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# Robotic-assisted minimally invasive pancreas surgery. Review



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Minimally invasive techniques have been increasingly used in oncologic surgery and pancreatic surgery in particular [1, 2]. Minimally invasive pancreatectomy (MIP) has been performed with increasing frequency in all pancreatic pathologies, including pancreatic neuroendocrine tumors (PNETs), including pancreaticoduodenectomy (PD), distal pancreatectomy (DP), and pancreatic enucleation [3, 4].

Robotic-assisted surgery using the DaVinci platform has accelerated the adoption of MIP. The proportion of robotic DP between 2015 and 2016 was nearly 4 times greater than between 2010 and 2012 (16 % vs 4 %), with a similar increase in proportion of robotic PD (7 % vs 2 %) over the same time frame [1]. Advantages of robotic surgery over laparoscopy include three-dimensional visualization, increased degrees of motion with endo-articulation, stable camera platform, surgeon ergonomics, and single surgeon's ability to control four instruments. Systematic adoption of MIP has been facilitated by the creation of multiple multicenter training programs in robotic DP and PD, aiming to standardize the oncologic safety and technical performance of these operations [5, 6].

Maintaining the quality of oncologic pancreatectomy with continued uptake of minimally invasive surgery remains the most critical challenge going forward. Variation in surgical quality directly impacts locoregional recurrence and long-term survival in patients with colorectal cancer [7]. In pancreatic cancer, obtaining a margin-negative resection is an independent predictor of survival [8]. In PD, complete clearance of

the lateral aspect of the superior mesenteric artery (SMA) is critical in improving chances of R0 resection [9]. Whether surgeons beginning to adapt MIP will be able to sustain these technical requirements are paramount to broader success of this approach. Given these concerns, the US Food and Drug Administration has cautioned against the use of robotic-assisted surgery for oncologic indications, given a lack of evidence demonstrating equivalent overall survival and oncologic outcomes [10].

Evidence supporting the association between MIP and decreased length of stay, lower blood loss, and equivalent complication rates has largely been reported at high-volume centers with experienced surgeons [11]. The Miami Guidelines for Minimally Invasive Pancreas Resection recommended minimally invasive DP in experienced hands for benign or low-grade malignant tumors suggest it is an equivalent approach in pancreas ductal adenocarcinoma and that insufficient data exist to recommend minimally invasive PD [12]. These international expert guidelines note that randomized controlled studies are needed for both DP and PD.

Perioperative multidisciplinary planning is the key to success of both open and MIP. Perioperative assessment of cardiovascular, nutritional, and functional status is paramount to both short-term and long-term outcomes after pancreatectomy, regardless of approach. Evidence continues to accumulate demonstrating the added value of nutritional evaluation

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and prehabilitation before pancreatectomy to enhance postoperative functional recovery [13]. In addition, in our experience, consistent operating room teams including nursing staff, surgical technicians, and anesthesiologists for MIP ensures the safest possible perioperative course.

Although the indications for MIP are the same to the open approach, careful case selection for MIP ensures adequate safety and success especially early in the learning curve. No randomized controlled data exist to guide patient selection, and one recent survey across Europe demonstrated that patient selection was largely driven by personal experience, rather than data [14]. We believe that evaluation of patient and surgical factors is critical in selecting the appropriate cases for MIP.

Patients at the extremes of body mass index (BMI) may pose technical challenges for both robotic and laparoscopic approaches. BMI has not shown to be associated with increased perioperative complications, particularly after minimally invasive DP, but may present added technical challenge in manipulation of the colonic mesentery and mobilization of the proximal jejunum [15]. Indeed, internal adiposity rather than BMI itself is more of a problem in MIS approach. Particularly in robotic approach, subcutaneous fat and abdominal thickness has small impact on surgical difficulty [16]. Preoperative exercise program with weight reduction diet would make the operation safer in morbidly obese patients by reducing internal obesity and creating more surgical space with pneumoperitoneum [17]. In low BMI patients, adequate port spacing and intrabdominal surgical working room may present a challenge.

Prior history of pancreatitis, metallic biliary stent placement, and receipt of radiation therapy anecdotally increases difficulty of MIP due to desmoplastic changes surrounding pancreas and vascular structures, although severity of such desmoplastic change is difficult to expect before surgery. If radiographically evident pancreatitis is seen, waiting for 8 to 12 weeks before attempting resection is encouraged. After administration of radiation therapy, it is recommended to wait less than 12 weeks before attempting MIP. Prior surgery history may increase complexity and operative time due to potentially lengthy lysis of adhesions. Particularly early in the learning curve when MIP has increased operative length, the addition of extended adhesiolysis is not recommended. Prior Roux-en-Y gastric bypass additionally adds complexity to operative conduct during minimally invasive PD.

Severe cardiopulmonary disease limiting pneumoperitoneum is a contraindication. Risks and benefits of MIS approach should be carefully considered for patients with marginal renal function as pneumoperitoneum reduces venous return and may affect renal arterial flow.

The need for multi-visceral or major vascular resection should represent a relative contraindication to MIP, especially early in the procedural learning curve. Although the robotic approach is technically feasible for vascular reconstruction, the lack of «surgeon's left hand» to control bleeding when it is needed is critical concern for safety in MIP. A. H. Zureikat et al. [11] demonstrated unchanged perioperative outcomes with increasingly complex R-PD, involving vascular resection, over the first 500 cases at their institution. Although these types of resections are not contraindications at highly experienced centers, they should be undertaken with caution. Tumors which require resection of the portal or superior mesenteric vein should be approached open outside of highly selected centers in highly selected circumstances. A thorough review of high-quality CT scan with arterial and portal venous phases is critical in planning of operative approach for MIP. Replaced or aberrant vascular anatomy should be identified and taken into account in selecting patients for MIP. Replaced right hepatic artery while increasing the complexity of resection is not an absolute contraindication unless involved in the tumor process [18]. For surgeons at the beginning of their learning curve selection of cases with imaging suggestive of dilated pancreatic and bile ducts facilitates ease of reconstruction and may minimize the risk of postoperative pancreatic or biliary fistulas.

Volume-outcome relationships in gastrointestinal surgery, including pancreatic surgery, have been widely studied [19, 20]. Although the case volumes of specific surgeries have been reported as meaningful in overcoming the learning curve of a new procedure, it is intuitive that experience with similarly complex foregut gastrointestinal procedures can accelerate the mastery of a similar procedure. In the Netherlands, L. A. D. Busweiler et al. [21] reported that the composite volume of gastric, esophageal, and pancreatic cancer resections at a given institution correlated with improvements in oncologic outcomes as well as overall survival after surgery for gastric cancer.

One of the largest obstacles to implementation of an MIP program is the learning curve, particularly in PD. As surgeons have been performing laparoscopic surgery

for far long, more data exist for the learning curve in laparoscopic PD. This previous work has demonstrated three phases in development of technical proficiency in laparoscopic PD: the initial learning period, technical competence, and challenging period — with step-wise decreases in blood loss, length of stay, and operative time and increases in lymph node harvest [22]. A wide variety of case volume has been reported as necessary for overcoming the learning curve in laparoscopic PD, from 10 to 60 cases, with most authors suggesting around 60 to 80 cases [23, 24]. Similarly, the learning curve needed to produce proficiency in robotic PD has been reported around 80 cases, with early optimization of blood loss and conversion to open around 20 cases, decreased rates of pancreatic fistula (POPF) and operative time after 40 and 80 cases, respectively [25]. The surgical group at the University of Pittsburgh has developed a robotic pancreatectomy program optimized to overcome this lengthy learning curve, with robust simulation and shared operative responsibilities [26, 27].

Minimally invasive DP follows a similar, though shorter, learning curve. In a recent meta-analysis K. S. Chan et al. [28] demonstrated both laparoscopic and robotic DP have a similar learning curve of 25.3 versus 20.7 cases respectively ( $p = 0.6$ ) using a composite learning curve metric. The Pittsburgh group has reported 40 cases needed for optimization of robotic DP, with precipitous decrease in operative time between the first 20 and 40 cases (266 min and 210 min, respectively) and readmissions [29].

As DP lacks the need for reconstruction, both laparoscopic and robotic DP have been widely adopted. MI DP is safe and feasible for benign and malignant indications [14]. For PNETs in particular, retrospective matched cohort studies demonstrated similar disease-free survival after laparoscopic resection, with significantly decreased rates of postoperative complications and length of stay [30]. Retrospective analyses have consistently demonstrated laparoscopic DP is associated with lower blood loss and length of stay, improved postoperative quality of life, and similar costs, without appreciable increases in postoperative POPF, short-term complications, mortality, or rate of R0 resections in comparison with open approach [31—33].

Randomized controlled data supports MI DP over the open approach. The LEOPARD-1 trial randomized one hundred and eight patients with left-sided pancreatic tumors, without evidence of vascular involvement, to MI DP (42 laparoscopic, 5 robotic) or open DP. Of note, patients were blinded to surgical approach

using a large abdominal dressing. MI DP demonstrated decreased time to functional recovery (4 versus 6 days,  $p < 0.001$ ), decreased rates of delayed gastric emptying (3 patients (6 %) vs 11 patients (20 %);  $p = 0.04$ ) without a difference in rate of POPF (39 % vs 23 % for MIDP and open DP, respectively [ $p = 0.07$ ]), or 90-day mortality. Follow-up analyses of cost and quality of life up to 1 year after surgery showed comparable costs after MI DP, with a probability of at least 0.654 of improved cost-effectiveness [34]. Long-term follow-up (up to 3 years) after DP demonstrated no differences in overall quality of life between MI and open DP. The LAPOP trial is an unblinded, parallel group, single-center superiority trial between laparoscopic open DP [35]. Twenty-nine patients were randomized to each group, demonstrating improvements in length of stay (5 vs 6 days,  $p = 0.007$ ) and blood loss (50 vs 100 ml,  $p = 0.015$ ) for laparoscopic and open DP, respectively. No differences were observed between Clavien-Dindo III + complications, rates of delayed gastric emptying or grade B/C POPF [36].

Retrospective studies have shown equivalent oncologic outcomes after MI DP compared with open although it is important to acknowledge that these retrospective studies may be subject to selection bias and that no randomized long-term survival data have been reported. The European Consortium on Minimally Invasive Pancreatic Surgery reported the results of a pan-European matched cohort study between MI and open DP in pancreatic ductal adenocarcinoma, matching 340 patients [37]. This study demonstrated decreases in median blood loss (200 vs 300 ml,  $p = 0.001$ ) and length of stay (8 vs 9 days,  $p < 0.001$ ), for MI versus open DP, respectively. No differences were seen in 90-day mortality (2 % vs 3 %) and Clavien-Dindo III + complications (18 vs 21 %) for MI and open DP, respectively. Most importantly, no differences were observed in median overall survival between MI DP and open DP (28 vs 31 months,  $p = 0.929$ ). However, MI DP was associated with higher rates of R0 resection (67 % vs 58 %,  $p = 0.019$ ) and lower lymph node yield (14 vs 22;  $p < 0.001$ ). As a result of these data, the same group is currently enrolling 258 patients in a multicenter, non-inferiority, randomized controlled trial between MI DP (laparoscopic or robotic) and open. Their primary outcome measure is the microscopically radical resection margin, and secondary outcomes include time to functional recovery and survival [38]. Several additional international trials are ongoing between MI and open DP, including a multicenter, non-inferiority,

non-blinded randomized controlled trial in Korea, with primary endpoint of 2-year survival [39]. The DISPACT-2 trial in Germany is currently enrolling, randomizing 294 patients between MI and open DP, with a primary outcome measure of postoperative morbidity and mortality [40, 41].

Robotic versus laparoscopic DP has been examined in multiple recent meta-analyses. These studies reported lower rates of open conversion and shorter hospital stay, with higher rates of spleen preservation after robotic DP, and no differences between morbidity and POPF rate [42]. However, robotic DP was associated with higher operative time. In PNETs in particular, robotic DP is associated with improved splenic preservation compared with laparoscopic DP (65.3 % vs 44.7 %,  $p < 0.0001$ ) in a retrospective analysis of 181 patients at four tertiary Italian referral centers [43, 44]. This study also reported no differences in short- or long-term perioperative outcomes, including overall and disease-free survival. Cost favored the laparoscopic approach, with mean total costs of 9235 vs 11226 €, for the laparoscopic and robotic DP, respectively ( $p < 0.0001$ ). Although these data likely represent selection bias, in appropriate hands both laparoscopic and robotic DP seem to be safe and effective options for the treatment of the spectrum of pancreatic tumors.

### SUMMARY

Minimally invasive techniques in pancreatectomy are increasingly being used. Minimally invasive DP seems to be the standard approach for most low-grade distal pancreatic lesions, and ongoing trials may further bolster its use in pancreatic adenocarcinoma. However, minimally invasive PD remains controversial, with selected high-volume centers reporting successful case series. Maintaining high levels of oncologic excellence, with negative-margin resection remains the challenge facing wide adoption of minimally invasive PD. Adherence to the key technical standards of pancreatic resection during a minimally invasive approach, while simultaneously traversing the learning curve of these procedures is the key to their ultimate success. Ongoing hospital-level and national-level planning should play a role in the development of safe MIP programs.

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## ABSTRACT

The use robotics in surgery is gaining momentum. This approach holds substantial promise in pancreas surgery. Minimally invasive techniques have been increasingly used in oncologic surgery and pancreatic surgery in particular. Minimally invasive pancreatectomy (MIP) has been performed with increasing frequency in all pancreatic pathologies, including pancreatic neuroendocrine tumors (PNETs), including pancreaticoduodenectomy (PD), distal pancreatectomy (DP), and pancreatic enucleation. Robotic-assisted surgery using the DaVinci platform has accelerated the adoption of MIP. The proportion of robotic DP between 2015 and 2016 was nearly 4 times greater than between 2010 and 2012 (16 % vs 4 %), with a similar increase in proportion of robotic PD (7 % vs 2 %) over the same time frame. Advantages of robotic surgery over laparoscopy include three-dimensional visualization, increased degrees of motion with endo-articulation, stable camera platform, surgeon ergonomics, and single surgeon's ability to control four instruments. Systematic adoption of MIP has been facilitated by the creation of multiple multicenter training programs in robotic DP and PD, aiming to standardize the oncologic safety and technical performance of these operations. Robotic surgery for pancreatic lesions and malignancies has become well accepted and is expanding to more and more center annually. The number of centers using robotics in pancreatic surgery is rapidly increasing. The most studied robotic pancreas surgeries are PD and DP. Most studies are in their early phases, but they report that robotic pancreas surgery is safe feasible. Robotic pancreas surgery offers several advantages over open and laparoscopic techniques. Data regarding costs of robotics versus conventional techniques is still lacking. Robotic pancreas surgery is still in its early stages. It holds promise to become the new surgical standard for pancreatic resections in the future, however, more research is still needed to establish its safety, cost effectiveness and efficacy in providing the best outcomes.

**Keywords:** pancreas, pancreatic surgery, pancreaticoduodenectomy, robotic surgery, minimally invasive surgery.

## РЕЗЮМЕ

**Роботизована малоінвазивна хірургія підшлункової залози. Огляд****T. Keck, H. Lapshyn***University Medical Center Schleswig-Holstein,  
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Дедалі частіше в хірургії використовують робототехніку. Цей підхід має значні перспективи в хірургії підшлункової залози. Малоінвазивні методи застосовують в онкологічній хірургії, зокрема в хірургії підшлункової залози. Мінімально інвазивну панкреатектомію (МІП) останнім часом частіше виконують при всіх патологіях підшлункової залози, зокрема при нейроендокринних пухлинах підшлункової залози, методами панкреатодуоденектомії (ПД), дистальної панкреатектомії (ДП) та енуклеації підшлункової залози. Роботизована хірургія з використанням платформи DaVinci прискорила впровадження МІП. Частка роботизованої ДП у 2015—2016 рр. у 4 рази перевищувала таку в 2010—2012 рр. (16 та 4 % відповідно), водночас збільшилася частка роботизованої ПД (з 2 до 7 %). Переваги роботизованої хірургії перед лапароскопією полягають у тривимірній візуалізації, підвищеному ступені рухливості з ендоартикуляцією, стабільній платформі камери, хірургічній ергономічності та можливості контролювати чотири інструменти одним хірургом.

Систематичному впровадженню МІП сприяло створення кількох багатоцентрових навчальних програм для роботизованих ДП і ПД, спрямованих на стандартизацію онкологічної безпечності й технічну ефективність цих операцій. Роботизована хірургія уражень підшлункової залози та злоякісних новоутворень отримала широке визнання та щороку впроваджується в нових центрах. Кількість центрів, які використовують робототехніку в хірургії підшлункової залози, стрімко зростає. Найбільш вивченими роботизованими методами хірургії підшлункової залози є ПД і ДП. У більшості досліджень ранні стадії, але отримані попередні дані свідчать, що роботизована операція на підшлунковій залозі є безпечною. Роботизована хірургія підшлункової залози має кілька переваг перед відкритими та лапароскопічними методами. Даних щодо витрат на робототехніку порівняно зі звичайними методами недостатньо. Роботизована хірургія підшлункової залози нині перебуває на початковій стадії. Метод обіцяє стати новим хірургічним стандартом для резекції підшлункової залози в майбутньому, але необхідно провести додаткові дослідження, щоб встановити його безпечність, економічну ефективність і ефективність у забезпеченні найкращих результатів.

**Ключові слова:** підшлункова залоза, операції на підшлунковій залозі, панкреатодуоденектомія, роботизована хірургія, малоінвазивна хірургія.

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