Editorial Commentary

Is open pancreatic surgery still relevant now in the era of minimally invasive pancreatic surgery?

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Minimally invasive pancreatic surgery (MIPS) has been shown to be associated with reduced length of stay (LOS), intra-operative blood loss and surgical site infections (1). However, the impact of MIPS on the commonly feared complications of pancreatic surgery—post-operative pancreatic fistula (POPF) and major morbidity—remains to be proven. Trial sequential analysis by Ricci *et al.* in 2023 showed that for laparoscopic pancreaticoduodenectomy (LPD) to reduce the relative risk (RR) of POPF by 25%, a cumulative sample size of 2,755 was required (only 818 patients were included in their review). They concluded that it is impossible to recruit enough patients for randomized controlled trials (RCTs) to show the benefit of MIPS in the near future (2). Nevertheless, there is an increasing adoption of MIPS, from 10% in 2010 to 13% in 2014 for laparoscopic pancreatic surgery (LPS), and from <1% in 2010 to 3% in 2014 for robotic pancreatic surgery (RPS) in the United States (3).

Unlike open pancreatic surgery (OPS) however, MIPS comes with a steep learning curve (LC) with similar high post-operative morbidity (4). It is therefore important for expert consensus to prevent unnecessary harm to patients. The Miami International Evidence-based Guidelines on Minimally Invasive Pancreas Resection (IG-MIPR) were established in 2019 (5); however, since then, several trials on MIPS have emerged and evidence needs to be consolidated and updated (6). The Brescia Internationally Validated European Guidelines on Minimally Invasive Pancreatic Surgery (EGUMIPS) was recently published in 2023 to address this need, where 98 recommendations covering 8 domains [terminology, indications, patients, procedures, surgical techniques and instrumentation, assessment tools, implementation and training, and artificial intelligence (AI)] were proposed (7). The authors clearly described the methodology used to develop these set of guidelines, where consensus statements were drafted using the Delphi method. While there are several points raised in the guidelines, this commentary aims to cover on a few controversial issues: (I) indications for LPS or RPS, (II) indications for OPS, (III) comparison of LPS *vs* RPS, (IV) LC of MIPS, and (V) application of AI in peri-operative care.

The EGUMIPS further divided the indications and contraindications for LPS and RPS based on the pathology—benign or pre-malignant, *vs* malignant disease. Unlike benign diseases, surgical resection for malignant diseases requires oncological principles to be obeyed. A total of five recommendations were made for the indications

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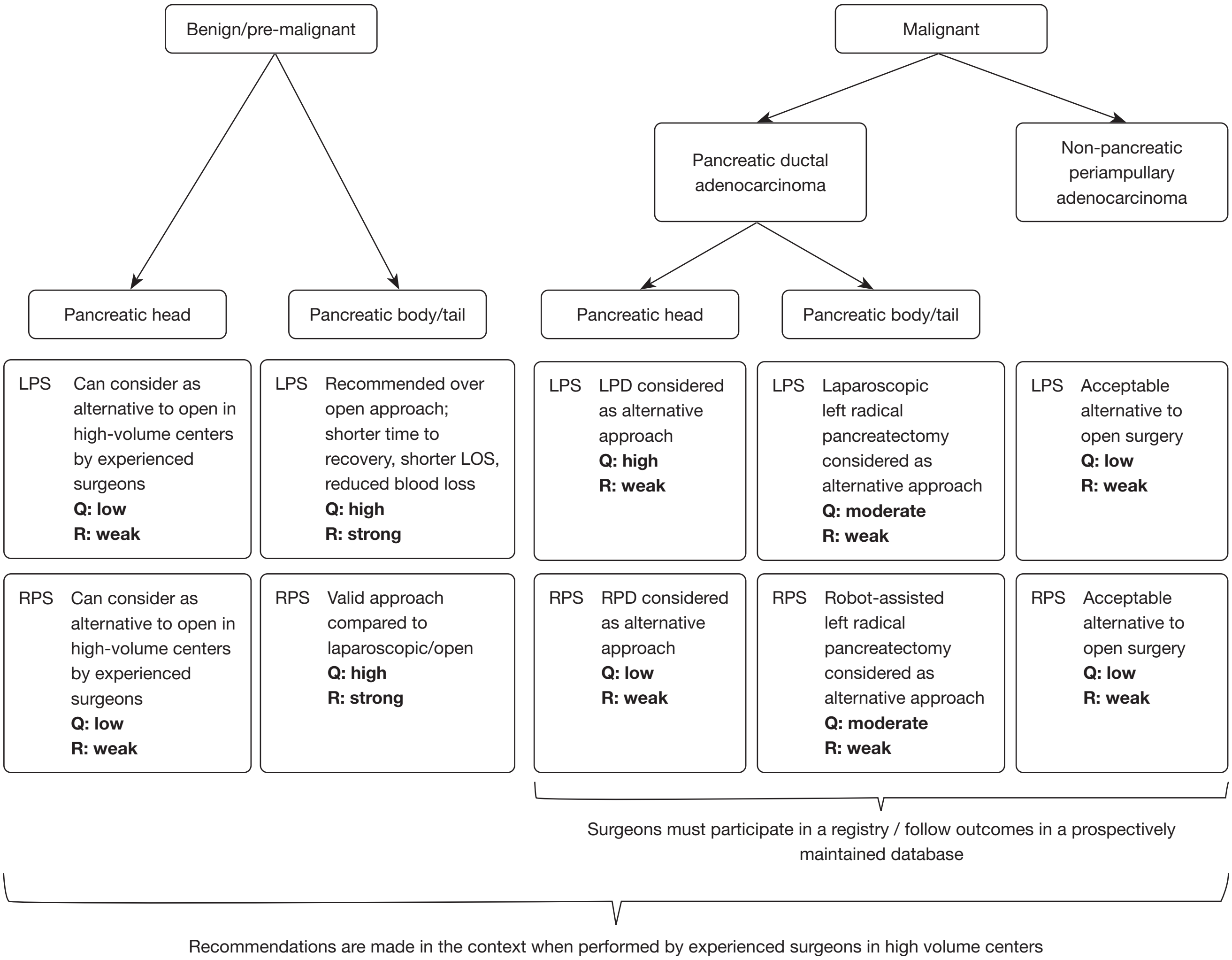

Figure 1 Diagram summarising the recommendations and quality of evidence on the role of LPS and RPS for various types of pancreatic lesions. LPD, laparoscopic pancreaticoduodenectomy; LPS, laparoscopic pancreatic surgery; LOS, length of stay; RPD, robotic pancreaticoduodenectomy; RPS, robotic pancreatic surgery; Q, quality of evidence; R, strength of recommendation based on GRADE framework; GRADE, Grading of Recommendations, Assessment, Development, and Evaluations.

of LPS and RPS each, for which we have summarised in *Figure 1*. In short, only weak recommendations were made for the use of LPS and RPS in pancreatic cancer (regardless of histology) compared to OPS. Strong recommendations were made for the use of LPS or RPS compared with OPS for benign and pre-malignant lesions. The main difference between benign/pre-malignant lesions *vs.* malignant disease would be the need for oncological resection for malignant disease (adequacy of margins, lymphadenectomy). It can be argued that RPS should be superior to open surgery since RPS provides ergonomic advantages and allows for more precise dissection and anastomosis.

However, one may also argue that surgery for malignant disease is more technically challenging due to the extent of disease with possibility of invasion into surrounding structures. This is compounded by the need to overcome the initial LC of MIPS, as well as patients with more advanced disease with invasion into surrounding structures (e.g., borderline resectable pancreatic cancer (BRPC) requiring vascular resection and reconstruction). The International Study Group of Pancreatic Surgery (ISGPS) in 2014 recommends for portomesenteric venous resection in patients with BRPC (8). However, literature is even more limited on the safety and oncological outcomes following

LPD with venous resection and reconstruction; Ma *et al.* demonstrated good outcomes following LPD (n=25) with major vascular resection and reconstruction, with lower intra-operative blood loss (200 *vs.* 400 mL, P<0.001) and shorter LOS (11 *vs.* 11 days, P=0.005) compared to open pancreaticoduodenectomy (n=38) (9). Additionally, there was no significant difference in post-operative morbidity (grade B or C POPF, delayed gastric emptying, abdominal infection, bile leak, or pancreatic haemorrhage) and oncological outcomes (R0 resection rate and number of lymph nodes harvested). While the results shown by this study is optimistic and promising, LPD with vascular resection and reconstruction is technically challenging and should only be performed in high-volume and experienced surgeons. Similarly, for locally advanced pancreatic cancer with invasion into adjacent structures, e.g., colon requiring multivisceral resection (MVR), there is still too little that is known. Laparoscopic MVR has only been shown to have acceptable oncological outcomes with good safety profile in patients with primary colonic or gastric cancer (10). Before any work is done to evaluate the role of MIPS in more extended resections, more studies are required to determine the short-term and long-term oncological benefits in standard pancreatic resections for pancreatic cancer first. OPS should still be the standard surgical approach for complex pancreatic surgeries requiring extended resections.

The third point of discussion would be comparison of short- and long-term outcomes between LPS and RPS. The EGUMIPS provide guidance on LPS *vs.* OPS, or RPS *vs.* OPS; however, there is no direct comparison between LPS and RPS. The EGUMIPS only provided weak recommendation for the use of RPS over OPS for pancreatic cancer; extrapolating from this, it is therefore assumed that the additional benefit of RPS would be even lesser if compared with LPS. Robotic surgery provides a 3-dimensional field of vision, depth perception, ergonomic advantages with endowrists and surgeons' comfort. One would then expect more precise dissection, better anastomosis, and reduced post-operative complications. A recent meta-analysis by Kamarajah *et al.* on 44 studies showed that robotic pancreaticoduodenectomy (RPD) was associated with lower risk of open conversion [odds ratio (OR) 0.45, P<0.001] and LOS (11 *vs.* 12 days, P<0.001) compared with LPD (11). Operating time, post-operative complications including POPF, and R0 resection rates were comparable. Traditionally, operating time for robotic surgery is longer than laparoscopic surgery due to the initial LC and docking time, but this has been largely mitigated by the latest Da Vinci Xi© system. This leads to the question of whether RPS should be recommended over LPS. The benefits showed by the large meta-analysis in RPD and LPD are promising (11), but may not be cost-effective. These benefits may also only be reaped after overcoming the initial LC, which further limits the clinical utility of RPS.

This brings us to the next topic of discussion—the LC. LC is an important topic of discussion in the field of MIS (12). While existing studies showed that MIPS reduces LOS, intra-operative blood loss and surgical site infections (1), these studies do not define the prior experience of included surgeons. It is unknown whether the superior outcomes reflected in these studies were during or after overcoming the LC. These studies should also report on the prior surgical experience to allow better interpretability of results. Additionally, in small-volume institutions, multiple consultant surgeons may be involved in the same surgery; what defines as "one case" of MIPS performed is also arbitrary, since multiple surgeons are involved in various parts of the surgery. These factors render calculation of LC extremely difficult and unrealistic. In order to truly define the LC of MIPS, the LC of a single-surgeon with no prior experience in MIPS (but with a defined number of cases of previous laparoscopic surgeries and OPS) should be reported. This is however extremely difficult realistically as such studies will have to be well-planned prospectively to start at the point when a surgical trainee finishes his or her exit examinations, and begin his or her first case of MIPS. This calls for a need to pool results from multiple studies and draw conclusions from there.

One may expect the LC to be shorter for RPS compared with LPS, since the natural progression for adoption of robotic surgery is from open to laparoscopic, and finally to robotic; this has been shown in the LC for MIS for other gastrointestinal malignancies (13,14). A recent systematic review by Chan *et al.* in 2021 showed that the number of cases required to overcome the LC for laparoscopic and robotic pancreaticoduodenectomy were 34.1 and 36.7 respectively, while that for laparoscopic and robotic distal pancreatectomy were 25.3 and 20.7, respectively, with no statistical significance between laparoscopic and robotic approaches (4). This raises the question on whether MIPS is warranted, especially since there is a sizable number of cases required to overcome the LC, and limited benefits of MIPS. The EGUMIPS similarly agreed on the difficulty to achieve at least 20 independent cases of MIPS per surgeon. However, consensus was eventually made to allow MIPS in lower volume centres in the presence of a well-trained multidisciplinary pancreas team where post-operative outcomes are acceptable; with correct proctorship, the primary surgeon may not have to overcome the LC to obtain similar post-operative outcomes as the supervising surgeon. Interestingly, a recent study found that experience in pancreaticoduodenectomy (PD) is not necessarily essential in achieving good post-operative outcomes (15). Centres with low volume in PD (<11 operations/year) but had high volume in gastric, hepatic, complex biliary or pancreatic operations other than PD (defined as >33 operations/year) did not have increased 30-day mortality [OR 1.258, 95% confidence interval (CI): 0.942–1.680, P=0.1203] or positive resection margins (OR 1.073, 95% CI: 0.948–1.214, P=0.2648). Future consensus statements may also consider the experience in pancreatic-adjacent operations on the recommendations on whether MIPS should be performed, even at low volume centers for pancreatic surgery.

With limited caseloads of pancreatic surgery, it is paramount to find alternative ways to improve surgical skills. Adjuncts for surgical training include computerised simulation, cadaveric workshops and online surgical videos. Viewing surgical videos pre-operatively is a convenient way to allow the surgeon to have a mental imagery to better prepare for surgery (16). Online surgical videos are often truncated to provide an overview of the key steps required and pitfalls to look out for. However, one caveat of online surgical videos is the quality of video watched; surgeons and/or trainees should be cognizant of the source of video and corroborate with other information sources. Advancements in technology have led to the evolution of the use of computerised simulation and AI to guide medical care (17). The EGUMIPS made recommendations on the use of AI for MIPS: use of AI for peri-operative care (e.g., pre-operative risk assessment and planning), AI together with computerised simulation such as augmented reality (AR) to improve post-operative outcomes and potential use of AI for automation of robots for surgery. However, these recommendations were weak and were based off low quality evidence.

The terminology "AI" has been widely used in literature; but what actually defines AI? AI is defined as a machine with intelligent behavior such as perception, reasoning, learning, or communication and the ability to perform human tasks (18). The utility of AI in surgery can be broadly classified into (I) medical education/surgical training (19), (II) peri-operative care (e.g., diagnosis, pre-operative risk assessment and surgical planning, risk prediction for post-operative complications), and (III) surgical treatment. One major role that AI can be used for surgical training would be its role as an adjunct to provide feedback for computerised simulation, such as virtual reality (VR) or AR simulators. For instance, an AI tool was developed to provide individualised performance feedback and grade the user's level of expertise on a neurosurgery VR simulator (20). To our knowledge however, the use of AI to provide individualised feedback has not been used in MIPS yet.

The role of AI is more focused for its use in pre-operative planning, especially due to the complexity of pancreatic surgery. AI allows for 3-dimensional (3D) reconstruction of computed tomography (CT) images to guide pre-operative surgical planning and determine resectability of disease. This is of great clinical significance especially in pancreatic cancer, where there is a subgroup of patients with borderline resectable (BR) disease (21). Unlike resectable pancreatic cancer, there is role for neoadjuvant chemotherapy; a recent meta-analysis on 6 randomised controlled trials (RCTs) showed that neoadjuvant treatment (chemotherapy/chemoradiation) improved R0 resection rate by approximately 20% in BRPC, even though overall survival (OS) and disease-free survival (DFS) were comparable with upfront surgery followed by adjuvant treatment (22). It is therefore important for accurate classification of patients into the BR group. Fang *et al.* showed that the use of the Medical Image 3D Visualization System (MI-3DVS) allowed for a better assessment of resectable PDAC, with an accuracy of 100% compared to that of CT angiography, with an accuracy of 82.5% only (23). Images obtained from 3D reconstruction can also be printed out as 3D models to allow surgeons to better visualise and plan for surgery (24). Other uses include the ability of AI to predict post-operative complications, especially POPF.

Traditionally, robotic surgery is performed by an operating surgeon without any ability for automation. However, this is now made possible with AI, where AI allows the robot to be granted certain extent of autonomy to perform parts of the surgery; for instance, in 2016, Shademan *et al.* reported autonomous robotic anastomosis of porcine intestine complete *in-vivo*, which outperformed human surgeons (25). However, the use of AI to perform RPS is still far from reality clinically; hence, recommendation was made for the need for a human surgeon and to promote data gathering to develop AI algorithms. Of course, there lies the problem of "who to blame" when complications arise, especially if robots are granted full autonomous control. While this discussion is important, it falls beyond the scope of this commentary and should be discussed separately.

In conclusion, while there is an emerging trend towards the use of MIPS worldwide, evidence on the benefits of MIPS is still lacking in general, warranting the need for international consensus to guide the patient selection process, surgical techniques and training process.

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Footnote

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