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CONSENSUS STATEMENT

Laparoscopic surgery for pancreatic neoplasms: the European association for endoscopic surgery clinical consensus conference

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Abstract

Background Introduced more than 20 years ago, laparoscopic pancreatic surgery (LAPS) has not reached a uniform acceptance among HPB surgeons. As a result, there is no consensus regarding its use in patients with pancreatic neoplasms. This study, organized by the European Association for Endoscopic Surgery (EAES), aimed to develop consensus statements and clinical recommendations on the application of LAPS in these patients.

Methods An international panel of experts was selected based on their clinical and scientific expertise in laparoscopic and open pancreatic surgery. Each panelist performed a critical appraisal of the literature and prepared evidence-based statements assessed by other panelists during Delphi process. The statements were further discussed during a one-day face-to-face meeting followed by the second round of Delphi. Modified statements were presented at the plenary session of the 24th International Congress of the EAES in Amsterdam and in a web-based survey.

Results LAPS included laparoscopic distal pancreatectomy (LDP), pancreatoduodenectomy (LPD), enucleation, central pancreatectomy, and ultrasound. In general, LAPS was found to be safe, especially in experienced hands, and also advantageous over an open approach in terms of intraoperative blood loss, postoperative recovery, and quality of life. Eighty-five percent or higher proportion of responders agreed with the majority (69.5%) of statements. However, the evidence is predominantly based on retrospective case–control studies and systematic reviews of these studies, clearly affected by selection bias. Furthermore, no randomized controlled trials (RCTs) have been published to date, although four RCTs are currently underway in Europe.

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Conclusions LAPS is currently in its development and exploration stages, as defined by the international IDEAL framework for surgical innovation. LDP is feasible and safe, performed in many centers, while LPD is limited to few centers. RCTs and registry studies are essential to proceed with the assessment of LAPS.

Keywords Laparoscopy · Pancreatoduodenectomy · Pancreatectomy · Enucleation · Consensus

First introduced in the mid 1990s, laparoscopic pancreatic surgery (LAPS) developed slowly, presumably due to anatomic complexity of the region and high postoperative morbidity [1, 2]. Although initially considered for staging purposes only, increasing experience in laparoscopy enabled the application of LAPS for more advanced procedures.

Today, more than 20 years after the first reports, none of the laparoscopic pancreatic resections has gained a uniform acceptance. A recent pan-European survey demonstrated that 73% of surgeons had experience with minimally invasive distal pancreatectomy, although the median proportion of this procedure per surgeon was only 30% [3]. At the same time, 45% of surgeons stated that they had insufficient training in laparoscopic distal pancreatectomy (LDP). According to the same survey, 21% of respondents had experience with minimally invasive pancreatoduodenectomy (MIPD), while 65% considered laparoscopic pancreatoduodenectomy (LPD) as technically challenging. These findings demonstrated that the role of LAPS in the treatment of pancreatic neoplasms remains unclear.

The objective of this study developed by the European Association for Endoscopic Surgery (EAES) was to provide evidence-based clinical recommendations for the use of LAPS in the treatment of pancreatic neoplasms.

Materials and methods

The project started in July 2015, when the expert panel was selected based on the scientific and clinical expertise of the candidates, as well as their experience in the field of laparoscopic and open pancreatic surgery (BE, MAH, MGB, MB, JMF, LFC, BG, SCK, and IH). The consensus conference was coordinated from Oslo University Hospital-Rikshospitalet (BE) and assisted by a surgical research fellow (MS).

Literature search and appraisal

First, the expert panel agreed on the list of topics to be included in the consensus conference. Each expert was assigned to two or more topics and asked to prepare evidence-based statements supported by the discussion of the current literature. The literature search and its critical appraisal were limited to the articles published in English during the period from 1994 to 2016. The searched databases were Medline and Cochrane Library. Medical subject headings (MeSH) and free-text words were used for searches. Reference lists from the included articles were manually checked for any additional studies, which were included when appropriate. Critical appraisal of the literature was carried out using the evidence level (EL) provided by Oxford Centre for Evidence-based Medicine, and the grade of recommendations (GoR) derived from the ELs (http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/).

Consensus development

Upon reviewing the literature, each expert drafted statements on specific topic(s) accompanied by supporting discussion. These statements were assessed by the members of the expert panel (first Delphi round) and discussed at one day face-to-face meeting in Copenhagen, 26 February 2016. Based on the comments and suggestions, the statements were modified and put in circulation for further evaluation (second Delphi round). All statements were approved by the expert panel prior to presenting for the online voting at the consensus conference (CC) during 24th International Congress of the EAES in Amsterdam, 17 June 2016. The plenary session was moderated by members of the expert panel.

After the congress, statements were posted on the EAES website for 3 months and sent to the EAES membership for further comments and voting. The latter included a total number of 148 respondents. Scientific community consensus (SCC) reflecting the level of approval of suggested statements was considered in the next round of document revision by the expert panel (third Delphi round). SCC was calculated as the mean percentage of the agreements obtained at the consensus conference and in the web-based survey. As a result, all statements were divided into four levels: level 1 (SCC ≥ 90%), level 2 (SCC: 85–89%), level 3 (SCC: 80–84%), and level 4 (SCC < 80%). The final version of the manuscript was reviewed and approved by all participants of this study.

Results

A total number of 23 statements were prepared, and ultimately 100% consensus was achieved among the panelists on all statements. Of these, 7 (30.4%) and 9 (39.1%) achieved SCC level 1 and 2, respectively (Table 1). Three statements had less than 80% SCC. As a result, the expert

Table 1 Levels of scientific community consensus on presented statements

Level	Scientific community consensus	Number of statements (%)
1	≥90%	7 (30.4%)
2	85–89%	9 (39.1%)
3	80–84%	4 (17.4%)
4	<80%	3 (13.1%)

panel agreed to drop two of these statements and present them in the discussion section.

Laparoscopic distal pancreatectomy

Laparoscopic distal pancreatectomy is a feasible and safe alternative to open approach in the treatment of benign and malignant pancreatic lesions, providing advantages in terms of reduced blood loss and enhanced postoperative recovery resulting in shorter hospital stay (EL: 3a; GoR: B). SCC: Level 1 (94%).

In 1994, Cuschieri reported the first LDP performed for chronic pancreatitis [1]. From then on, the interest in LDP and in the range of its indications grew exponentially. However, it took more than 10 years until the first comparative series on LDP vs open distal pancreatectomy (ODP) were published [4, 5]. Comparative studies for non-malignant diseases found similar baseline characteristics such as age, BMI, and tumor size, although Yoon et al. reported younger patients in the laparoscopic group [6–13]. Recent nationwide evaluation in the US suggests that benign disease and BMI of 30-40kg/m^2 have been the selection factors for minimally invasive technique, whereas pancreatic ductal adenocarcinoma (PDAC), tumor size > 5 cm, and multivisceral resections resulted in ODP [14].

The early series on LDP mostly included patients with pancreatic cysts and neuroendocrine neoplasms [4, 5, 15, 16]. In a meta-analysis from Mehrabi et al., the indications for LDP in 59% of patients were cysts [17]. When indications for cystic lesions are specified, the mucinous cystic neoplasia (MCN) represents the first indication, followed by serous cystic neoplasia (SCN), solid pseudopapillary neoplasm (SPN), intrapapillary mucinous neoplasm (IPMN), pseudocyst, and true congenital cysts [18–20]. In a study on 62 patients with pancreatic cysts, Anonsen and coworkers reported on 46.7% of SCN and 61% of benign lesions in total [21]. The authors concluded that preoperative investigations such as endoscopic ultrasound examination and fine needle aspiration should be considered to reduce the likelihood of resecting benign cysts. Although LDP has been proposed for all types of cysts in the body or tail of the pancreas, the majority of studies focused on MCN and SPN [22–26], whereas less data are published on IPMN [27]. Only case reports were found on lymphoepithelial, epidermoid, and true congenital cysts [28–30].

Most of the comparative studies found 1–2 h longer operative time for laparoscopy [6–13], but only in three of those, the difference was statistically significant [6, 7, 12]. On the other hand, estimated blood loss (EBL) decreased with 200–300 mL by LDP [6–13], and two studies found that LDP was associated with higher spleen preservation rate [7, 8]. LDP was not shown to reduce the postoperative morbidity, although some studies still suggest lower rate of complications compared with ODP [11, 12]. Laparoscopy also seems to be advantageous in terms of postoperative recovery resulting in a significantly shorter hospital stay (with 1–9 days) observed in 6 studies [6, 7, 9, 11–13].

A recent meta-analysis from Mehrabi et al., including 29 observational studies and 5 systematic reviews, demonstrated the superiority of LDP over ODP in terms of EBL (308 ml less), time to first oral intake (1.3 days less) and length of hospital stay (3.8 days less) [17]. However, no difference was found in postoperative pancreatic fistula (POPF) (21.8 vs 21.6%), postoperative morbidity (34 vs 38%), and mortality (0.4 vs 1.1%). In all, systematic reviews confirm that LDP is both feasible and safe in patients with lesions in the body and tail of the pancreas [31–33]. Nevertheless, the real-life benefits of LDP including quality of life and cost analysis are still to be determined in randomized controlled trials (RCTs). In Europe, such trials are currently underway—the LEOPARD-1 multicenter RCT in the Netherlands (http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=5188) and the LAPOP single-center RCT in Sweden (http://www.isrctn.com/ISRCTN26912858).

The rate of pancreatic fistula is similar after laparoscopic and open distal pancreatectomy, independent from the technique of pancreatic stump closure (EL: 3b). SCC: Level 2 (88%).

Three single-center case-matched studies and one multicenter case-matched study showed that laparoscopy did not reduce the POPF rate when compared to open surgery [4, 34–36]. The same result was reported based on an unmatched comparison of 131 laparoscopic vs 637 open procedures [37]. Two meta-analyses on comparative non-randomized studies found that LDP led to a statistically not significant reduction of grade B/C fistula [38, 39]. At the same time, POPF highly varied from study to study due to different criteria used for its definition.

A case-matched study compared results in patients with LDP (86 linear stapler and 14 hand-sewn) and ODP (92 hand-sewn and 8 linear stapler) operated between 2010 and 2013 [34]. POPF rate was 53% after LDP and 51% after ODP. About 70% of POPF in both groups were grade A, and no difference was found between the stapler and hand-sewn closure techniques. Taylor et al. assessed the outcomes in 46 consecutive patients with LDP and found no significant difference in POPF, when using linear stapler and hand-sewn technique (13 vs.19%, $p = 0.43$) [40]. These findings are consistent with the RCTs in open surgery [41, 42]. Marangos et al. examined the effect of TachoSil® patch and found no improvement in the rate of POPF [43].

All in all, the vast majority of the literature on POPF prevention in the setting of LDP is currently represented by retrospective studies with small sample sizes.

Spleen-preserving laparoscopic distal pancreatectomy can be considered in patients with benign tumors (EL: 3b; GoR: B). SCC: Level 1 (100%).

Splenectomy is reportedly associated with an increased postoperative morbidity, hematologic complications, and impaired primary immune response [44]. As a result, patients are at a risk of developing respiratory tract infections and overwhelming postsplenectomy infection any time after removal of the spleen [45]. Nevertheless, the experimental and clinical studies demonstrated significantly improved outcomes after using vaccines against Streptococcus pneumoniae, Haemophilus influenzae, and Neisseria meningitides, leading to a decrease in mortality from OPSI [46–48].

A comparative study from Choi et al. suggests that spleen-preserving LDP (SP-LDP) is associated with significantly longer operative time ($p = 0.02$) but less postoperative complications ($p < 0.01$), POPF ($p = 0.03$), and shorter hospital stay ($p < 0.01$) compared with the standard technique [49]. Furthermore, the latter impaired the quality of life based on the results of follow-up survey. Mekeel and co-workers also report on non-significantly lower rate POPF after SP-LDP, speculating that preservation of the splenic blood vessels may improve perfusion to the pancreatic stump and decrease the risk of leak [50]. On the contrary, Fernández-Cruz et al. observed higher rate of postoperative complications after SP-LDP compared to standard LDP [16]. Nonetheless, the application of SP-LDP was encouraged in the majority of patients with cystic neoplasms, but not in case of suspected malignancy. Bruzoni et al. concluded that SP-LDP is a feasible and safe procedure suitable in selected cases with cystic and low-grade neoplasms [51]. These findings have been confirmed in further studies [52–55].

Only a few reports on SP-LDP for pancreatic cancer were found in the literature [56, 57]. Kawaguchi et al. described the experience with SP-LDP with the ligation of splenic vessels and sparing lymphadenectomy in the splenic hilum in 17 patients with adenocarcinoma in the distal pancreas [56]. Median survival was 28 months, and 5-year survival was 33%. However, SP-LDP is usually not recommended in patients with pancreatic cancer, as it may jeopardize the oncologic completeness of the procedure by not removing the lymph nodes residing in the splenic hilum [58].

In all, literature on SP-LDP vs LDP is represented by relatively small number of comparative studies with small sample sizes. However, the majority of these articles consider patients with benign tumors as good candidates for SP-LDP [59–62].

Spleen-preserving laparoscopic distal pancreatectomy with preservation of splenic vessels seems to be advantageous over the Warshaw technique in terms of postoperative outcomes, particularly splenic infarction (EL: 3a; GoR: B). SCC: Level 3(82%).

Comparative studies demonstrate that SP-LDP with the splenic vessel preservation (VP-SPLDP) is associated with significantly reduced EBL, morbidity, clinically relevant POPF (CR-POPF), splenic infarctions (5 vs. 39% ; $p < 0.01$), and shorter hospital stay compared with the vessel ligation (VL-SPLDP) [44, 60, 63]. Furthermore, two meta-analyses report significantly lower incidence of splenic infarction, gastric varices, as well as postoperative splenectomy after VP-SPLDP [64, 65]. Some studies also recommend attempting VP-SPLDP whenever possible, but switching to VL-SPLDP in case of bleeding or difficulties during dissection [60, 63]. According to Choi et al., the following conditions are unfavorable for VP-SPLDP and may be potential indications for VL-SPLDP: relatively large tumor (1) associated with chronic pancreatitis (2), tumor abutting splenic vascular structures (3), and bleeding during the VP-SPLDP (4) [49]. On the other hand, Fernández-Cruz et al. assumed that splenomegaly is a contraindication for VL-SPLDP due to insufficient nourishment of an increased mass by short gastric vessels [16]. Another comparative study from Butturini and co-workers found no significant differences between the two techniques in terms of operative time, postoperative complications, and hospital stay [61]. Although gastric or perigastric varices were detected in 60% of patients with VL-SPLDP at 12 months from the index operation, no cases of gastrointestinal bleeding were observed during the long-term follow-up. These results were also confirmed by Zhou et al. [66]. Several reports observed longer operative time and higher EBL in patients with VP-SPLDP [63, 67].

Yoon et al. described impaired patency of the splenic vein after VP-SPLDP, resulting in an increased risk of left-sided portal hypertension [68]. The splenic vein was presumed to be occluded due to a manipulation during the dissection, as well as because of its susceptibility to thrombosis and inflammation, caused by the lack of muscle and elastic fibers. However, these results were not confirmed in a retrospective study by Hwang et al., who did not observe impaired vascular patency in splenic vessels or secondary changes in the spleen [69]. A recent study by Yoon and co-workers comparing the outcomes following open and laparoscopic VP-SPLDP found that vessel preservation and EBL were prognostic factors for compromised splenic vein patency [13]. Interestingly, it was significantly less frequent in patients operated during the late study period, indicating an improvement with the increasing surgical experience and minimizing the EBL.

Laparoscopic distal pancreatectomy is associated with the significantly better quality of life compared to open approach (EL: 2b). SCC: Level 2 (87%).

Two studies compared the quality of life (QoL) following LDP and ODP [10, 34]. Braga et al. performed a prospective cohort study with propensity score-matched analysis (1:1) in 200 patients [34]. The 8-item Short-Form Health Survey (SF-8) was used to assess the QoL 1- and 3-month postoperatively. This questionnaire consisted of 8 questions concerning general health, physical functioning, role-physical (impairment due to physical health), bodily pain, vitality (energy level), social functioning, emotional problems, and role-emotional (impairment due to emotional problems). The results after 1 month showed a significant improvement in general health perception ($p = 0.03$) and vitality ($p < 0.01$) favoring the laparoscopic group. All other items were similar for both groups. There were no differences in QoL parameters found at 3-month follow-up.

A retrospective study by Ricci et al. assessed the QoL 1-year postoperatively using the European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire C-30 (EORTC QLQ C-30) and the EuroQoL five dimensions (EQ-5D) Questionnaire [10]. The first questionnaire consisted of 5 generic questions regarding QoL. The EORTC QLQ C-30 consisted of one global domain, five functional domains as well as eight symptom scales. Eighty-one patients (41 LDP and 40 ODP) were included in this study, and the analysis of the QoL was available in only 54 patients (34 LDP and 20 ODP) due to loss to follow-up and denial of participation. After 1 year, patients who had undergone LDP scored significantly better regarding physical functioning (daily activities) ($p = 0.04$) and role functioning (impairment in work, leisure, or other daily activities) ($p = 0.03$). The improvement on these scales was also observed in the multivariable analysis (physical functioning $p = 0.05$ and role functioning $p = 0.04$). The latter also showed a significant improvement in cognitive functioning scores for the LDP group ($p = 0.03$). On the symptom scales, LDP patients presented with a significantly higher diarrhea scale ($p = 0.03$) and a lower sleep disturbance scale ($p = 0.05$), which was also confirmed during multivariable analysis ($p = 0.05$).

Although both studies showed better QoL outcomes after LDP, they used different questionnaires and were not randomized. This may have influenced the results and makes generalization difficult.

Laparoscopic distal pancreatectomy is feasible and safe in patients with pancreatic neuroendocrine tumors providing satisfactory postoperative and oncologic outcomes (EL: 3a; GoR: B). *SCC: Level 1 (96%).*

Surgery is the only curative modality for pancreatic neuroendocrine tumors (NETs). Recent studies have demonstrated the improved survival rates across all stages of the disease, advocating resection of the primary tumor in the settings of localized, regional, as well as (selectively) metastatic disease [70–73]. However, experience with LDP for NET remains small.

A systematic review on laparoscopic vs open surgery for NETs from Drymousis et al. suggests that LAPS is associated with less EBL, lower morbidity, and shorter hospital stay [74]. However, this study included a heterogeneous cohort of patients undergoing predominantly LDP and laparoscopic enucleation. A similar systematic review from Tamburrino et al. reported less EBL and shorter hospital stay following LAPS [75]. Haugvik et al. assessed the long-term outcomes in 65 patients, who had undergone LAPS for NETs (51 LDP and 14 LPE) and found 5-year disease-specific survival of 90% [76]. Two studies reported on LDP in a total number of 26 patients with NETs [16, 77]. Perioperative outcomes in these patients did not substantially differ from those reported for ODP. No CR-POPF were reported. These rates of POPF were lower than previously reported for LAPS for NETs (29%) or LDP for all lesions (21.8%) [17, 74]. Finally, the comparative study from Xourafas et al. found lower morbidity, shorter hospital stay, comparable oncologic outcomes, and survival after LDP compared with ODP in patients with NETs [11]. Radical resection (R0) of NETs in the body and tail of the pancreas has been previously reported to be feasible by laparoscopy [16, 76, 77].

Laparoscopic distal pancreatectomy is feasible and safe in patients with pancreatic ductal adenocarcinoma, providing favorable outcomes in terms of estimated blood loss and hospital stay when compared with open technique. Short- and long-term oncologic outcomes are similar (EL: 3a; GoR: B). SCC: Level 2 (85%).

Although numerous studies had described successful utilization of LDP in patients with benign and low-grade malignancies, its role in the treatment of PDAC remained unclear. Limited evidence in this area hindered ultimate conclusions, and a recent pan-European survey found that one-third of pancreatic surgeons were concerned about the application of LDP for PDAC [3].

Malignant tumors in the body and tail of the pancreas are typically presented in a more advanced stage than those of the proximal gland. On the other hand, significant advances in pancreatic imaging using multi-modality approach may enable to detect PDAC in the early stages. Furthermore, a magnified view through the laparoscopic approach has an advantage of providing improved visualization of the anatomy for dissection of complex vessels or lymphadenectomy [78].

The outcomes of LDP vs ODP for PDAC are described in a limited number of comparative studies. Hu et al. reported similar operative time and EBL after LDP and ODP [79], while some studies found less EBL following LDP [80, 81]. Larger comparative studies observed reduced blood transfusion rates and shorter hospital stay after LDP [82–84]. Case–control studies found identical rates of postoperative morbidity, mortality, and POPF [81–83, 85–87]. Finally, a meta-analysis from Ricci et al. demonstrated longer operative time but less EBL and shorter hospital stay compared to ODP, although tumor size was smaller in LDP group (p = 0.04) [85].

Yet, the major concern has been the oncologic adequacy of LDP. Baker et al. demonstrated significantly higher amount of retrieved lymph nodes after ODP compared with LDP [88]. However, this finding was not confirmed in further studies suggesting comparable lymph node yield, pN1 and R1 resection rates following LDP and ODP [58, 79, 80, 83]. Furthermore, Sharpe et al. demonstrated that LDP was associated with the higher rate of R0 margins [82]. Studies also found no significant differences in terms of recurrence (both local and distant) and median survival after LDP and ODP [79–81, 86]. A propensity score-matched comparative single-center study by Shin et al. demonstrated 5-year survival of 32.5% after LDP, which was comparable with the survival after ODP [83]. In the French multicenter study, Sulpice et al. reported improved survival following LDP compared to ODP with 3- and 5-year survival rates of 63.7% vs 50.8% and 50.6% vs 37.1%, respectively [84]. However, the authors mentioned selection bias in the laparoscopic group characterized by smaller tumors and less multivisceral resections. A recent multicenter study also reported satisfactory oncologic outcomes of LDP in a relatively large cohort of patients with PDAC [89]. In the recent meta-analysis, Ricci et al. demonstrated similar short- and long-term oncologic outcomes after LDP and ODP, concluding that laparoscopic approach did not affect overall survival rate ($p = 0.32$) [85]. However, no RCTs have been performed up to date, although the pan-European DIPLOMA group is now addressing this topic [3].

Several studies emphasized the role of careful patient selection when considering LDP for PDAC [79, 82, 87, 90, 91]. Adam et al. recommended minimally invasive approach in patients with the small tumors located in the body and tail of the pancreas [90]. Conversely, Fernández-Cruz demonstrated that tumor size did not compromise surgical and oncologic outcomes of LDP [92]. Yonsei selection criteria were suggested for LDP when considered in patients with PDAC (tumor confined to pancreas, intact fascial layer between distal pancreas and the left adrenal gland/kidney, tumor located more than 1–2 cm from the celiac axis) [87]. At the same time, Marangos et al. reported 21 consecutive PDACs operated by LDP with only one patient converted to ODP [93]. Thus, patient selection criteria must be evaluated separately in each expert center.

Laparoscopic radical antegrade modular pancreatosplenectomy is feasible for the treatment of pancreatic ductal adenocarcinoma. Currently, the choice of surgical technique should be left to the surgeon's discretion (EL: 4; GoR: C). SCC: Level 2 (88%).

Small series including well-selected patients with PDAC reported on technical feasibility and oncologic safety of laparoscopic radical antegrade modular pancreatosplenectomy (RAMPS) devised to increase the rate of negative resection margins and complete lymph node dissections [87, 91]. Song et al. employed RAMPS in 34 patients with PDAC achieving the mean number of 10.3 harvested lymph nodes and 92% R0 resection rate [20]. Fernández-Cruz et al. reported 10 cases with PDAC operated by modified RAMPS (the superior mesenteric artery was not skeletonized and left renal vessels were not dissected) with 90% negative margins and median survival of 14 months [16]. Kawaguchi et al. recommended performing RAMPS to obtain negative tangential margins [56], while Abu Hilal et al. suggested "hanging" the pancreas with Gerota's fascia during LDP, followed by a clockwise dissection, which resulted in the R0 rate of 76% [94]. At the same time, Kooby et al. had previously indicated that margin positive resection rate in pancreatectomy for PDAC is difficult to interpret due to a lack of defined standard for histological margin assessment [80]. Marangos et al. presumed that dissection planes for conventional left-to-right technique of the LDP could be chosen based on visualization of the relevant anatomy and combined with intraoperative ultrasonography, while lymphadenectomy can be performed only for the enlarged or suspicious local lymph nodes [93]. This study reported on R0 rate of 93%, median survival of 23 months, and 3-year survival of 30% after LDP for PDAC. Asbun et al. applied a clockwise technique starting with mobilization of the left colon flexure and continuing along the lower border of the pancreas in 5 patients with adenocarcinoma [95]. The median number of retrieved lymph nodes and the rate of R0 resection were 19 and 100%, respectively. It was concluded that this technique shares some similarities with RAMPS, as it allows for a wide exposure of the pancreas and makes it feasible to resect the left adrenal gland if needed.

Comparative studies in open surgery have not found survival benefits in RAMPS when compared with the standard approach [96, 97]. No comparative studies between laparoscopic RAMPS and conventional LDP have been published up to date. Hence, true oncologic benefits of RAMPS remain unclear [83]. Further studies focused on a surgical technique are essential to define the role of laparoscopic RAMPS in the treatment of PDAC.

Extended laparoscopic distal pancreatectomy (defined by the International Study Group for Pancreatic Surgery) is associated with surgical outcomes similar to standard procedure. Despite decreased survival compared with the standard procedure, it may still be of use in selected patients with tumors extending beyond the pancreas (EL: 4; GoR: C). SCC: Level 3 (80%).

A consensus from the International Study Group for Pancreatic Surgery (ISGPS) recommends performing extended pancreatic resections in selected patients with locally advanced tumors within the specialized centers [98]. The study suggests that despite possible increase in postoperative morbidity long-term results are favorable over palliative chemo- and/or radiochemotherapy alone. At the same time, only a handful of studies have examined the outcomes of extended laparoscopic distal pancreatectomy (ELDP). Hu et al. assumed that laparoscopy is not suitable for extended resections and should not be applied for tumors growing to the adjacent organs [79]. French all-inclusive national observational study showed significantly less multivisceral resections performed during LDP when compared with ODP [84]. In fact, according to the pan-European survey, 60% of pancreatic surgeons consider tumor involvement of at least one adjacent organ a contraindication for minimally invasive surgery [3].

Cho and co-workers have described LDP with en bloc resection of the celiac axis resection as a safe and feasible procedure helping to achieve R0 resection margins in highly selected patients with locally advanced PDAC [99]. Furthermore, a multicenter study by Sahakyan et al. found similar postoperative outcomes after standard LDP and ELDP [89]. The latter was associated with the significant decline in survival compared to LDP with the median survival of 20.2 months and 3-year survival of 26.3%. These findings may support the application of ELDP in selected patients with PDAC. Although the evidence on ELDP in the setting of PDAC is very scarce, it can be of use in these patients providing advantages over chemotherapy or radiochemotherapy alone.

A significant reduction in operative time during laparoscopic distal pancreatectomy can be obtained after 10–17 procedures. Other possible indicators for learning curve are conversion rate and intraoperative blood loss (EL: 3b; GoR: B). SCC: Level 2 (86%).

Four single-center studies have focused on the learning curve for LDP [18, 100–102]. In a study from Braga et al., the results were compared in the three consecutive groups of 10 patients [100]. Reduction of conversion rate, operative time, and EBL was found in the second and third groups compared with the first group. Therefore, a cut-off of 10 procedures has been suggested to complete the learning curve. No differences in postoperative morbidity and length of hospital stay were found in the three groups. A reduction of operative time after 10 procedures was also reported in series of 25 patients [101], while a cut-off of 17 procedures was needed to reduce the operative time in another study on 32 patients [102]. Conversion rate did not change with an increasing number of LDP in both studies. Similar operative time and conversion rate were also observed in a series of 100 patients operated between 1999 and 2012 [18]. Finally, a systematic review from Barrie et al. identified a 10-procedure cut-off necessary to obtain operative time reduction and 6-procedure cut-off for reducing the EBL [101]. Relevant factors influencing the learning curve were the hospital volume and staff experience in both open pancreatic surgery and gastrointestinal laparoscopic surgery.

Laparoscopic distal pancreatectomy is associated with higher operative costs and lower postoperative costs compared with open technique resulting in comparable cost for both procedures (EL: 3b). SCC: Level 1 (90%).

Ten studies have assessed costs for LDP vs ODP and 8 of those evaluated operative, postoperative, and total costs separately. Five studies found significant differences in operative costs between the two approaches [10, 103–106]. In 4 of them, LDP was associated with significantly increased operative costs up to 2800 USD, related to the higher costs of surgical equipment and the increased operative time [10, 104–106].

Yet the most obvious benefit of LDP is the enhanced postoperative recovery resulting in a shorter length of hospital stay [17]. Since postoperative morbidity is suspected to be comparable for ODP and LDP [17], the postoperative costs should therefore be lower for LDP than for ODP. This hypothesis was confirmed in 6 studies, in which lower postoperative costs up to 6,500 GBP were observed [11, 103–107]. Consequently, total costs of LDP vs ODP were less or comparable in the majority of studies [11, 34, 103–105, 107, 108].

One study has assessed the influence of implementation of the enhanced recovery program for LDP, which was found to decrease the length of hospital stay with 3 days resulting in a significant total cost reduction of 2000 GBP per patient ($p < 0.01$) [109]. Reduction of the postoperative pancreatic fistula rate and implementation of the enhanced recovery program can further decrease mean total costs per patient.

Laparoscopic pancreatoduodenectomy

For surgeons who highly experienced in laparoscopic pancreatoduodenectomy, indications are the same as for open pancreatoduodenectomy (EL: 3a; GoR: B). SCC: Level 4 (70%).

LPD is a technically demanding procedure. As a result, early series on LPD predominantly included patients with small benign or early-stage malignant lesions located in head of the pancreas, ampulla of Vater, and distal common bile duct with no signs of vascular invasion [110–112]. Patients with ampullary tumors, mucinous cystic neoplasms, and IPMNs were considered as good candidates for LPD since the lesions were located distant from the major vascular structures.

The vast majority of studies have been conducted in high-volume centers demonstrating that LPD is a feasible, safe, and effective approach in patients with benign and malignant pancreatic lesions [113, 114]. The criteria for patient selection did not significantly change with regard to the technique applied in these centers. A recent meta-analysis from De Rooij et al. found no substantial differences in preoperative characteristics of patients undergoing OPD and MIPD, except the fact that the latter was less often employed for pancreatic cancer [115].

On the other hand, the analysis of the experience with LPD in the United States demonstrated a two-fold increase in the rate of perioperative mortality compared with OPD in low-volume centers (performing < 10 LPDs within 2 years) [116]. These results may be attributed to the early learning curve in these centers. At same time, before performing LPD surgeons should obtain a structured training and carefully consider the type of surgery in order to minimize the risk for patients. In particular, surgeons in their early learning curve should exclude obese patients and limit the procedure to small tumors, confined to the pancreatic head without suspicion for vascular involvement [113, 116–118]. With an increasing experience in LPD, these factors will become less relevant.

All in all, LPD is feasible and safe in experienced hands, however, it should be considered in selected cases and probably not in the low-volume centers.

Laparoscopic pancreatoduodenectomy seems to be advantageous over open approach in terms of blood loss, rate of delayed gastric emptying, and hospital stay, but results in longer operative time (EL: 3a). It also provides better quality of life within the first 6 months after surgery (EL: 4). SCC: Level 3 (84%)

A number of systematic reviews have compared the outcomes of minimally invasive (including laparoscopic, hand-assisted, laparoscopy-assisted, and robot-assisted techniques) and open pancreatoduodenectomy [115, 119–122]. These studies demonstrate that MIPD is associated with less EBL and shorter hospital stay, but longer operative time compared with OPD. These findings were confirmed in the comparative studies between LPD vs OPD [114, 123–127]. Furthermore, several studies suggest significantly lower blood transfusion rates following LPD [128, 129].

Previous meta-analyses found no difference between MIPD vs OPD in terms of overall morbidity, POPF and CR-POPF rates [115, 119–122]. At the same time, De Rooij et al. observed significantly lower rate of delayed gastric emptying (DGE) after MIPD [115]. Comparative studies also report similar morbidity and POPF after LPD and OPD [114, 118, 123, 124, 126, 127, 130], although Dokmak et al. found significantly more grade C POPF in the laparoscopic group [125]. As previously mentioned, the obvious advantage of MIPD and, particularly, LPD is a fast recovery resulting in a shorter hospital stay [114, 115, 118–122, 126, 130]. In patients with PDAC, these advantages of laparoscopy provide premises for timely initiation of the adjuvant therapy [118].

Langan et al. reported the first and only study on QoL after MIPD [131]. Although utilized for laparoscopy-assisted pancreaticoduodenectomy, the study demonstrates that it is associated with favorable QoL within the first 6 months compared with open surgery. Apparently, more data is needed to assess the QoL following LPD.

Short-term oncologic outcomes (harvested lymph nodes /positive resection margins) and survival are comparable between laparoscopic and open pancreatoduodenectomy (EL: 3a and 3b, respectively). SCC: Level 2 (88%).

Data on oncologic outcomes of LPD are insufficient. Only two out of 5 meta-analyses on MIPD vs OPD found significant differences in terms of total number of harvested lymph nodes and the rate of positive resection margins [115, 121]. Correa-Gallego et al. reported higher lymph node harvest and rate of negative margins following MIPD [121], whereas De Rooij and co-workers found no differences in a total number of retrieved lymph nodes but observed a lower rate of positive margins in MIPD group [115].

Two comparative studies between LPD and OPD report greater number of lymph nodes, retrieved by LPD [114, 130]. Croome et al. found that LPD was advantageous over OPD in terms of securing the margin-free resection in patients with major vascular resection [130]. In a matched case–control study, Song et al. found no differences in survival among patients with periampullary cancer following LPD and OPD [126]. Palanivelu et al. reported 5-year survival of 32% in patients with periampullary cancer following LPD [132]. Another study from the same center reported 5-year survival of 20.9% in patients with PDAC [133]. However, both studies included only patients with early-stage cancer ($T_{1-2}N_{0-1}M_0$). Comparative studies on LPD vs OPD for PDAC found no statistically significant differences in survival [118, 129]. These findings were subsequently confirmed by Croome et al., when analyzing the results of LPD and OPD combined with major vascular reconstruction [130].

Laparoscopic pancreatoduodenectomy becomes a standardized procedure after performing 30–60 procedures. Operation time, intraoperative blood loss, conversion, postoperative complication rate, and length of hospital stay are the indicators for learning curve assessment (EL: 4; GoR: C). SCC: Level 2 (86%).

Several studies suggest that LPD can be safely performed by experienced HPB surgeons, skilled in laparoscopy during their early learning curve [127, 134]. At the same time, increased mortality (7.5%) in low-volume centers, demonstrated in the analysis of the American National Cancer Database, underscores the necessity of appropriate training, as well as hospital volume in successful application LPD. Only one study focused on the learning curve for LPD has been published to date [112]. Kim et al. suggest that surgeon must be familiar with the "laparoscopic anatomy" of the region before considering LPD [112]. Analysis of the published data demonstrates that standardization of LPD leads to a significant reduction in operative time and EBL, which was shown within the first 30–60 cases [110, 126, 127].

Currently, there is no standardized training process adopted for LPD. Training out of the operation room was proven to have a positive impact on basic skills during real laparoscopic procedures. Several studies have assessed simulation for basic laparoscopic skills [120, 135, 136]. A further step in laparoscopic simulation is to train surgeons in complex procedures, requiring more advanced technical skills, such as gastric and colorectal procedures, hepatectomy, or pancreatectomy. The aim of this training is to reduce the learning curves and provide safe implementation of real procedures, especially for junior surgeons with limited access to advanced laparoscopic procedures.

Special models have been designed for training the technical skills in pancreatojejunostomy and hepaticojejunostomy during LPD [137]. Furthermore, LPD can be favorable over OPD in terms of the teaching process due to visual advantages provided by laparoscopy [138]. As a result, such training may enhance the understanding of the surgical anatomy.

Laparoscopic pancreatic enucleation

Indications for laparoscopic pancreatic enucleation do not differ from those in open surgery (EL: 3b; GoR: B). SCC: Level 1 (93%).

Indications for performing laparoscopic pancreatic enucleation (LPE) include insulinomas, non-functioning pancreatic NETs, serous and mucinous pancreatic neoplasms, and branch duct IPMN [138–140]. Some authors also advocate that pancreatic metastases from renal cell carcinoma can be removed by LPE in selected cases, since lymph node dissection is not mandatory [141, 142]. Tumor size must be "small." Different authors claim that ideal tumor size should be up to 4 cm [138, 143], although tumors sized up to 10 cm were shown to be successfully removed by LPE [25].

Other key points are accurate localization of the lesion and assuring prudent distance from the main pancreatic duct (MPD). Since LPE lacks manual palpation, intraoperative ultrasound is an essential tool that aids in identifying the lesion and avoiding MPD trauma. Recently, Laliotis et al. suggested a needle-guided LPE of insulinomas after localization of the lesion with the ultrasound [144]. Failure to correctly locate and identify the lesion is one of the main causes of conversion to open surgery, together with such issues as intraoperative hemorrhage, oncologic concerns, or reduced vision of the operative field [145]. According to the literature, conversion rate among published series ranges from 0 to 44% [146].

The minimal distance between the tumor and MPD should range from 2 to 3 mm in order to avoid the injury of MPD, which usually results in POPF [147, 148]. MRI cholangiopancreatography and LUS are the ideal imaging modalities for determining this distance in the preoperative and intraoperative settings, respectively [149]. Other methods of identifying the MPD, such as intraoperative pancreatography using an endoscopic naso-pancreatic drain, also have been described in the literature [141].

Another important issue is lymph node dissection. In most cases, LPE is performed without dissecting any local lymph node. However, since even NETs smaller than 4 cm have the ability to develop lymph node metastases (<1 cm: 14%; 1–1.9 cm: 9%; 2–2.9 cm: 37%; 3–3.9 cm: 56%), some authors advocate for performing routine nodal sampling [117, 150] or selective removal of the regional enlarged lymph nodes [151]. If the frozen section reveals lymph node metastasis, the surgeon should switch to formal pancreatoduodenectomy or distal pancreatectomy [8, 150].

Recent ENETS consensus guidelines consider enucleation possible for the management of insulinoma, gastrinoma and non-functional pancreatic NETs > 2 cm [152].

Although the results of laparoscopic and open enucleation are similar, laparoscopy results in reducing the operative time, blood loss, and postoperative pain (EL: 3b). SCC: Level 1 (91%).

The results of LPE in terms of postoperative and long-term outcomes should not be directly compared with the results of other pancreatic resections, since it is usually performed for benign lesions. Given the fact that these lesions generally do not induce fibrotic changes in the pancreatic gland, the risk of POPF is increased, although it is clinically non-significant in the majority of cases. On the other hand, since these lesions are benign and most of the patients are young, the long-term outcomes are especially important in terms of preserving pancreatic endocrine and exocrine functions.

LPE was shown to carry the advantages of shorter operative time, reduced blood loss, and less postoperative pain when compared with its open counterpart [148, 153]. The main complication arising after LPE is POPF. The published series report POPF after LPE with the average rate of 30–35%, which is similar to POPF reported for OPE [154]. Recently published comparative studies showed comparable fistula rates after laparoscopic and open enucleations [148, 153]. Thus, POPF seems to be more related to the distance between the tumor and the MPD than to the surgical approach itself. In contrast with pancreatoduodenectomy or distal pancreatectomy, transection line along the lesion during enucleation can be larger in case of tumor > 3 cm. Furthermore, the secondary branches of the MPD might be involved. In addition, since there is usually no obstruction of the MPD by tumor, the pancreatic texture remains soft, fragile and particularly prone toward developing POPF. Recently, Heeger et al. demonstrated that CR-POPF and overall complications rates were higher in patients with less than 3 mm between the tumor and the MPD [149]. At the same time, Fernández-Cruz et al. noted that CR-POPF was more frequent following LPE compared with the standard pancreatic resections [155]. Unfortunately, only a few reports mention CR-POPF, which usually ranges between 4 and 27% [143, 153, 155, 156].

Some studies found that right-sided LPE (for lesions in the head/uncinate process of the pancreas) was associated with longer operative time, higher rates of CR-POPF, postoperative complications and prolonged hospital stay compared with the left-sided LPE (for tumors in the body and tail of the pancreas) [157, 158]. However, Afridi et al. report satisfactory outcomes in patients with the SPN located in the pancreatic head/uncinate process [25]. A comparative study from Sahakyan et al. suggests similar outcomes for left- and right-sided LPE [156]. Moreover, the latter is a reasonable alternative to pancreatoduodenectomy in selected cases.

Since patients subjected to LPE usually have benign or low-grade malignant tumors, the oncologic results in terms of local recurrence are excellent in the reported series. However, the majority of studies do not report on tumor recurrence. Although for many of them it is 0%, some studies found tumor recurrence as high as 25% [159]. One of the studies report recurrence rate of 19% in patients with NETs, although this series include patients who had undergone open surgery [158].

Laparoscopic central pancreatectomy

Laparoscopic central pancreatectomy is feasible and safe in selected patients with small benign and low-grade malignant lesions in the pancreatic neck and proximal body (EL: 3b). SCC: Level 2 (87%).

Since the first publication in 2006, relatively small series have been described in the literature, and the largest study included 26 patients [160]. Laparoscopic central pancreatectomy (LCP) is indicated in patients with benign or potentially low-grade malignant lesions, including cases where LPE should not be recommended due tumor proximity to the MPD. LCP is also indicated for lesions in the pancreatic neck, when LDP would sacrifice a considerable portion of healthy pancreatic parenchyma.

Two aspects of LCP have raised concerns among surgeons. First, it is a technically more demanding procedure than LDP, since there is a need of pancreatic anastomosis. Second, POPF is a serious problem in the setting of LCP given the fact that there are two potential sources of pancreatic juice leak (proximal pancreatic transection point in the head of the pancreas and the anastomosis in the pancreatic body). Furthermore, usually normal parenchyma and non-dilated MPD lead to a higher likelihood of leakage. Small experience in LCP reported in the literature hinders setting recommendations for its application.

Song et al. assessed the results of laparoscopic and open central pancreatectomy and found longer operative time but shorter hospital stay after LCP [160]. Other perioperative outcomes were similar in the two groups. The efficacy of LCP in preservation of the pancreatic endocrine and exocrine functions has been proven to be excellent compared to LDP. Crippa et al. report reduced endocrine and exocrine insufficiency rates following open central pancreatectomy compared with ODP (4% vs. 38% and 5% vs. 15.6%, respectively) [161]. While many reports do not explicitly explain long-term results of LCP, some series found no exocrine impairment but worsening of the endocrine function in up to 14.3% of cases [160, 162–165].

The most discussed topic, however, is probably the pancreatic anastomosis given the two possible options, such as pancreaticojejunal and pancreaticogastric anastomoses (PJA and PGA, respectively). At the same time, there are a few points to consider on this issue. First, no studies published have compared PGA and PJA in the setting of LCP. Second, the evidence in the literature favoring PGA over PJA comes from the RCTs on pancreatoduodenectomy including patients mainly with the malignant pancreatic disease, which results in chronic obstruction of the MPD and subsequent hard pancreas with the dilated MPD [166–168]. In contrast, patients undergoing LCP usually have non-dilated MPD and soft pancreatic gland, which can affect the incidence POPF. Third, pancreatic anastomosis during LCP can be even more challenging compared with pancreatoduodenectomy. Finally, despite contradictory results, there are concerns about the effect of PGA on long-term endocrine and exocrine pancreatic functions [169, 170]. This may be an important subject to consider in patients with benign lesions due to a presumably long life expectancy. As there is no clear advantage of one of the anastomosis over another one, its choice seems to be a matter of preference for each surgeon.

Laparoscopic vs robotic pancreatic surgery

Robotic distal pancreatectomy does not seem to be advantageous over laparoscopic approach in terms of surgical and oncologic outcomes (El. 3a; GoR: B). SCC: Level 2 (89%).

Robotic pancreatoduodenectomy is a new technology that does not provide any clear benefits over laparoscopic pancreatoduodenectomy. Its role should be estimated in further studies (EL: 3b; GoR: B). SCC: Level 2 (84%).

The first cases of robot-assisted pancreatoduodenectomy (RPD) and robot-assisted distal pancreatectomy (RDP) have been introduced more than 10 years ago [171, 172]. Some studies consider the robotic approach advantageous over laparoscopy with regard to reduction of natural tremors, absence of fulcrum effect, three-dimensional and high-definition vision, seven degrees of freedom compared to three (EndoWrist technology®), and improved ergonomics for the surgeon [37, 173]. In order to translate these advantages into clinical practice, a number of non-randomized, comparative studies between robotic and laparoscopic techniques have been carried out [173–176]. Some of them report shorter length of hospital stay and higher rate of spleen preservation after RDP [59, 103, 177–179], although these findings were not confirmed in a study from Lee et al. (22% vs 8% for LDP vs RDP, respectively) [37]. Daouadi and co-workers experienced no conversions and demonstrated shorter operative time following RDP when compared with LDP (0% vs 16% and 293 vs 372 min, respectively) [175]. In patients with PDAC, RDP resulted in a higher rate of negative resection margins (100% vs 64%) and increased lymph node yield (19 vs 9). According to the Italian multicenter study, RDP results in lower conversion rate (0% vs 21%) and intraoperative blood loss (462 vs 26mL), but longer operative time (291 vs 217 min) compared with LDP [178]. At the same time, no differences were found between the two techniques in terms POPF and postoperative complications. In contrast with these findings, Goh et al. report shorter operative time and lower conversion rate in laparoscopic group [179]. Furthermore, a prospective non-randomized study from Butturini et al. found no advantages in RDP demonstrating similar intra- and postoperative outcomes, when compared to LDP [173]. Kang et al. report longer operative time and also a two-fold increase in costs associated with RDP [59]. On the contrary, Waters et al. found similar costs after RDP and LDP [103]. Interestingly, the actual operative time (excluding approximately 30 min required to dock and undock the robot) was comparable to LDP.

To date, three meta-analyses have been published on RDP vs LDP [176, 180, 181] all of which concluded that RDP is as safe and feasible as LDP. A study from Zhou et al. including seven non-randomized controlled studies suggests longer operative time, but less blood loss, higher spleen preservation rate, and shorter hospital stay after RDP [180]. Conversely, a meta-analysis from Huang and co-workers, based on nine comparative studies, found no advantages over LDP with regard to intra- and postoperative outcomes [176]. Gavriilidis et al. observed less EBL, but higher readmission rate following RDP and no differences in postoperative complications and POPF [181].

The evidence on RPD is limited to case-series with the largest study including 200 patients [182]. Orti-Rodriguez et al. conducted a comparative review between LPD and RPD including case series on more than five patients (284 vs 147 patients, respectively) [183]. Operative time, morbidity, and mortality were similar in the two groups, whereas the EBL, POPF, and conversion rates were higher in RPD group (346 vs 173mL, 28% vs 13%, and 11.6% vs 5.6%, respectively). Consequently, the length of stay was longer after RPD (13.8 vs 11.1 days). Although these results may favor LPD, a smaller experience in RPD should be taken into account.

Intraoperative laparoscopic ultrasound

Compared with preoperative imaging, intraoperative laparoscopic ultrasound is an efficient tool, essential in the setting of laparoscopic pancreatic surgery (EL: 4; GoR: C). SCC: Level 1 (94%).

The usefulness of laparoscopic ultrasound (LUS) has been reported for several indications in pancreatic surgery. However, its role has been most thoroughly examined in the laparoscopic staging of pancreatic tumors, as well as in LAPS for insulinoma and NETs. In 1995, John TG et al. reported results in 40 consecutive patients with the potentially resectable pancreatic or periampullary cancer, who underwent staging laparoscopy with LUS [184]. Occult metastases were found in 14 patients (35%). Furthermore, LUS detected unresectable tumor in 23 patients (59%) and changed the decision regarding tumor resectability in 10 patients (25%). Thomson BN et al. examined the results of utilizing laparoscopic staging and LUS for presumably non-metastatic pancreatic or ampulllary tumors after the assessment of vascular involvement by a triple-phase CT scan [185]. Vascular involvement was graded from A (fat plane separating tumor from the adjacent vessels) to F (tumor occluding the vessels), and grade A-D on a CT scan corresponded to potentially resectable tumor. Of 152 patients with LUS, 56% were deemed unresectable (31% in grades A-D, 59% in grade E and 100% in grade F). As a result, LUS was concluded to be mainly indicated in patients with the grade A-D involvement. A meta-analysis from Handgraaf et al. including 17 studies found that sensitivity of LUS for determining unresectability was 76%, whereas the negative predictive value (patients, correctly diagnosed with resectable disease) was 82% [186].

Other advantages are that LUS aids to confirm the location of solitary tumor, detect additional tumors, locate "non-visible" tumors, and determine whether enucleation or pancreatic resection is more appropriate. LUS is particularly useful in surgery for insulinoma. Grover et al. reported that LUS identified 12 of 14 insulinomas (86%) and was equivalent to angiography with the venous sampling [187]. The combination of preoperative CT scan and LUS helped determine the precise localization of tumor in 13 of 14 cases (93%). Further studies on insulinoma also suggest that LUS is an effective tool for detecting the tumor and determining the extent of surgery [188–190]. At the same time, LUS requires a sufficient exposure of the pancreas; surgeon experienced in LUS and/or radiologist present at the operation room. All in all, LUS seems to be an indispensible tool in the setting of LAPS.

Discussion

In this first European consensus on LAPS, a total number of 23 statements have been initially presented and 16 achieved ≥ 85% SCC indicating high level of agreement. At the same time, several issues, such as cost-effectiveness of LPD and combined major vascular resections, have been discussed by the expert panel, but ultimately dropped from the list of statements due to low SCC and scarce data in the literature.

Only a few studies, mostly case reports have been published on vascular resections during LPD [130, 191, 192]. Today, a limited number of centers report their experience in superior mesenteric/portal vein resection during LPD [130, 191–194]. The Mayo Clinic group reported less EBL during laparoscopic procedure and similar rates of postoperative morbidity and mortality compared with the open technique [130]. Several reports conclude that venous reconstruction can be safely performed by laparoscopy in case of tumor involvement of the superior mesenteric/portal vein [130, 193, 194]. At the same time, none of the studies examined potential benefits of LPD over OPD in patients with borderline resectable cancer. There are also no reports on the use of LPD in patients with the downstaged tumors after neoadjuvant chemotherapy. Type of venous reconstruction also seems to be influenced by LPD since it can more difficult to close the venous defect transversely due to increased difficulty in mobilizing the vein and colon laparoscopically. As a result, patch may more often be needed to close the defect on the venous wall. The feasibility of arterial resections in the setting of LPD is unclear. The review of the literature found only one report on laparoscopic arterial resection based on two cases [130]. However, this procedure is associated with poor short- and long-term outcomes. Further studies are warranted to determine the role of arterial resection in the setting of PD.

Only two studies compared costs associated with LPD and OPD [124, 127]. Mesleh et al. found that LPD leads to equivalent overall cost compared with OPD [124]. Interestingly, although the operating time and supply cost were higher for LPD, they seem to be balanced by decreased costs due to reduced postoperative hospital stay. A study from Tan and co-workers found that LPD was linked to higher cost for surgery and anesthesia, but lower admission cost compared with OPD [127].

This study demonstrates that LAPS is currently in its development and exploration stages, as defined by the international IDEAL framework for surgical innovation [195]. The literature is mostly based on retrospective case–control studies and systematic reviews on these studies, while no RCTs have been published to date. The International Clinical Trials Registry Platform of the World Health Organization was searched to identify ongoing RCTs. Two RCTs were found on LDP vs ODP: the multicenter LEOPARD-1 RCT for all indications that is currently being performed in 17 centers of the Dutch Pancreatic Cancer Group, and the results are expected in 2017 (http://apps.who.int/trialsearch/Trial2.aspx?TrialID=NTR5188) and the single-center LAPOP RCT from Sweden assessing the length of hospital stay following LDP and ODP in 60 patients with lesions the body and tail of the pancreas (http://apps.who.int/trialsearch/Trial2.aspx?TrialID=ISRCTN26912858). Searching of the International Clinical Trials Registry Platform of the World Health Organization also yielded RCTs on LPD vs OPD for all indications. A trial from India focusing on postoperative morbidity according to the expanded Accordion Severity Grading System in 60 patients (http://apps.who.int/trialsearch/Trial2.aspx?TrialID=CTRI/2013/09/004016) has been completed, so results are awaited. The monocenter PADULAP trial on LPD vs OPD is ongoing in Spain and will include 66 patients (http://apps.who.int/trialsearch/Trial2.aspx?TrialID=ISRCTN9316893). The multicenter LEOPARD-2 phase 2/3 RCT conducted by the Dutch Pancreatic Cancer Group is currently ongoing and investigates the safety and time to functional recovery after LPD and OPD (http://apps.who.int/trialsearch/Trial2.aspx?TrialID=NTR5689).

Compliance with ethical standards

Disclosures Drs. Bjørn Edwin, Mohammad Abu Hilal, Marco Braga, Jean-Michel Fabre, Laureano Fernandez-Cruz, Brice Gayet, Song Cheol Kim, Igor E. Khatkov and Mushegh A. Sahakyan have no conflicts of interest or financial ties to disclose. Dr. Marc G. Besselink is funded by Ethicon International.

Appendix

The following investigators participated in this study as collaborator (upon acceptance of this manuscript, please list as collaborator in PubMed)

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