Editorial

Pancreatic morbidity following minimally invasive radical gastrectomy

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Minimally invasive gastrectomy has been now almost universally accepted as a valid option for the treatment of gastric cancer, with special reference to stage I malignancies (1-4). Actually, the well-known merits of minimally invasive surgery, such as reduced postoperative morbidity and shorter hospitalization with earlier return to daily activities are combined with the expected oncological outcomes. Nevertheless, there has been an increasing attention for pancreas-related morbidity following minimally invasive radical gastrectomy along the last years (5-9).

Acute pancreatitis and postoperative pancreatic fistula are unusual but potentially life-threatening occurrences in the postoperative course of radical gastrectomy (6,7,9). Despite this, it is likely that the real incidence of such events is underrated in clinical practice, essentially because of the lack of a systematic investigation of specific clinical, laboratory or radiological postoperative data. Indeed, the reported rates of pancreatic fistula and acute pancreatitis following gastrectomy vary significantly in the existing literature, though such variability probably depends more on diagnostic precision than on surgical outcomes *per se* (6,9-11). At this regard, it is noteworthy that, when systematically assessed, pancreatic complications revealed higher incidences than commonly believed (6,9,11,12).

Obama *et al.* from the University of Kyoto (6) compared laparoscopy and open surgery in terms of pancreatic complications analyzing a consecutive series of more than 200 patients receiving gastrectomy for cancer. The authors revealed a higher incidence of clinically relevant (grade B and C) pancreatic fistula following minimally invasive surgery (7% *vs.* 2%), together with a statistically higher amylase concentration in drainage fluids. Moreover, the group of patients undergoing laparoscopic surgery had worse outcomes despite more favorable baseline characteristics such as lower tumor stage, BMI, and rate of upper tumor localization needing total gastrectomy. In the seminal paper by Hu *et al.* (2) a multicentric, randomized trial investigated morbidity and mortality following laparoscopic versus conventional distal gastrectomy with D2 lymphadenectomy for advanced gastric cancer. More than 1,000 patients were included in the analysis from 14 institutions in China. Overall, the incidence of postoperative complication did not differ significantly between the two methods (15% in the laparoscopic group and 13% in the open group). Interestingly, although limited, the incidence of postoperative pancreatic was 0.4% and zero following laparoscopic and conventional surgery, respectively. Similar results were shown by Inokuchi and co-workers (13), who analysed laparoscopic versus open gastrectomy with the propensity-score matching method on patients with poor physical status. Again, postoperative pancreatic fistula was experiences only by patients in the laparoscopic group (4 % *vs.* zero).

More recently, Hiki *et al.* reported on the surgical outcomes of nearly 5,300 patients receiving gastrectomy in Japan (7). After propensity score matching, a total of 1,067 patients receiving laparoscopic gastrectomy were compared to 1,067 patients receiving conventional surgery. Apart

of for the rate of surgical site infection and the length of hospital stay (which favored minimally invasive surgery over conventional celiotomy), there was not significant difference on surgical outcomes between the two surgical approaches. The rate of clinically relevant postoperative pancreatic fistula was significantly higher for laparoscopy than for open surgery, 2.2% and 1% being the relative incidences, respectively.

It is clear that the attention paid to postoperative morbidity related to the pancreas has increased importantly also as a consequence of the dramatic penetration of minimally invasive gastrectomy into surgical practice (6,8,11,14,15). Despite several reviews and meta-analyses comparing minimally invasive versus conventional gastrectomy have been made available during the last decade (1,3,4), none of them has focused the rates of postoperative complications related to the pancreas.

We recently published the results of a comprehensive, systematic meta-analysis of the literature investigating the rates of pancreatic complications of radical gastrectomy (9). Our analysis also analyzed possible differences between conventional celiotomy and minimally invasive surgery. More than 7,000 patients from 20 primary studies were included in the final analysis. Overall, the incidence of postoperative complications related to the pancreas ranged between <0.5% and >6%, being approximately 1% on average. At the analysis of pooled data comparing standard surgery with the minimally invasive counterpart, there was an odd ratio (OR) of 1.6 favoring open over minimally invasive surgery. Particularly, the group of patients receiving minimally invasive surgery had increased risk of both acute pancreatitis (OR, 2.69) and postoperative pancreatic fistula (OR, 1.13).

A number of events are likely to take part in the development of pancreatic complications after gastrectomy, especially in the case of oncological procedures featuring formal lymphadenectomy. Firstly, some critic modification of local blood supply may occur as a result of surgical dissection. Concurrently, the direct manipulative trauma of certain surgical procedures, together with the thermal injury caused by energy devices may also play an important role (5,6,9).

Essentially, it is evident that a careful manipulation to the pancreas is crucial, especially when dissecting the fat tissue from the surface of the pancreas during infrapyloric and suprapancreatic lymphadenectomy (6,9,11,16,17).

In this respect, the technique recently introduced by Tsujiura and colleagues merits particular consideration. Tsujiura *et al.* recently reported on their experience (18) on suprapancreatic lymphadenectomy without direct compression of the pancreas. The authors describe the relative outcomes of a consecutive series of 96 patients receiving laparoscopic radical gastrectomy with either conventional or a so-called pancreas-compressionless suprapancreatic lymph nodes dissection. Basically, according to the proposed technique, the surgical assistant controls the peripancreatic connective tissues instead of the pancreatic body itself and avoids the direct manipulative trauma on the pancreas (7,18). In the compressionless group there was a decreased incidence of postoperative pancreatic fistula (2.2% *vs.* 11.8%, P=0.1) and a significantly lower amylase concentration in the drainage fluids postoperative day 1. In general, all measures directed at improving the intraoperative view and surgical dexterity are to be taken into consideration. Particularly, the use of additional trocars, increasing the pneumoperitoneum and ameliorating the position of the patient are crucial during laparoscopic gastrectomy (9,16,17,19). This is important not only to limit pancreatic compression, but also in order to avoid prolonged use of energy devices in the peripancreatic area that may cause direct thermal injury (9,18,19).

At this regard, one area that merits particular attention is the penetration of robotic surgery in surgical practice. Along the last few years several reports have suggested that the use of the robot may be utile in reducing pancreas-related morbidity (20-22). Actually, the utilization of robotic platforms in surgical practice has been evolving and expanding over the recent years to perform almost all abdominal surgeries, with special emphasis for those surgeries requiring fine dissections in narrow surgical spaces (5,9). As a result, robotic radical gastrectomy has been increasingly performed worldwide and its competency has been demonstrated by a number of experiences (3,7,16). Actually, the use of the robot is thought to be technically advantageous for nodal dissection and some evidence exists suggesting improved outcomes in terms of pancreas-related complications, especially in the case of locally advanced disease (5,6,21).

Son et al. (23) analysed more than 100 minimally invasive spleen-preserving total gastrectomies with D2 lymphadenectomy and compared the robot with conventional laparoscopy on the mean number of harvested and positive lymph nodes. The two groups were well-matched for preoperative data including BMI, tumor stage, and previous surgery. Overall, the mean amount of harvested lymph nodes was 47.2 and 42.8 for robotic and

laparoscopic surgery, respectively. Particularly, perigastric lymph node dissection resulted in 30.8 and 26.6 lymph nodes. Interestingly, the volume of extra-perigastric dissection favored significantly robotics over laparoscopy (15.9 *vs.* 12.2), specifically in the case of stations 10 (splenic hilum), 11 (splenic artery) and in the suprapancreatic stations (7-12). Overall, there was no significant difference in the number of metastatic nodes between the two groups, except for peripancreatic lymphadenectomy, for which robotic surgery retrieved an higher amount of metastatic nodes. The authors concluded that in the setting of total gastrectomy, the robot might provide some advantages compared to conventional laparoscopy, despite there was not significant differences between the two methods on overall and disease-free survival. One of the most substantive experience is that of Suda and associates (5), who in 2015 published their Institutional retrospective analysis of more than 500 minimally invasive gastrectomies (both laparoscopic and robotic) performed during a period of 4 years. Pancreatic complications did not occur in the robotic group, while both pancreatic fistula (4.3%) and acute pancreatitis (0.5%) were observed in the group of patients receiving conventional laparoscopic interventions. Similarly, Seo *et al.* (21) studied the incidence of postoperative pancreatic fistula following minimally invasive gastrectomy in their series including 40 patients. The authors compared the conventional laparoscopic to the robotic technique. Overall, the rates of postoperative fistula were significantly different between the two groups (20% *vs.* 10%), in favor of the robot. Kim and colleagues (24) recently presented similar data comparing laparoscopy with robotics in performing suprapancreatic nodal dissection during radical distal gastrectomy. A total of 272 patients were included. Overall, the robotic group had significantly higher amount of lymph nodes yield, particularly at extra-perigastric area and number 11 station. Noshiro and associates (22) recently published the results of a prospective trial comparing standard laparoscopic and robotic distal gastrectomy for gastric malignancy. The authors compared the two techniques on 181 consecutive patients (whereby 160 receiving laparoscopies and 21 receiving surgery with the robot). While laparoscopic gastrectomy was performed with the aid of ultrasonic-activated devices, the robot was used employing only monopolar/bipolar energy. Overall, the robot was associated with higher number of retrieved lymph nodes compared to laparoscopy (44±19 *vs.* 40±15). Interestingly, despite the higher extent of lymphadenectomy, the incidence of postoperative pancreatic fistula tended to be lower after robotic surgery than following laparoscopic surgery.

Due to the relative lack of high-level evidences and the absence of specifically focused trials, definitive data on possible methods to avoid pancreatic complication following minimally invasive gastrectomy cannot be drawn. Currently, the application of meticulous compressionless operative techniques, along with the improved dexterity provided by the robot seem to show a propensity for lower rates of pancreatic fistula and pancreatitis (5,6,9,11,15,18). However, the tendency toward increased postoperative morbidity related to the pancreas following minimally invasive surgery as compared to conventional surgery can still be of concern and specific trials addressing this issue are strongly warranted (5,9,15,16,25).

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Footnote

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