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**Contemporary review of minimally invasive pancreaticoduodenectomy**

Dai R *et al.* Contemporary review of minimally invasive pancreaticoduodenectomy

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**Abstract**

***AIM***

To assess the current literature describing various minimally invasive techniques for and to review short-term outcomes after minimally invasive pancreaticoduodenectomy (PD).

***METHODS***

PD remains the only potentially curative treatment for periampullary malignancies, including, most commonly, pancreatic adenocarcinoma. Minimally invasive approaches to this complex operation have begun to be increasingly reported in the literature and are purported by some to reduce the historically high morbidity of PD associated with the open technique. In this systematic review, we have searched the literature for high-quality publications describing minimally invasive techniques for PD-including laparoscopic, robotic, and laparoscopic-assisted robotic approaches (hybrid approach). We have identified publications with the largest operative experiences from well-known centers of excellence for this complex procedure. We report primarily short term operative and perioperative results and some short term oncologic endpoints.

***RESULTS***

Minimally invasive techniques include laparoscopic, robotic and hybrid approaches and each of these techniques has strong advocates. Consistently, across all minimally invasive modalities, these techniques are associated less intraoperative blood loss than traditional open PD (OPD), but in exchange for longer operating times. These techniques are relatively equivalent in terms of perioperative morbidity and short term oncologic outcomes. Importantly, pancreatic fistula rate appears to be comparable in most minimally invasive series compared to open technique. Impact of minimally invasive technique on length of stay is mixed compared to some traditional open series. A few series have suggested that initiation of and time to adjuvant therapy may be improved with minimally invasive techniques, however this assertion remains controversial. In terms of short-terms costs, minimally invasive PD is significantly higher than that of OPD.

***CONCLUSION***

Minimally invasive approaches to PD show great promise as a strategy to improve short-term outcomes in patients undergoing PD, but the best results remain isolated to high-volume centers of excellence.

**Key words:** Pancreaticoduodenectomy; Whipple; Pancreatic adenocarcinoma; Minimally invasive surgery; Periampullary malignancy

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**Core tip:** In this contemporary review, we systematically review current literature regarding minimally invasive techniques and outcomes for pancreaticoduodenectomy. This review will be highly educational to providers-surgical and nonsurgical alike-who care for patients with resectable periampullary malignancies.

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**INTRODUCTION**

Pancreaticoduodenectomy (PD) remains the only potentially curative therapy for periampullary malignancies, including, most commonly, pancreatic adenocarcinoma. Despite advances in minimally invasive techniques over the last 2 decades, the vast majority of PDs are still performed with the standard open technique (OPD) that has evolved from the original Whipple procedure described in 1935[1]. Even with modern improvements in perioperative care, contemporary complication rates after OPD range from 25% to 65%, and thus highlight the need for surgical innovation aimed at reducing perioperative morbidity[2-9].

In general, minimally invasive techniques have been shown to provide shorter postoperative length of stay, decreased postoperative pain, fewer wound complications, and quicker return to daily activities. Despite this evidence for the benefit of minimally invasive surgery across a broad array of surgical procedures, minimally invasive approaches to PD have not been widely adopted and remain confined to large tertiary referral centers with highly experienced surgeons[10,11]. PD is a highly complex operation with a steep learning curve. This complexity has led some to question whether the advantages of minimally invasive approaches, seen in other general surgical procedures, translate to PD. In this review, we evaluate the published literature to date on contemporary approaches to minimally invasive PD-including laparoscopic, robotic, and hybrid approaches-in regards to perioperative morbidity and short-term outcomes.

**MATERIALS AND METHODS**

Appropriate articles were identified by manually searching through PubMed and Google Scholar databases between January 1st, 2005 to January 1st, 2015, using “laparoscopic” or “robotic” or “minimally invasive” AND “pancreaticoduodenectomy” or “Whipple.” Subsequent full-text papers were screened, and only the most recent publications from individual groups were used. We only included manuscripts that distinguished among or singularly published data from laparoscopic, robotic or hybrid PDs. Similarly, we only focused on studies which included greater than 5 patients, in order to assure the surgeon’s experience with the technique. We only included studies which distinguished among laparoscopic, robotic or robotic assisted laparoscopic PDs (RALPDs).

Study variables included: (1) Minimally invasive technique (laparoscopic, robotic, or hybrid approach); (2) number of patients; (3) age range; (4) BMI range (5) American Society of Anesthesiologist physical status classification[12]; (6) estimated blood loss; (7) operative time; (8) length of stay; (9) pancreatic fistula rate; and (10) postoperative mortality. The data are represented as average ± standard deviation (SD), unless otherwise indicated in the text or table.

Average American Society of Anesthesiologist physical status classification (ASA) is used as a surrogate for an independent evaluation of how well the patient presents prior to the procedure[13]. The higher the score, the more complicated the patient, where ASA I is defined as a normal healthy patient, and ASA III is someone with severe systemic disease. Overall complication is defined, if available, as the number of patients with post-operative complications with a graded Clavien-Dindo classification (≥ grade I)[14]. Postoperative mortality is defined as surgical-related deaths within 30 d of procedure.

***Surgical techniques***

This manuscript focuses on primarily three minimally invasive surgical techniques for PD. The first is LPD, which uses laparoscopic instrumentation to dissect, extract, and reconstruct intestinal continuity[15]. Robotic PD (RPD) uses a robotic system (da Vinci Surgical System) in lieu of handheld laparoscopic instruments (Intuitive Surgical, Inc., Sunnyvale, CA)[16]. Finally, hybrid RALPDs uses both laparoscopic and robotic techniques for various steps in the PD, most commonly laparoscopic dissection and specimen extraction followed by robotic reconstruction[17].

**RESULTS**

***LPD***

Since its introduction by Gagner and Pomp[18] in 1994, wide-spread adoption of LPD has been limited by a steep learning curve confounded by modest case volumes seen in most centers. Despite these challenges, LPD has clearly been shown to be technically feasible and is purported to have tremendous potential in improving patient outcomes. Six LPD studies without robotic components were analyzed, two of which directly compare laparoscopic with open techniques[18,19,22-26]. There were no distinct differences in the patient populations (Table 1).

In the two studies which compared LPD outcomes to matched open cases at the same institution, the authors reported advantages of LPD over open PDs (OPD)[19,26]. Asbun *et al*[19] noted that LPD had significantly less intraoperative blood loss (*P* < 0.001), reduced rate of transfusion (*P* < 0.001), length of hospital stay (*P* < 0.001), and length of ICU stay (*P* < 0.001). Both Asbun *et al*[19] and Zureikat *et al*[25] noted that operative time was significantly higher for LPD, but there were no differences in overall complications, pancreatic fistula rate, or delayed gastric emptying[19,26].

There were no significant differences in oncologic outcomes in these two studies. Asbun *et al*[19] found that LPD had higher number of lymph nodes retrieved (*P* = 0.007), more favorable lymph node ratio (*P* < 0.001), less estimated blood loss, transfusions, and length of stay for laparoscopic procedures, while Zureikat *et al*[25] found no significant difference in R0 resection rate, lymph node harvest, and estimated blood loss, transfusions, and length of stay.

Of the four studies that examined only LPD, all found that LPD was safe and feasible[22-25]. Kendrick *et al*[23] reported that only 3 of the 65 patients enrolled in the study converted to OPD, and of the 62 patients who underwent LPD, 26 experienced post-operative morbidity, including pancreatic fistula (*n* = 11), delayed gastric emptying (*n* = 9), bleeding (*n* = 5), and deep vein thrombosis (*n* = 2). There was one postoperative mortality within 30-d of operation. Median operating time reported was 368 min (range 258-608) and median length of hospital stay was 7 d (range 4-69 d)[23].

Dulucq *et al*[22] reported three of the 25 patients enrolled in the study converted to OPD, and of the 22 patients who underwent unconverted LPD, seven patients experienced postoperative complications and one patient died of a cardiac event three days after an uncomplicated surgery. A mean of 18 ± 5 lymph nodes were retrieved for malignant lesions, and all resected margins were free. Only two patients with metastatic disease received adjuvant therapy. The mean hospital stay was 16.2 ± 2.7 d. Mean operating time was 287 ± 39 min[22].

Palanivelu *et al*[24] also reported 5-year survival rates for the 42 patients enrolled in the study. They found that after 5-years, 32% survival over all malignancies, 30.7% with ampullary adenocarcinoma, 33.3% for pancreatic cystadenocarcinoma, 19.1% for pancreatic head adenocarcinoma, and 50% for common bile duct adenocarcinoma. The study presented with similar perioperative statistics with 8 patients with comorbidities, including gastrojejunostomy obstruction, postoperative pancreatic fistula, postoperative bile leak, pulmonary complications, intraabdominal abscess, and deep vein thrombosis. Mean operating time was 370 min, with 13 mean lymph nodes harvested, and 65 mL mean of estimated blood loss[24].

Pugliese *et al*[18] found that of the 19 patients undergoing LPD, 6 patients required conversion to laparotomy, 3 for bleeding and 3 for difficulties in dissection. The study recorded no mortality, but noted that 3 of the converted PDs resulted in complications including bile leakage, hemorrhage, and pulmonary embolism. The mean operating time was 461 ± 90 min, and hospital stay of 18 ± 7 d. An average of 13 ± 4 (range 4-22) lymph nodes were harvested[18].

***RPD***

Robotic technology has many of the advantages ascribed to laparoscopic surgery by virtue of using laparoscopic ports and minimal incision size and was first reported by Guilianotti *et al*[19] in 2003. Robotic instrumentation provides 3-dimensional visibility, increased degrees of freedom, and improved ergonomics though possibly less haptic advantage[20,21]. Advocates of robotic surgery suggest that the advantages in robotics provide obvious benefits for complex procedures such as PD surgeries[27]. However there is little comparative data available to support the routine use of robotics over laparoscopy for pancreatic resections (Table 2).

This review describes four robotics experiences, of which two incorporated comparison studies with OPD[26-29].Buchs *et al*[26] found that despite the RPD group having statistically significant older (63 years old RPD *vs* 56 years old OPD; *P* = 0.04) and heavier patients (BMI 27.7 RPD *vs* 24.8 OPD; *P* = 0.01), with a higher American Society of Anesthesiologist score (RPD 2.5 *vs* OPD 2.15; *P* = 0.01), when compared to OPD group, there were no significant differences in complications, mortality rates, and length of hospital stays between the two groups[27]. The study found that RPD surprisingly had shorter operative time (444 min *vs* 559 min; *P* = 0.0001), reduced blood loss (387 mL *vs* 827 mL; *P* = 0.0001), and higher number of lymph nodes harvested (16.8 *vs* 11; *P* = 0.02).

Similarly, Zhou *et al*[28] found that RPD group had longer operative times than OPD (718 min RPD *vs* 420 min OPD; *P* = 0.011), but less intraoperative blood loss (153 mL RPD *vs* 210 mL OPD; *P* = 0.04), fewer complications (25% RPD *vs* 75% OPD, *P* = 0.05), and decreased hospital stay (27.5 h RPD *vs* 96 h, *P* = 0.000). There was no significant difference in R0 resection rate between the two groups.

Boggi *et al*[27] reported for 34 patients undergoing RPD, the mean operating time was 597min (range 420-960 min) and mean intraoperative blood loss was 220 mL (range 150-400 mL), with 4 patients requiring blood transfusions. Nineteen of the 34 patients in the study developed postoperative complications (utilizing the Clavien-Dindo classification), five of which had a classification of III or higher. The mean number of lymph nodes retrieved in the study was 32 (range 15-76). Thirty-day mortality was 0%[27].

Chan *et al*[29] reported 55 patients undergoing robotic hepatobiliary and pancreatic surgeries, of which eight were pancreaticoduodenectomies. Of the patients undergoing pancreatic resections, Chan *et al*[29] found that the operating time had a media of 478 min, ranging from 270-692 min, with blood loss of 200 mL (range 30-300 mL). There were 4 complications resulting in pancreatic fistula and biliary fistula, but all were treated conservatively and healed without any significant sequelae. There was no mortality in the postoperative hospital stay of a median 12 d (range 6-21 d).

**RALPD:** Hybrid techniques (RALPD) include a combination of laparoscopic and robotic utilization for PD. We report five hybrid studies here, three of which are comparison studies to OPD[30-34]. In all 3 comparison studies, RALPD demonstrated significantly lower intraoperative blood loss. In the first reported RALPD study, Chalikonda *et al*[30] found that there was a significant increase in operative time (476.2 min RALPD *vs* 366.4 min OPD; *P* = 0.005), but decreased length of stay for RALPD (9.79 d RALPD *vs* 13.26 d OPD; *P* = 0.043)[25]. The study found that there was no significant difference between the two techniques in postoperative morbidity (30% RALPD *vs* 44% OPD; *P* = 0.14), or reoperation (6% RALPD *vs* 24% OPD; *P* = 0.17). The study noted that there were 3 patients (12%) undergoing RALPD that were converted to OPD due to excessive bleeding (Tables 3).

Similarly, Kuroki *et al*[32] found decreased intraoperative blood loss with RALPD (376 mL RALPD *vs* 1509.5 mL OPD; *P* < 0.01), but there was also a significantly higher number of blood transfusions compared with OPD (0 blood transfusions in RALPD *vs* 13 in OPD; *P* < 0.01)[32]. The study found that there was no significant difference between the two techniques in operative time or postoperative complications.

Lai *et al*[33] reported that RALPD had a significantly longer operative time (491.5 min RALPD *vs* 264.9 min; *P* = 0.01), decreased blood loss (247 mL RALPD *vs* 774.8 mL OPD; *P* = 0.03), and shorter hospital stay (13.7 d RALPD *vs* 25.8 d OPD; *P* = 0.02)[33]. Conversion rate from RALOPD to OPD was 5%, and the study did not find a significant difference between the two groups in overall complication rates (50% RALPD *vs* 49.3%; *P* = 0.95), mortality rates (0% RALPD *vs* 3% OPD; *P* = 0.43), rate of reoperation (2 or 10% RALPD *vs* 3 or 4.5% OPD; *P* = 0.04), R0 resection rate (11 or 73.3% RALPD *vs* 34 or 64.1% OPD; *P* = 0.92), and harvested lymph node numbers (10 ± 6 RALPD *vs* 10 ± 8 OPD; *P* = 0.99).

Of the 2 noncomparison studies, Giulianotti *et al*[31] published the largest series of robotic pancreatic surgery to date with 134 patients, 60 of which were PD[31]. This study reported similar outcomes to previous studies, including mean operative time with 331 min (range 75-660 min), mean length of hospital stay at 9.3 d (range 3-85 d), postoperative complication rate at 26%, and mortality rate of 2.23% (3 patients).

Zeh *et al*[34] examined 50 patients undergoing RALPD, 8 of which required conversion to open procedure (16%). Overall, 28 patients (56%) experienced postoperative complications, 13 of which were Clavien I/II. Intraoperative blood loss had a median of 350 mL (interquartile range: 150-625), with 11 patients (22%) requiring transfusions. The median length of stay reported by the study was 10 d (IQR 8-13). The median number of lymph nodes collected was 18 (IQR 5) and Zeh *et al*[34] report that 89% of the resections had negative margins.

***Pancreatic fistula***

Pancreatic leak at the pancreaticojejunostomy anastomosis is one of the most serious and common postoperative complications after PD, and can lead to erosion of adjacent tissues, bleeding from large vessels, severe pancreatitis, peritonitis, and sepsis. The complexity of this anastomosis has often been cited as the primary obstacle to widespread adoption of minimally invasive techniques for PD. Broadly, there did not appear to be significant differences in pancreatic fistula rates between minimally invasive and open techniques. Pancreatic leaks can be classified according to the International Study Group on Pancreatic Fistula criteria[35]. In Asbun *et al*[19], there were 29 (13.5%) pancreatic fistulas in the open group (Grade A = 14, B = 5, C =10), and 7 (13.2%) in the laparoscopic group (Grade A = 3, B = 1, C = 3), with a nonsignificant *P*-value[19]. Similarly, there is no significant difference in the pancreatic fistula rate between robotic and open groups as demonstrated in Buchs *et al*[26], where both open and robotic had 8 pancreatic fistulas at a rate 21% (Grade A = 5, B = 1, C = 2) and 18% (Grade A = 4, B = 3, C = 1) respectively, with a *P* = 1. The same could be seen between open and RAL groups, such as in Chalikonda *et al*[30], where there were 5 (16.7%) in the open group (Grade B = 2, C = 5), and 2 (6.7%) in the RAL group (Grade B = 1, C = 1)[30].

***Cost analysis***

In 2013, Mesleh *et al*[36] published an analysis of a single institution analysis of the cost of LPD *vs* OPD. Using a similar dataset as Asbun *et al*[19], Mesleh *et al*[36] found that of 123 patients who underwent PD, with 48 OPD (39%) and 75 LPD (61%), there was no significant difference in overall cost of LPD compared to OPD, because of increased postoperative cost of OPD.

Consistent with other studies, Mesleh *et al*[36] found that the intraoperative cost of LPD was significantly higher than that of OPD, due to increased equipment expense and mean operative time (*P* < 0.0001, OPD 355 min, range 199-681; LPD 551 min, range 390-819). Similarly, they determined that both OPD and LPD had similar rates of morbidity of 31% for both groups, with median hospital stay for OPD at 8 d (range 5-63), and 7 d (range 4-68) for LPD (*P* = 0.5). However in postoperative categories, OPD represented slightly higher cost per unit in anesthesia, critical care, pathology, pharmacy, nursing, and radiology. Because admission accounted for 65%-70% of the total cost, the increased postoperative cost of OPD balanced the excess intraoperative cost of LPD.

Similarly, Boggi *et al*[27] reported a cost analysis of RPD compared to OPD, and found that RPD’s intraoperative cost significant exceeds that of OPD by approximately 6193 euros, or $5034.90 based on the currency exchange rate used in the study on 15 August 2012 (http://www.x-rates.com/calculator.html). In the United States, according to Chalikonda *et al*[30], the cost of disposables of robotic and laparoscopic equipment can be as high as $4000-5000 per case, plus the associated significant higher operative time.

Thus, in an era of limited health care dollars, cost issues associated with minimally invasive techniques, especially robotic platforms, are important considerations as these techniques are adopted more broadly into less experienced centers.

With the emergence of newer technologies and improving minimally invasive techniques, it is important to understand the potential benefits of laparoscopic, robotic, and robotic assisted techniques. From this systematic review of the data presented, LPD, RPD, and RALPD in general appear to have less intraoperative blood loss than OPD, but in exchange for longer operating times. However, it is important to realize that all of these studies are subject to heavy selection bias, with the most difficult cases still typically being performed with open technique.

Most studies have failed to show any significant difference between the open and minimally invasive techniques in terms postoperative mortality and overall complications, though mortality may be higher with minimally invasive PD at less experienced centers[37,38]. This issue is an extraordinarily important consideration for centers with lower surgeon volume and potentially less expertise with minimally invasive techniques. Regarding pancreatic fistula, there does not appear to be a significant difference between minimally invasive and open techniques. As the learning curve improves and technology improves, differences between techniques may begin to emerge. This issue has been most consistently touted by robotics advocates. Finally, minimally invasive techniques also appear to be equivalent in terms of short-term oncologic endpoints.

In the context of broader oncologic issues, Some studies suggest that more favorable short-term outcomes including decreased pain, quicker return to daily activities, and potentially fewer wound issues may favor increased utilization of and shorter time to adjuvant therapy[39-42]. This issue too remains somewhat unproven but is an important consideration given the dismal outcomes with surgery alone for this disease[24,43-45].

In summary, there remain many hurdles before the widespread use of laparoscopic and RPD take hold, the most significant of which is the steep learning curve associated with minimally invasive PD[46,47]. Currently, minimally invasive PDs require extensive training and advanced equipment, and so are only performed by select surgeons for select patients at select tertiary centers[48]. Robotic approaches may shorten the learning curve for minimally invasive PD but this has yet to be definitely proven[49]. Even for OPD, the learning curve is steep, and a robust literature has shown tremendous variations in outcome for patients, depending on surgeon volume, hospital volume, and multidisciplinary collaboration. Thus, minimally invasive approaches to PD appear to be feasible and safe in the hands of highly experienced surgeons at centers of expertise, but widespread adoption remains a challenge given the steep learning curve, limitations of technology, and important cost considerations in an era of limited health care resources.

**COMMENTS**

***Background***

Pancreaticoduodenectomy (PD) remains the only potential curative therapy for periampullary malignancies, including, most commonly, pancreatic adenocarcinoma. Despite advances in minimally invasive techniques over the last 2 decades, the vast majority of PDs are still performed with a standard open technique (OPD) that has evolved from the original Whipple procedure described in 1935**.**

***Research frontiers***

Even with modern improvements in perioperative care, contemporary complication rates after OPD range from 25% to 65%, and thus highlight the need for surgical innovation aimed at reducing perioperative morbidity.

***Innovations and breakthroughs***

Despite a growing body of evidence supporting minimally invasive techniques to expedite post-operative recovery, decrease postoperative pain and reduce wound complications, minimally invasive approaches to PD have not been widely adopted and remain confined to large tertiary referral centers with highly experienced surgeons.

***Applications***

In general, minimally invasive techniques have been noted to provide shorter hospitalizations, fewer post-operative complications, and less time to adjuvant therapy. However, whether the advantages of minimally invasive approaches, seen in other general surgical oncologic procedures, translate to PD remains unclear. Here, the authors review current data regarding the applicability of minimally invasive approaches to PD.

***Peer-review***

This is an interesting and timely study.

**REFERENCES**

1 **Schnelldorfer T**, Sarr MG. Alessandro Codivilla and the first pancreatoduodenectomy. *Arch Surg* 2009; **144**: 1179-1184 [PMID: 20026839 DOI: 10.1001/archsurg.2009.219]

2 **Stauffer JA**, Nguyen JH, Heckman MG, Grewal MS, Dougherty M, Gill KR, Jamil LH, Scimeca D, Raimondo M, Smith CD, Martin JK, Asbun HJ. Patient outcomes after total pancreatectomy: a single centre contemporary experience. *HPB* (Oxford) 2009; **11**: 483-492 [PMID: 19816612 DOI: 10.1111/j.1477-2574.2009.00077.x]

3 **Cirocchi R**, Partelli S, Trastulli S, Coratti A, Parisi A, Falconi M. A systematic review on robotic pancreaticoduodenectomy. *Surg Oncol* 2013; **22**: 238-246 [PMID: 24060451 DOI: 10.1016/j.suronc.2013.08.003]

4 **Cameron JL**, Riall TS, Coleman J, Belcher KA. One thousand consecutive pancreaticoduodenectomies. *Ann Surg* 2006; **244**: 10-15 [PMID: 16794383 DOI: 10.1097/01.sla.0000217673.04165.ea]

5 **Del Chiaro M**, Segersvärd R. The state of the art of robotic pancreatectomy. *Biomed Res Int* 2014; **2014**: 920492 [PMID: 24982913 DOI: 10.1155/2014/920492]

6 **Cameron JL**, He J. Two thousand consecutive pancreaticoduodenectomies. *J Am Coll Surg* 2015; **220**: 530-536 [PMID: 25724606 DOI: 10.1016/j.jamcollsurg.2014.12.031]

7 **Tran TB**, Dua MM, Worhunsky DJ, Poultsides GA, Norton JA, Visser BC. The First Decade of Laparoscopic Pancreaticoduodenectomy in the United States: Costs and Outcomes Using the Nationwide Inpatient Sample. *Surg Endosc* 2016; **30**: 1778-1783 [PMID: 26275542 DOI: 10.1007/s00464-015-4444-y]

8 **Doula C**, Kostakis ID, Damaskos C, Machairas N, Vardakostas DV, Feretis T, Felekouras E. Comparison Between Minimally Invasive and Open Pancreaticoduodenectomy: A Systematic Review. *Surg Laparosc Endosc Percutan Tech* 2016; **26**: 6-16 [PMID: 26836625 DOI: 10.1097/SLE.0000000000000228]

9 **Wright GP**, Zureikat AH. Development of Minimally Invasive Pancreatic Surgery: an Evidence-Based Systematic Review of Laparoscopic Versus Robotic Approaches. *J Gastrointest Surg* 2016; **20**: 1658-1665 [PMID: 27412319 DOI: 10.1007/s11605-016-3204-1]

10 **Strijker M**, van Santvoort HC, Besselink MG, van Hillegersberg R, Borel Rinkes IH, Vriens MR, Molenaar IQ. Robot-assisted pancreatic surgery: a systematic review of the literature. *HPB* (Oxford) 2013; **15**: 1-10 [PMID: 23216773 DOI: 10.1111/j.1477-2574.2012.00589.x]

11 **Jossart GH**, Gagner M. Pancreaticoduodenal resection. *J Hepatobiliary Pancreat Surg* 2000; **7**: 21-27 [PMID: 10982587 DOI: 10.1007/s005340000070021.534]

12 **Dripps RD**. New classification of physical status. *Anesthesiol* 1963; **24**: 111

13 **Fitz-Henry J**. The ASA classification and peri-operative risk. *Ann R Coll Surg Engl* 2011; **93**: 185-187 [PMID: 21477427 DOI: 10.1308/147870811X565070a]

14 **Clavien PA**, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, de Santibañes E, Pekolj J, Slankamenac K, Bassi C, Graf R, Vonlanthen R, Padbury R, Cameron JL, Makuuchi M. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg* 2009; **250**: 187-196 [PMID: 19638912 DOI: 10.1097/SLA.0b013e3181b13ca2]

15 **Ammori BJ**, Ayiomamitis GD. Laparoscopic pancreaticoduodenectomy and distal pancreatectomy: a UK experience and a systematic review of the literature. *Surg Endosc* 2011; **25**: 2084-2099 [PMID: 21298539 DOI: 10.1007/s00464-010-1538-4]

16 **Zureikat AH**, Breaux JA, Steel JL, Hughes SJ. Can laparoscopic pancreaticoduodenectomy be safely implemented? *J Gastrointest Surg* 2011; **15**: 1151-1157 [PMID: 21538192 DOI: 10.1007/s11605-011-1530-x]

17 **Nguyen KT**, Zureikat AH, Chalikonda S, Bartlett DL, Moser AJ, Zeh HJ. Technical aspects of robotic-assisted pancreaticoduodenectomy (RAPD). *J Gastrointest Surg* 2011; **15**: 870-875 [PMID: 21512900 DOI: 10.1007/s11605-010-1362-0]

18 **Gagner M**, Pomp A. Laparoscopic pylorus-preserving pancreatoduodenectomy. *Surg Endosc* 1994; **8**: 408-410 [PMID: 7915434]

19 **Asbun HJ**, Stauffer JA. Laparoscopic vs open pancreaticoduodenectomy: overall outcomes and severity of complications using the Accordion Severity Grading System. *J Am Coll Surg* 2012; **215**: 810-819 [PMID: 22999327 DOI: 10.1016/j.jamcollsurg.2012.08.006]

20 **Zhang J**, Wu WM, You L, Zhao YP. Robotic versus open pancreatectomy: a systematic review and meta-analysis. *Ann Surg Oncol* 2013; **20**: 1774-1780 [PMID: 23504140]

21 **Zenoni SA**, Arnoletti JP, de la Fuente SG. Recent developments in surgery: minimally invasive approaches for patients requiring pancreaticoduodenectomy. *JAMA Surg* 2013; **148**: 1154-1157 [PMID: 24154790 DOI: 10.1001/jamasurg.2013.366]

22 **Dulucq JL**, Wintringer P, Mahajna A. Laparoscopic pancreaticoduodenectomy for benign and malignant diseases. *Surg Endosc* 2006; **20**: 1045-1050 [PMID: 16736311 DOI: 10.1007/s00464-005-0474-1]

23 **Kendrick ML**, Cusati D. Total laparoscopic pancreaticoduodenectomy: feasibility and outcome in an early experience. *Arch Surg* 2010; **145**: 19-23 [PMID: 20083750 DOI: 10.1001/archsurg.2009.243]

24 **Palanivelu C**, Jani K, Senthilnathan P, Parthasarathi R, Rajapandian S, Madhankumar MV. Laparoscopic pancreaticoduodenectomy: technique and outcomes. *J Am Coll Surg* 2007; **205**: 222-230 [PMID: 17660068 DOI: 10.1016/j.jamcollsurg.2007.04.004]

25 **Zureikat AH**, Nguyen KT, Bartlett DL, Zeh HJ, Moser AJ. Robotic-assisted major pancreatic resection and reconstruction. *Arch Surg* 2011; **146**: 256-261 [PMID: 21079111 DOI: 10.1001/archsurg.2010.246]

26 **Buchs NC**, Addeo P, Bianco FM, Ayloo S, Benedetti E, Giulianotti PC. Robotic versus open pancreaticoduodenectomy: a comparative study at a single institution. *World J Surg* 2011; **35**: 2739-2746 [PMID: 21947494 DOI: 10.1007/s00268-011-1276-3]

27 **Boggi U**, Signori S, De Lio N, Perrone VG, Vistoli F, Belluomini M, Cappelli C, Amorese G, Mosca F. Feasibility of robotic pancreaticoduodenectomy. *Br J Surg* 2013; **100**: 917-925 [PMID: 23640668 DOI: 10.1002/bjs.9135]

28 **Zhou NX**, Chen JZ, Liu Q, Zhang X, Wang Z, Ren S, Chen XF. Outcomes of pancreatoduodenectomy with robotic surgery versus open surgery. *Int J Med Robot* 2011; **7**: 131-137 [PMID: 21412963 DOI: 10.1002/rcs.380]

29 **Chan OC**, Tang CN, Lai EC, Yang GP, Li MK. Robotic hepatobiliary and pancreatic surgery: a cohort study. *J Hepatobiliary Pancreat Sci* 2011; **18**: 471-480 [PMID: 21487754 DOI: 10.1007/s00534-011-0389-2]

30 **Chalikonda S**, Aguilar-Saavedra JR, Walsh RM. Laparoscopic robotic-assisted pancreaticoduodenectomy: a case-matched comparison with open resection. *Surg Endosc* 2012; **26**: 2397-2402 [PMID: 22437947 DOI: 10.1007/s00464-012-2207-6]

31 **Giulianotti PC**, Sbrana F, Bianco FM, Elli EF, Shah G, Addeo P, Caravaglios G, Coratti A. Robot-assisted laparoscopic pancreatic surgery: single-surgeon experience. *Surg Endosc* 2010; **24**: 1646-1657 [PMID: 20063016 DOI: 10.1007/s00464-009-0825-4]

32 **Kuroki T**, Adachi T, Okamoto T, Kanematsu T. A non-randomized comparative study of laparoscopy-assisted pancreaticoduodenectomy and open pancreaticoduodenectomy. *Hepatogastroenterology* 2012; **59**: 570-573 [PMID: 21940382 DOI: 10.5754/hge11351]

33 **Lai EC**, Yang GP, Tang CN. Robot-assisted laparoscopic pancreaticoduodenectomy versus open pancreaticoduodenectomy--a comparative study. *Int J Surg* 2012; **10**: 475-479 [PMID: 22732431 DOI: 10.1016/j.ijsu.2012.06.003]

34 **Zeh HJ**, Zureikat AH, Secrest A, Dauoudi M, Bartlett D, Moser AJ. Outcomes after robot-assisted pancreaticoduodenectomy for periampullary lesions. *Ann Surg Oncol* 2012; **19**: 864-870 [PMID: 21947670 DOI: 10.1245/s10434-011-2045-0]

35 **Bassi C**, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, Neoptolemos J, Sarr M, Traverso W, Buchler M. Postoperative pancreatic fistula: an international study group (ISGPF) definition. *Surgery* 2005; **138**: 8-13 [PMID: 16003309 DOI: 10.1016/j.surg.2005.05.001]

36 **Mesleh MG**, Stauffer JA, Bowers SP, Asbun HJ. Cost analysis of open and laparoscopic pancreaticoduodenectomy: a single institution comparison. *Surg Endosc* 2013; **27**: 4518-4523 [PMID: 23943116 DOI: 10.1007/s00464-013-3101-6]

37 **Sosa JA**, Bowman HM, Gordon TA, Bass EB, Yeo CJ, Lillemoe KD, Pitt HA, Tielsch JM, Cameron JL. Importance of hospital volume in the overall management of pancreatic cancer. *Ann Surg* 1998; **228**: 429-438 [PMID: 9742926]

38 **Adam MA**, Choudhury K, Dinan MA, Reed SD, Scheri RP, Blazer DG, Roman SA, Sosa JA. Minimally Invasive Versus Open Pancreaticoduodenectomy for Cancer: Practice Patterns and Short-term Outcomes Among 7061 Patients. *Ann Surg* 2015; **262**: 372-377 [PMID: 26158612 DOI: 10.1097/SLA.0000000000001055]

39 **Oshiro EO**, Dziakova J, Lasses Martinez B. Outcomes of hepatopancreatic robotic surgery: update from the literature-pancreatic surgery. *OA Robotic Surgery* 2014; **2**: 1-7

40 **Oettle H**, Post S, Neuhaus P, Gellert K, Langrehr J, Ridwelski K, Schramm H, Fahlke J, Zuelke C, Burkart C, Gutberlet K, Kettner E, Schmalenberg H, Weigang-Koehler K, Bechstein WO, Niedergethmann M, Schmidt-Wolf I, Roll L, Doerken B, Riess H. Adjuvant chemotherapy with gemcitabine vs observation in patients undergoing curative-intent resection of pancreatic cancer: a randomized controlled trial. *JAMA* 2007; **297**: 267-277 [PMID: 17227978 DOI: 10.1001/jama.297.3.267]

41 **Neoptolemos JP**, Stocken DD, Friess H, Bassi C, Dunn JA, Hickey H, Beger H, Fernandez-Cruz L, Dervenis C, Lacaine F, Falconi M, Pederzoli P, Pap A, Spooner D, Kerr DJ, Büchler MW. A randomized trial of chemoradiotherapy and chemotherapy after resection of pancreatic cancer. *N Engl J Med* 2004; **350**: 1200-1210 [PMID: 15028824 DOI: 10.1056/NEJMoa032295]

42 **Vanderveen KA**, Chen SL, Yin D, Cress RD, Bold RJ. Benefit of postoperative adjuvant therapy for pancreatic cancer: A population-based analysis. *Cancer* 2009; **115**: 2420-2429 [PMID: 19301434 DOI: 10.1002/cncr.24269]

43 **Nussbaum DP**, Penne K, Stinnett SS, Speicher PJ, Cocieru A, Blazer DG, Zani S, Clary BM, Tyler DS, White RR. A standardized care plan is associated with shorter hospital length of stay in patients undergoing pancreaticoduodenectomy. *J Surg Res* 2015; **193**: 237-245 [PMID: 25062813 DOI: 10.1016/j.jss.2014.06.036]

44 **Lesurtel M**, Cherqui D, Laurent A, Tayar C, Fagniez PL. Laparoscopic versus open left lateral hepatic lobectomy: a case-control study. *J Am Coll Surg* 2003; **196**: 236-242 [PMID: 12595052 DOI: 10.1016/S1072-7515(02)01622-8]

45 **Giger U**, Michel JM, Wiesli P, Schmid C, Krähenbühl L. Laparoscopic surgery for benign lesions of the pancreas. *J Laparoendosc Adv Surg Tech A* 2006; **16**: 452-457 [PMID: 17004867 DOI: 10.1089/lap.2006.16.452]

46 **Gumbs AA**, Rodriguez Rivera AM, Milone L, Hoffman JP. Laparoscopic pancreatoduodenectomy: a review of 285 published cases. *Ann Surg Oncol* 2011; **18**: 1335-1341 [PMID: 21207166 DOI: 10.1245/s10434-010-1503-4]

47 **Pilka R**, Marek R, Dzvinčuk P, Kudela M, Neubert D. ["Learning curve" robotic radical hysterectomy compared to standardized laparoscopy assisted radical vaginal and open radical hysterectomy]. *Ceska Gynekol* 2013; **78**: 20-27 [PMID: 23607379]

48 **Speicher PJ**, Nussbaum DP, White RR, Zani S, Mosca PJ, Blazer DG, Clary BM, Pappas TN, Tyler DS, Perez A. Defining the learning curve for team-based laparoscopic pancreaticoduodenectomy. *Ann Surg Oncol* 2014; **21**: 4014-4019 [PMID: 24923222 DOI: 10.1245/s10434-014-3839-7]

49 **Shakir M**, Boone BA, Polanco PM, Zenati MS, Hogg ME, Tsung A, Choudry HA, Moser AJ, Bartlett DL, Zeh HJ, Zureikat AH. The learning curve for robotic distal pancreatectomy: an analysis of outcomes of the first 100 consecutive cases at a high-volume pancreatic centre. *HPB* (Oxford) 2015; **17**: 580-586 [PMID: 25906690 DOI: 10.1111/hpb.12412]

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| **Table 1 Laparoscopic procedures** | | | |  |  |  |  |  |  |  |  |  |  |  |
| **Ref.** | **Year** | **Robotic, open, Lap, or RAL** | **No. of patients** | **Age of patients** | **BMI of patients** | **ASA classification** | **EBL (mL)** | **Transfusio*n* (#)** | **Op time (min)** | **Conversion (#)** | **Overall complications (# of patients)** | **Panc fistula** | **Length of stay** | **Postop death** |
| **Asbun *et al*[19]** | **2012** | **Lap** | **53** | **62.9 ± 14.14** | **27.64 ± 27.64** | **2.73** | **195 ± 136** | **17** | **541 ± 88** | **Counted as open** | **13** | **7** | **8 ± 3.2** | **3** |
| **Dulucq *et al*[22]** | **2006** | **Lap** | **25** | **621 ± 14** | **NR** | **1.391 ± 0.5** | **107 ± 48** | **3** | **2871 ± 39** | **3** | **7** | **0** | **16.2 ± 2.7** | **0** |
| **Kendrick *et al*[23]** | **2010** | **Lap** | **65** | **661** | **261** | **31** | **2401** | **NR** | **3681** | **3** | **11** | **NR** | **71** | **1** |
| **Palanivelu *et al*[24]** | **2007** | **Lap** | **42** | **61** | **NR** | **Only I and II** | **65** | **NR** | **370** | **0** | **8** | **3** | **10.2** | **1** |
| **Pugliese *et al*[18]** | 2008 | Lap | 19 | 64 ± 12 | < 35 | 2.3 | 180 |  | 461 | 6 | 7 | 3 | 19 | 0 |
| **Zureikat *et al*[16]** | **2011** | **Lap** | **14** | **69.8 ± 10.2** | **28.5** | **2.64** | **3001** | **4** | **4561** | **2** | **9** | **5** | **81** | **1** |

1Indicates statistically significant compared to open procedures. RAL: Robotic Assisted Laparoscopy; BMI: Body Mass Index; ASA: American Society of Anaesthesiologists physical status classification; EBL: Estimated Blood Loss; NR: Not reported.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
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| **Table 2 Robotic procedures** | | |  |  |  |  |  |  |  |  |  |  |  |  |
| **Ref.** | **Year** | **Robotic, open, Lap, or RAL** | **No. of patients** | **Age of Patients** | **BMI of patients** | **ASA classification** | **EBL (mL)** | **Transfusion (#)** | **Op time (min)** | **Conversion (#)** | **Overall complications (# of patients)** | **Panc fistula** | **Length of stay** | **Postop death** |
| **Boggi *et al*[27]** | **2013** | **Robotic** | **34** | **601** | **24.41** | **2.82** | **220** | **4** | **517.9** | **0** | **19** | **13** | **23** | **0** |
| **Buchs *et al*[26]** | **2011** | **Robotic** | **44** | **63 ± 14.5** | **27.7 ± 5.4** | **2.5 ± 0.5** | **387 ± 334** | **10** | **444 ± 93.5** | **NR** | **16** | **8** | **13 ± 7.5** | **2** |
| **Chan *et al*[29]** | **2011** | **Robotic** | **8** | **71.5** | **NR** | **NR** | **200** | **NR** | **478** | **0** | **4** | **0** | **12** | **0** |
| **Zhou *et al*[28]** | **2011** | **Robotic** | **8** | **64.4 ± 9.1** | **NR** | **NR** | **153.8 ± 43.4** | **NR** | **718.8 ± 186.7** | **0** | **2** | **NR** | **16.38 ± 4.1** | **0** |

1Indicates statistically significant compared to open procedures. RAL: Robotic Assisted Laparoscopy; BMI: Body Mass Index; ASA: American Society of Anaesthesiologists physical status classification; EBL: Estimated Blood Loss; NR: Not reported.

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| **Table 3 Robotic assisted procedures** | | | |  |  |  |  |  |  |  |  |  |  |  |
| **Ref.** | **Year** | **Robotic, open, Lap, or RAL** | **Number of patients** | **Age of Patients** | **BMI of patients** | **ASA classification** | **EBL (mL)** | **Transfusion (#)** | **Op time (min)** | **Conversion (#)** | **Overall complications (# of patients)** | **Panc fistula** | **Length of stay** | **Postop death** |
| **Chalikonda *et al*[30]** | **2012** | **RAL** | **30** | **62** | **24.8** | **2.6** | **485** | **NR** | **476** | **3** | **9** | **2** | **9.79** | **1** |
| **Giulianotti *et al*[31]** | **2010** | **RAL** | **60** | **58** | **NR** | **NR** | **394** | **6** | **421** | **11** | **No PD only** | **19** | **22** | **2** |
| **Kuroki *et al*[32]** | **2012** | **RAL** | **20** | **71.2 ± 8.8** | **21.9** | **1.5 ± 0.6** | **376.6** | **0** | **656.6** | **NR** | **9** | **12** | **NR** | **NR** |
| **Lai *et al*[33]** | **2012** | **RAL** | **132** | **66.4** | **NR** | **1.9** | **247** | **NR** | **491.5 ± 94** | **1** | **10** | **7** | **13.7 ± 6.1** | **0** |
| **Zeh *et al*[34]** | **2012** | **RAL** | **50** | **68 ± 16** | **27 ± 5** | **2.6** | **3501** | **11** | **5681** | **8** | **28** | **11** | **101** | **1** |

1Indicates statistically significant compared to open procedures. RAL: Robotic Assisted Laparoscopy; BMI: Body Mass Index; ASA: American Society of Anaesthesiologists physical status classification; EBL: Estimated Blood Loss; NR: Not reported.