Editorial

Minimally invasive pancreaticoduodenectomy for periampullary disease: it's time for a randomized control trial!

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During the 1980's, the introduction of laparoscopy as support to abdominal surgery changed in a revolutionary and innovative way the thoughts and the habits of the surgeons.

The first laparoscopic pancreatoduodenectomy (LPD) was described by Gagner and Pomp in the early 90's (1). There LPD is commonly performed using two different procedures. The laparoscopic-assisted PD or hybrid laparoscopic PD, consisting of the laparoscopic en-bloc resection of the pancreatic head followed by an auxiliary abdominal incision to reconstruct the digestive tract. Whereas if the procedure is wholly performed intracorporeally, the technique is defined as totally laparoscopic PD. All the procedures are also described using the robotic technology (2).

During the past years, minimally invasive PD (MIPD) has reached a considerable diffusion and has become increasingly popular (3,4). However, MIPD has still not reach the same boost and encouragement in the surgical community as other minimally invasive gastrointestinal procedures. This can be explained by the low volume and high complication rate of the pancreatic surgery, especially considering the several challenges of this troublesome surgery, regarding the complicated and different procedure that characterized PD, including pancreatic and biliary anastomoses (5), the high rate of complication and mortality (6), and the oncological radicality (7).

Postoperative pancreatic fistula (POPF) is still the most threatening complication after PD detected, even in high-volume centers, in one third of the patients (8,9). Several studies have shown a reduction of postoperative morbidity and mortality rates and especially a described a better compliance and results of the enhance postoperative recovery pathways in the treatment of the periampullary lesion with MIPD compared with open pancreatoduodenectomy (OPD) (10). Unfortunately, the majority of these studies are retrospective series or nonrandomized trials, while case series and high-quality comparative studies are still limited, and selection bias could likely influence these findings (11).

Chen *et al.* performed a comprehensive systematic review of all published studies to evaluate the safety, feasibility, and efficacy of MIPD, comparing data of the MIPD and conventional OPD (12).

The authors identified 100 studies for the initial systematic review and 26 out of them were included in the meta-analysis. Most of the articles analyzed were case reports or non-control case series studies. No prospective randomized studies have been published yet. The authors included a total of 3,402 patients in the analysis. MIPD was performed in 1,064 patients (31.3%), whereas 2,338 patients (68.7%) were submitted to OPD. The majority of the papers included patients with a benign and malignant disease, whereas five studies only figure out the research on cancers. Even if MIPD has been described for all stage periampullary tumors, also for locally advanced malignant disease involving surrounding organs or mesenteric vessels, most studies excluded patients with a clear infiltration of the vascular structures or with a huge dimension of the tumor. Usually, the reconstruction of the pancreas was performed

by a duct-to-mucosa, end-to-side pancreaticojejunostomy with or without stents. Some authors reported a pancreaticogastrostomy anastomosis.

The systematic review showed a conversion rate of MIPD to OPD ranged from 0% to 40%. The POPF rates widely vary between 3.8% and 50%. The results of the meta-analysis proved that MIPD had a significantly longer operative time, lower estimated blood loss, lower intraoperative transfusion rate, and shorter length of stay. No differences were found in time to oral intake, postoperative complications, POPF, reoperation, readmission, perioperative mortality, and number of retrieved lymph nodes.

Selection bias is a frequent problem especially in this cohort study, as confirmed by the exclusion of patients affected by locally advanced neoplasm or huge size of the tumor undergoing MIPD in this review. The typical patient, selected for MIPD, has a small tumor, ideally different from pancreatic ductal adenocarcinoma, no comorbidity, and no previous abdominal surgery. Even if in the study is reported a comparable rate of vascular resection for MIPD and OPD, no data are available about the neoadjuvant chemotherapy, and this is probably because most series excluded these patients. Notwithstanding the operative blood loss and other pathological variables, such as lymph node harvest or R0 resection rates, are inferior or comparable in MIPD, the initial selection bias could influence these outcomes.

The study reports relevant results of MIPD that allow considering this technique very promising. The surgical outcomes, such as major postoperative complication, reintervention, and readmission rates, are comparable with OPD, whereas the length of hospital stay is reduced in patients submitted to MIPD. These conclusions are still difficult to support and validate due to the presence of publication bias that could modify the results about the safety of the procedure. Furthermore, data about the POPF rate are misrepresented due to the study period and methods analyzed; not all studies classified the postoperative complication, especially POPF, with the International Study Group on Pancreatic Surgery definitions (13-15).

These data are confirmed by the results of previous systematic review and meta-analysis of comparative cohort and registry studies (16). Particularly, de Rooij *et al.* (16) focused on a crucial point; several studies report a higher mortality rate after MIPD performed in low-volume hospitals, such as less than 10 MIPDs per year (17). It is clear and logical that the surgical learning curve plays an essential part of the outcome of individual studies. Structured training programs should be performed in order to improve the surgeons' skills to implement new surgical procedures, such as MIPD safely. Indeed, high-volume centers, that may already have completed the surgical learning phase, report lower mortality rate. For this reason, the minimally invasive procedures should be part of the background and the skills of a pancreatic surgeon, independently by the future applications of the techniques.

The systematic review and meta-analysis demonstrate that MIPD is technically feasible and safe, especially in experienced hands. The study results should be interpreted considering the limitation reported by the authors and particularly the patient selection bias that could be present in the studies analyzed. Considering the evolution of technology and the structured training surgical program, MIPD could have a satisfying diffusion, even if probably will not replace the open procedure but will be applied to selected patients and in high-volume centers. Notably, patient selection should be not automatically a negative aspect and may protect the patients during the learning curve. MIPD needs probably to be implemented exclusive in high-volume centers within a structured training program. Strong and well-conducted prospective comparative studies and randomized clinical trials are needed, especially in high-volume centers, before a more comprehensive diffusion and recommendation of MIPD.

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