Editorial Commentary

The current status of minimally invasive pancreatectomy and implications of the Brescia guidelines

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Minimally invasive surgery, typically characterized by laparoscopic and in recent decades, robotic approaches, is one of the main surgical advances of the 21st century. Although pancreatic surgery largely remains an open operative procedure, minimally invasive pancreatic surgery (MIPS) is now a part of the armamentarium of the experienced pancreas surgeon. Several randomized controlled trials and retrospective studies have compared minimally invasive pancreas surgery against the conventional open approach. These studies have demonstrated mixed results regarding the efficacy of laparoscopic pancreatoduodenectomy as compared to open pancreatoduodenectomy in terms of perioperative complications, and oncologic as well as overall outcomes (1-4). On one end of the spectrum, some studies have shown both laparoscopic and robotic surgery have inherent benefits of minimally invasive surgery, such as decreased operative blood loss with reduced rates of transfusion, fewer surgical site infections and pulmonary complications, a shorter length of hospital stay, and earlier return to work. On the other end of the spectrum, as demonstrated in LEOPARD-II, laparoscopic pancreatoduodenectomy was associated with more complication-related deaths compared to open pancreatoduodenectomy, and no difference was observed between groups in time to functional recovery (5). There has been limited reported significant difference between minimally invasive and open techniques for pancreatic fistulas, other major complications, and short-term mortality (5-10). As discussed by Fung *et al.*, the learning curves associated with both laparoscopic and robotic pancreatic surgery could factor into these varying outcomes. Specifically, they found that for robotic approaches in both pancreatoduodenectomy (PD) and distal pancreatectomy (DP), more cases must be performed in order to achieve the learning curve. This can be attributed to the technically demanding nature of PD and robotics (11). However, some meta-analyses have reported more favorable oncological outcomes with minimally invasive techniques, demonstrating significantly higher number of lymph nodes examined compared to open surgery. Some studies even report the greatest probability of achieving R0 resection with the robotic approach (12,13). Although these contradictory findings dampen enthusiasm for a larger transition to MIPS, they illuminate possibilities for both future research and practice.

Despite these advances, pancreatic surgery continues to be one of the most complex and technically challenging procedures. Dr. Kausch performed the first PD in 1909, which was then popularized by Dr. Allen Old father Whipple. However, due to the high perioperative mortality rate of up to 30%, this procedure did not gain widespread adoption until the 1980s. Eventually, patients

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were increasingly being referred to high volume referral centers for pancreatic surgery, which lead to a reduction in the perioperative mortality rate for PD to less than 5%. Despite these efforts, major pancreatic resections continue to carry a significant morbidity rate with high volume centers reporting numbers in the 30–40% range (14). However, these outcomes seem to be improving with the use of minimally invasive techniques. Using the ACS-NSQIP data, Beane *et al.* demonstrated that from 2013 to 2017, robotic PD increased from 2.5% to 4.2% with multiple postoperative outcomes showing significant improvement, including decreased operative times, fewer transfusions, and decreased overall morbidity, mortality, and postoperative length of stay. This study also reported a significant increase in the rate of optimal pancreatic surgery, from 53.7% to 56.9% for PD and from 53.3% to 58.5% for DP (15). Similarly, these outcomes have also shown improvement with effective chemotherapy. Using the ACS-NSQIP data, another recent study demonstrated that between 2014 and 2019, the use of neoadjuvant therapy increased from 24.2% to 42.7% and that neoadjuvant therapy was associated with reduced rates of serious morbidity, clinically relevant postoperative fistulas, and organ space infections. These improved outcomes in turn lead to a lesser need for percutaneous drainage, reoperation, and a decrease in prolonged length of stay over time. Therefore, with the increase in neoadjuvant therapy, the rate of optimal pancreatic surgery has improved during this time period (16). These studies demonstrate that although pancreas surgery is a major surgery with significant risks for morbidity, use of minimally invasive techniques and neoadjuvant chemotherapy can lead to improvement in the rate of optimal pancreas surgery.

Minimally invasive approach to pancreas surgery was pioneered by Gagner and Pomp in 1994, who described the first laparoscopic PD (17). Just 6 years later, Giulianotti *et al.* performed the first robotic assisted PD in 2001 (18). By 2012, seven centers worldwide had reported an experience of 30 or more patients who had undergone laparoscopic PD with 33 robotic pancreatoduodenectomies performed in 2010 alone. Between 2014 to 2019, the overall proportion of pancreatoduodenectomies being performed using minimally invasive techniques in the American College of Surgeons National Surgical Quality Improvement Project database increased from 7% to 11% (19). With 1,141 robotic cases during this time period, the overall proportion of pancreatoduodenectomies being performed robotically increased from 2.8% to 7.5%. By 2019, robotic cases accounted for a greater portion of minimally invasive operations than laparoscopic approach (20). In their meta-analysis, Pfister *et al.* demonstrated that a minimally invasive approach in pancreatic surgery seems feasible and safe in comparison to the traditional open approach. The spectrum of MIPS is increasing as robotic surgery's benefits, compared with laparoscopy, may play a fundamental role in pancreatic resections in the future, tackling the technical issues specifically related to laparoscopic pancreatectomy (21). As surgeons continue to get more experience and robotic access continues to expand, we can expect to see a rise in the number of pancreas surgeries being done with minimally invasive techniques (18-20).

Despite these trends, there is currently no nationally sanctioned training program for robotic pancreas surgery. Given the complexity of these procedures and the high postoperative morbidity rates, minimizing the risk for patients calls for stringent, evidence-based guidelines and an appropriate curriculum for trainees (22). The challenge with robotic PD lies in the suggested learning curve of at least 20–40 cases to achieve proficiency. A recent study using the ACS-NSQIP data demonstrated that despite more robotic pancreatoduodenectomies taking place in recent years, the number of cases being performed in North America is still not adequate for most fellows to achieve proficiency before graduation (20). Therefore, to optimize robotic pancreatoduodenectomies training opportunities, development and implementation of formalized robotic PD training curriculum is required. This type of curriculum is already being implemented at a select few institutions (23-25). Data from these institutions demonstrate that fellows who completed the curriculum have improved posttest operating time and fewer operative errors (26). The ability to achieve similar outcomes following formalized training as compared to obtaining experience through building case volume alone (i.e., the current default) is a marker of success for these training curricula (27).

The Brescia guidelines on MIPS aim to build upon the surgeon's understanding and practice of pancreatic surgery. The article's presented guidelines focus on the differences between robotic, laparoscopic, and open approaches across eight unique domains of pancreatic surgery. In total, five committees were tasked with the development of the Brescia guidelines. All committees were formed with a balance of knowledge and expertise, to ensure a holistic understanding of pancreatic surgery throughout guideline development. The steering committee was responsible for identifying the members of the other four committees:

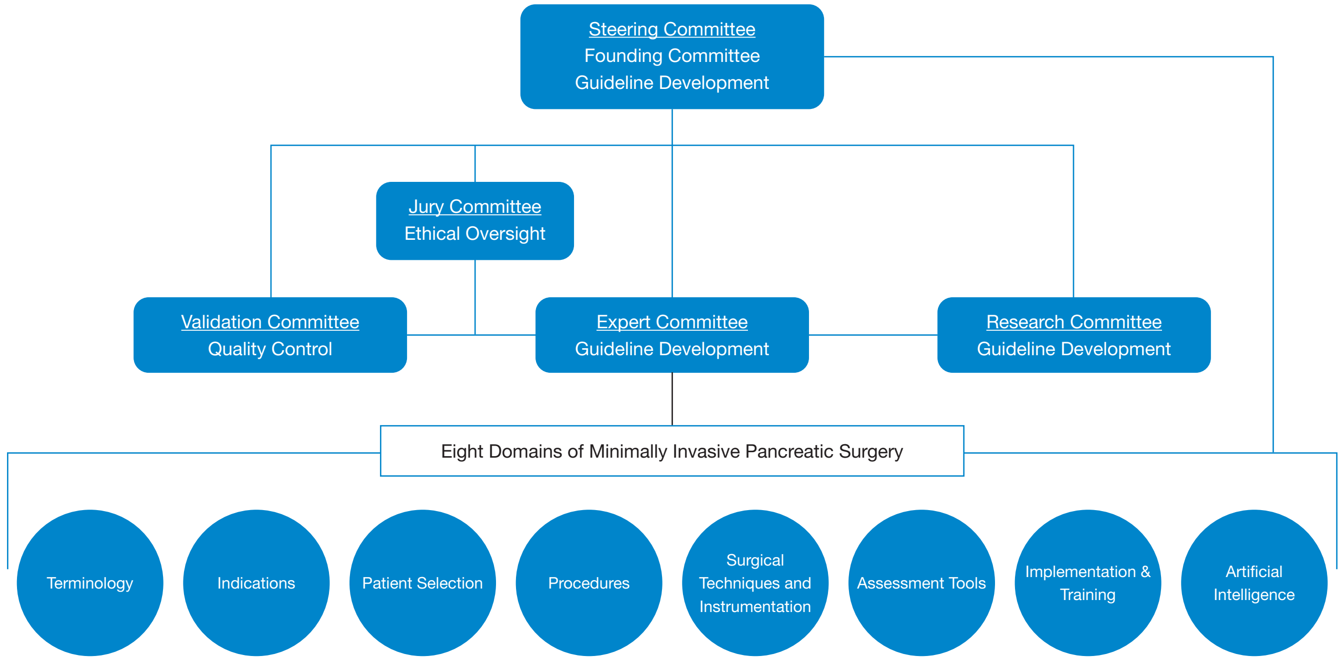

Figure 1 Structural development of the Brescia guidelines for minimally invasive pancreas surgery.

expert committee, validation committee, jury committee, and research committee. The expert committee, research committee, and steering committee were split into subgroups that focused on eight unique domains of MIPS and were tasked with guideline development. The validation committee acted peripherally in ensuring quality control throughout the duration of the study. The Jury committee provided oversight in ensuring appropriate, ethical interaction between the expert and validation committees. Three validated methodologies were utilized in the creation of the Brescia guidelines—the Scottish Intercollegiate Guidelines Network (SIGN) for evidence assessment and guideline development, The Delphi Method to establish a consensus on guidelines, and the AGREE II-GRS Tool for quality assessment and external validation (*Figure 1*).

Across the eight identified domains of MIPS, 98 evidence-based recommendations were established. Many of the recommendations were similar for both laparoscopic and robotic surgery, however, there were some significant differences for the topics of learning curves, cost-effectiveness, and artificial intelligence. The eight identified domains' significant findings are abbreviated as follows (22):

(I) Terminology: definitions were established for the different types of surgical approaches and conversions. The Brescia guidelines expand upon the traditional open, laparoscopic, and robotic surgical categorizations. More specifically, roboscopic, hand-assisted, single port approaches, among others are further defined in the guidelines.

(II) Indications: robotic and laparoscopic approaches can be considered effective alternatives to open DP and open pancreaticoduodenectomy in the treatment of both benign and malignant lesions. These recommendations are stronger for DP.

(III) Patients selection: no contraindications were identified for laparoscopic and robotic pancreatic resections regarding age, obesity, previous abdominal surgery, and size of the lesion. There is limited evidence to significantly analyze the use of vascular resection and neoadjuvant therapy in these populations, and they serve as a topic of future study.

(IV) Procedures: both laparoscopic and robot-assisted approaches were considered appropriate alternatives to enucleations, total pancreatectomy, and both vessel-sparing & vessel-resecting spleen-preserving DP. The role in central pancreatectomy has yet to be elucidated. Furthermore, there is insufficient evidence to establish the optimal anastomotic technique in both robotic and laparoscopic pancreaticoduodenectomy.

(V) Surgical techniques and instrumentation:

recommendations provided for techniques in pancreaticoduodenectomy, DP, vessel and hemorrhage control, stump closure after DP, and drain management are detailed in the Brescia guidelines. Evidence-based recommendations are detailed in the Brescia guidelines—from important landmarks in a laparoscopic Kocher Maneuver to dissection of both relevant vasculature and the biliary tree.

(VI) Assessment tools: identified severe morbidity, mortality, post-operative pancreatic fistulas, conversion rates, and patient-reported outcomes as assessment tools that could help determine ideal approaches to pancreatic surgery. These outcome measures were further categorized as core outcomes for pancreatic ductal adenocarcinoma (PDAC), patient reported outcome measures (PROM), and Quality Adjusted Life Years (QALY).

(VII) Implementation and training: center volumes, learning curves, and cost-effectiveness are topics that were widely debated among the committees. The learning curve for robotic MIPS is reportedly shorter compared to laparoscopic MIPS. However, despite the shorter learning curve, surgeons struggle to attain proficiency in robotic MIPS due to decreased case volumes world-wide. Laparoscopic MIPS is cost-effective, while the cost-effectiveness of robotic MIPS remains unclear.

(VIII) Artificial intelligence: A.I. will impact all areas of surgical practice including pre-operative risk assessment, surgical planning, and intra-operative augmentation. Artificial Intelligence is expected to be crucial in robotic MIPS, while the impact on laparoscopic MIPS remains unclear. However, at this time, surgery should not be performed without a human surgeon as there is still limited evidence on this topic. Given the lack of data, surgeons are encouraged to prioritize gathering data to better understand the role of artificial intelligence in the field of surgery.

Learning curves and case volume were some of the most highly debated topics among the committees. There is a fear that the proposed minimum number of cases-per-year considered acceptable for maintaining skills cannot be achieved worldwide, mostly because of the low volume in many countries as well as the lack of centralization. Furthermore, even in centralized systems, there are potential difficulties in maintaining skills. More specifically, a central system with a large number of surgeons would likely dilute the existing volume of cases; other centers may have multiple surgeons scrubbed into a single case with only one surgeon acting as the primary operator, which makes it difficult to assess a surgeon's true number of cases. In addition to sheer case volume limitations, there is limited established evidence needed to create a standardized framework to measure the learning curve for MIPS. A standardized reporting structure with explicit, defined outcome measures across the learning curve will help facilitate substantiated cross-study comparisons that can be applied to better predict performance (23). These challenges make it difficult to assess an accurate learning curve. Limited evidence is available on the best anastomotic techniques in MIPS and cost-effectiveness in robotic-assisted approach to MIPS. These topics can serve as topics of future studies to further enhance the growing knowledge of MIPS.

In conclusion, the Brescia guidelines form comprehensive recommendations across eight distinct domains of MIPS. To further expand on the Miami International Guidelines on MIPS, the Brescia guidelines specifically delineate the differences between laparoscopic and robotic approaches to MIPS. However, despite these advancements in understanding, work remains to be done to better elucidate the shortcomings of case volume and learning curves. While MIPS can provide a compelling alternative to open pancreatic surgery, scarce case volume and subsequent shortcomings in surgical proficiency create a barrier to adoption. Despite this barrier, pancreatic surgeons should refer to the Brescia guidelines to better utilize and understand MIPS. These guidelines can be used by surgeons, policy-makers, and patients alike to make the most out of MIPS for years to come.

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