (6.0% versus 15.7% with conversion to open, OR 3.25, P=0.04) in an propensity score matched ACS-NSQIP analysis by Hester *et al*. Conversion to open was accompanied by an increase in overall and major complication including hemorrhage (15). A decrease in UCO with RPD has many down-stream benefits, clearly favoring this approach over LPD.

Operating room time

Unplanned conversion to open prolongs operative time with ACS-NSQIP data finding the median operative time for an UCO PD of 444 minutes compared with 360 minutes for a pure open approach and 425 minutes for a minimally invasive approach. In comparing LPD and RPD, the NSQIP database reveals no difference in mean operative time (LPD 424 minutes, RPD 399 minutes, P=0.588);

however, these data are biased by selection and include many centers performing well-below the necessary number of MIPD to achieve proficiency (8,9,16). At single centers past the learning curve for RPD, RPD has been shown to in fact be faster than LPD (RPD 387 minutes, LPD 442 minutes, P=0.015) (17). Operative time is a known predictor for postoperative complication (18,19). As the technology matures and more surgeons become accustomed to robotic HPB surgery, the operative time and associated morbidity is predicted to continue to improve.

Post-operative pancreatic fistula

Considering the 2014–2015 ACS-NSQIP data, no significant difference was identified between MIPD and OPD for International Study Group on Pancreatic Fistula clinically relevant postoperative pancreatic fistula (CR-POPF) on risk-adjusted multivariate analysis (OR 1.05 CI: 0.87–1.26, P=0.60) (20). In a large systematic review and meta-analysis, Kostakis *et al*. found no significant difference for pancreatic leak between LPD and RPD (CI: 0.85–1.39, P=0.52) nor for bile leak (CI: 0.17–1.71, P=0.30). RPD was also found to be non-inferior to OPD for pancreatic leak in a meta-analysis of 13 studies with 1086 RPDs and 10526 OPDs (CI: 0.70–1.24, P=0.64) (6,21,22). Similar trends are highlighted in recent ACS-NSQIP data, with approximately a 20% postoperative pancreatic fistula rate in both LPD and RPD (P=0.075) (8). Cai *et al*., at a high volume MIPD center, were able to demonstrate a reduction in CR-POPF with RPD compared to OPD (6.7% versus 15.8%, P<0.001) even when propensity score matched while a 2017 meta-analysis by Shin *et al*. was not able to identify any trials with better CR-POPF rates in LPD compared to OPD (23). Given the severity of CR-POPF and its sequelae, the ability of RPD to reduce its incidence represents a major benefit of the approach.

Estimated blood loss

Laparoscopic and robotic approaches reduce blood loss (EBL) in a variety of gastrointestinal operations compared to the equivalent open approach including pancreaticoduodenectomies (7). Decreased blood loss is associated with improved survival in pancreaticoduodenectomy, and thus EBL is a key factor when deciding on the non-inferiority of alternatives to OPD (24). Superiority of blood loss with MIPD compared to OPD has been widely described (25-27). Nassour *et al*. found no difference in hemorrhage requiring transfusion between LPD and RPD in the ACS-NSQIP database (18.7% versus 14.0%, P=0.190), although, there was a greater rate of vascular resection and multivisceral resection in the laparoscopic cohort. In a large meta-analysis, however, the weighted mean difference (WMD) for EBL in LPD was −240.34 compared to open (CI: −579.29, 98.60) compared with −205.70 with RPD (CI: −367.58, −43.82, P=0.022) suggesting that RPD may in fact be associated with less blood loss than a laparoscopic approach. A recent systematic review and meta-analysis of 44 studies found significantly less transfusion requirements with RPD than LPD (OR 0.60, P=0.002) (28). This trend is further supported by data from single-center studies at high volume pancreas centers (17).

Hospital admission

Length of stay (LOS) has extensive quality implications and is one of the main advantages of minimally invasive surgery. Zimmerman *et al*. found no significant difference in LOS between LPD and RPD, but a significant reduction when either MIPD approach was compared to OPD (P=0.381 comparing LPD and RPD, P<0.001 and P=0.002 when LPD and RPD compared with OPD) (6). Interestingly, a meta-analysis of the PLOT, PADULAP, and LEOPARD-2 trials by Nickel *et al*. demonstrated no difference between LPD and OPD LOS (MD −2.68, CI: −8.10, 2.74, P=0.33) (29). Meta-analysis of five distal pancreatectomy studies reported a statistically shorter LOS of 1 day with robotic assist compared to laparoscopic approach (WMD −0.97, CI: −1.73, −0.22, P=0.01) (30). Some single-center trials have also found decreased LOS with RPD compared in LPD; in a Chinese trial of 52 patients, mean LOS was 17 days for RPD and 24 for LPD (P=0.012). Adjusting for cultural impact on LOS, these data suggest that in a mature pancreas center, the benefits of minimally invasive surgery are significant compared to open pancreas resection and the robotic approach may yield even greater benefit.

Oncologic outcomes

Multi-institutional studies

To be considered a reasonable alternative to an established standard, new operative approaches should demonstrate at a minimum, non-inferior oncological outcomes. Oncological indications for pancreaticoduodenectomy include pancreatic adenocarcinoma (PDAC) and periampullary carcinomas.

Previously identified predictors of survival are time to adjuvant chemotherapy, completion of 6-month course of adjuvant therapy, and an R0 margin at the index operation. Three RCTs, PLOT, PADULAP, and LEOPARD-2, found no difference between LPD and OPD for R0 resection (OR 1.43, CI: 0.71–2.88, P=0.32) nor for lymphadenectomy (MD −0.17, CI: −3.15, 2.82, P=0.91) (29,31). In the largest multi-center retrospective study, Zureikat *et al*. found no difference in R1 margins nor adequate lymph node harvest in 522 operations on multivariate analysis when comparing RPD to OPD for PDAC (4). A recent 2019 retrospective review of the American College of Surgeons National Cancer Database (NCDB) revealed a R0 rate of 81.9% with RPD compared to 78.7% with OPD (P=0.396) (7). The 2010–2015 NCDB cohort of pancreatic cancers also demonstrated no difference between MIPD and OPD for R1 margins, adequate lymphadenectomy, or receipt of adjuvant chemotherapy. A multivariate, subgroup analysis of the RPD and LPD cohorts during the same period found no difference in margin status (OR 1.05, CI: 0.78–1.41, P=0.755), adequate lymphadenectomy (OR 0.83, CI: 0.64–1.08, P=0.176), or receipt of adjuvant chemotherapy (OR 0.78, CI: 0.60–1.04, P=0.095) (32). Overall, MIPD has non-inferior short-term oncologic outcomes compared to OPD, with no significant differences between RPD and LPD; additional research is required to understand the long-term consequences.

Single institution studies

Several high volume pancreas centers have published long-term experiences with MIPD. From the University of Pittsburgh, Girgis *et al*. reviewed institutional data across five years and in comparing 163 RPDs with 198 OPDs, found no difference in R0 resection (78.5% *vs*. 78.3%, P=0.955), predicted receipt of adjuvant chemotherapy (OR 0.918, CI: 0.609–1.383, P=0.681), and time to adjuvant chemotherapy (65 *vs*. 62 days, P=0.056) (7). An older review of the Mayo Clinic outcomes by Croome *et al*. compared LPD with OPD found no difference in R0 resection (P=0.81) and faster time to adjuvant chemotherapy with LPD (48 *vs*. 59 days, P=0.001) (33). MIPD has comparable oncological outcomes with OPD at technically mature institutions.

Feasibility

Proficiency in RPD has been an area of significant inquiry given the novelty of the platform and the complexity of the operation. There are several described advantages: magnification, stereoscopic vision, 7 degrees of freedom, portable training modules, and training programs which facilitate ease of learning and operating with the robotic approach (34). In applying any new approach to an operation, understanding the learning curve is crucial. In a single-center analysis of three surgeons performing OPD, 60 cases was identified as the number required to reduce EBL, shorten operative time, and achieve superior oncologic outcomes (35). These are similar to described case load to achieve proficiency with RPD (4). The optimal number of cases to achieve comparable results between LPD and OPD is less clear; however, Wang *et al*. and Speicher *et al*. suggesting 40–50 cases as necessary to achieve proficiency (29). Notably, a recent meta-analysis of single-arm LPD and RPD studies found only 11 studies with at least 50 LPDs, highlighting the technical difficulty and limited scope of the approach (28).

Discussion

With the widespread proliferation of robotic surgery, the time has come to bring pancreatic resection into the future. The benefits of robotic surgery are well-described, including reduced postoperative ileus, better recovery time, decreased length of stay, and reduced incisional hernia. Laparoscopic surgery was first introduced to pancreatic resection in the 1990s; however, outside of distal pancreatectomy, it has failed to make significant headway in the realm of pancreaticoduodenectomy; while in a relatively short time, robotic pancreaticoduodenectomy has become a rapidly adopted approach. For a new approach to be considered viable, it must demonstrate non-inferiority or superiority with regards to perioperative outcomes, safety, oncological outcomes, and feasibility. Robotic pancreaticoduodenectomy fulfills all of these criteria. The laparoscopic approach has some of the same advantages as RPD compared to open, better EBL, reduced LOS, and comparable oncologic outcomes; however, the data is limited and at high risk of selection bias and the learning curve unclear. While proponents of the laparoscopic approach cite the increased cost and operative time of RPD, cost is predicted to decrease as robotic technology evolves and new systems enter the market. Operative time of RPD has also seen improvements as more centers achieve proficiency. The advantages of the robotic platform are numerous; wristed instruments, stereoscopic vision, ergonomic comfort, high fidelity simulation, and dual-consoles all make RPD a more attractive approach compared with traditional laparoscopy; however, access and availability may be more limited outside the United States. This continues to be a developing area of research and further studies comparing laparoscopic, robotic and open approaches should be conducted. The long-term outcomes comparing these three approaches is also unclear. Based on our current understanding of the technology, robotic pancreaticoduodenectomy offers an attractive, safe, and feasible alternative to the open and laparoscopic operations.

Conclusion

There is an absence of level one data comparing RPD to LPD. National multi-institutional studies show many similarities in RPD and LPD compared to open, but the most striking difference is the two- to three-fold increase in conversion in LPD compared to RPD. With the knowledge that conversion increases mortality, OR time, and LOS this repeated finding cannot be ignored. Single institution comparisons are also limited due to the fact that most centers perform either RPD or LPD but rarely both. One study does show that in a center that can do both LPD and RPD, there is a time advantage to RPD which is one of the major criticisms of robotics. The data in this area still needs more time to mature. The lack of randomized data opens criticism of a selection bias and national studies lack granularity to assess training and proficiency. However, the body of data supports feasibility and safety of RPD and LPD with an advantage to RPD.

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Footnote

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