Editorial

Is pylorus resecting pancreaticoduodenectomy a better surgical alternative than pylorus preserving pancreaticoduodenectomy regarding delayed gastric emptying?

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Pylorus preserving pancreaticoduodenectomy (PPPD) has been popularized as the surgical approach for patients with periampullary lesions by Traverso and Longmire since 1978 (1). It was first hypothesized to reduce the occurrence of dumping, diarrhea, bile reflux gastritis and improve overall nutritional status compared with classic pancreaticoduodenectomy, also known as classic Whipple (CW). Based on the Cochrane database review in 2016, there was no difference between PPPD and CW in terms of tumor recurrence, overall survival and relevant morbidity parameters (2). However, PPPD was associated with increased rate of delayed gastric emptying (DGE) (31.4% *vs.* 23.5%; OR 3.03, 95% CI, 1.05–8.7, P=0.04). DGE was the most common complication after pancreaticoduodenectomy with reported incidence between 7–61% (3). Subtotal stomach-preserving pancreaticoduodenectomy (SSPPD) or pylorus resecting pancreaticoduodenectomy (PRPD) was therefore designed during 1990s to preserve the pooling ability of stomach and decrease the rate of this frustrating complication. Meta-analysis at 2015 including 650 patients showed that PRPD had lower rates of DGE compared to PPPD (OR 2.75; 95% CI, 1.75–4.30, P<0.00001) (4). However, lack of randomization and retrospective in design of most included studies limited its validity. Pylorus resection or pylorus preservation in partial pancreaticoduodenectomy (PROPP study) was aimed to investigate the effect of pylorus resection on postop DGE incidences (5).

As the currently largest, randomized controlled trial, PROPP study included 188 patients with statistical superiority hypothesis (pylorus resection is associated with less DGE than pylorus preservation). In the control group, duodenum was divided 2 cm distal to the pylorus. An antecolic end-to-side (ETS) duodenojejunostomy was performed 50 cm distal to the hepaticojejunostomy. No pyloric dilatation or pyloromyotomy was performed. While in the intervention group, stomach was resected within 1 cm proximal to the pyloric ring. An antecolic ETS gastrojejunostomy was also performed 50 cm distal to the hepaticojejunostomy. This study failed to detect a significant difference in DGE rate within 30 days between PPPD and PRPD group (25.3% *vs.* 31.2%, OR 1.534, 95% CI, 0.788–2.978; P=0.208). Higher BMI, indigestion and intraabdominal major complication were significant risk factors for DGE. However, interpretation and clinical application of these data are needed with great cautions.

There are two other randomized clinical trials (RCTs) currently available in comparing surgical outcome between PPPD and PRPD prospectively. Kawai *et al.* enrolled 130 patients and demonstrated significant difference of DGE incidence between PPPD and PRPD group (17.2% *vs.* 4.5%, P=0.0244) (6). On the other hand, Matsumoto *et al.* recruited 100 patients but found no significant difference of DGE rate between PPPD and PRPD group (20% *vs.* 12%, P=0.414) (7). All of these studies assessed the incidence of DGE by ISGPS, which eliminated the limitation of prior studies (4). Meta-analysis of these existing RCTs failed to show any statistical significance between postop morbidities

of those two procedures, including DGE rate (8). Thus non-superiority of pylorus resection was confirmed by the result. Noticeably, these two studies from Japan tended to use more conservative postop management [for example, remove nasogastric tube (NGT) if daily output lower than 200 mL] comparing to the generalized enhanced recovery after surgery (ERAS) concept in German (NGT was removed as soon as mechanical ventilation stopped, usually at the end of the operation). Overall hospital stays of Japan study were longer than those of PROPP study, but DGE rates were relatively lower than those of the German study. Patient population with associated BMI difference, one of the independent prognostic factor in PROPP study (OR 1.09, 95% CI, 1.01–1.19, P=0.043), and variable indications for surgical intervention may also contribute to the insignificance.

More importantly, none of current RCT addressed with oncologic outcomes between PRPD and other PD approach despite most of the pancreaticoduodenectomy cases were indicated for pancreatic head or periampullary cancer. Sakai *et al.* summarized that the infrapyloric lymph node metastatic rate from pancreatic head cancer was about 12% (9). Adequate dissection and sampling during oncological resection are crucial for accurate staging and prognosis estimation. There are also emerging evidences that side to side (STS) gastrojejunostomy may be superior to ETS anastomosis in term of DGE incidence. Nakamura *et al.* retrospectively analyzed 160 patients between 2007 and 2012 (10). The incidence of DGE was 21.3% in the SSPPD-ETS group compared with 2.5% in the SSPPD-STS group (P=0.0002). In multivariate analysis, end to side gastrojejunostomy was the only independent significant risk factor (OR 9.85, 95% CI, 2.51–66.03, P=0.0005). Murata *et al.* enrolled 137 patients which divided into two subgroups, stapled STS anastomosis (SA group, n=57) and conventional hand-sewn end to side anastomosis (HA group, n=80) (11). Overall postop DGE incidence was significant lower in SA group (21.1% *vs.* 46.3%, P=0.003). Moreover, primary DGE incidence was noticed to be significant lower in SA group (8.8% *vs.* 28.8%, P=0.002) while secondary DGE incidence was comparable between those two subgroups. Furthermore, several reports have also suggested that the postoperative intraabdominal complication such as pancreatic fistula, biliary fistula and fluid collection are important risk factors associated with secondary DGE. Sato *et al.* concluded that pancreatic leak was the sole risk factor for secondary DGE after SSPPD (OR 6.63, 95% CI, 2.86–15.74; P<0.001) (12). Primary and secondary DGE should be defined separately since they had different mechanism and management algorithm. Walters *et al.* compared 194 PD patients, with 28 CW, 82 PPPD and 84 long gastrojejunostomy for PD (LGPD) with 9 cm anastomosis (13). DGE incidence was reported to be 46.4%, 37.8% and 16.7% respectively (P=0.001). They concluded that LGPD was associated with significantly decreased DGE compared to SPD and PPPD. Lastly, with the rising rate of neoadjuvant therapy (NAT) applied to borderline resectable and locally advanced pancreatic cancer in the last few years, its association with DGE incidence after PD was still unknown. Marchegiani *et al.* analyzed 445 patients with pancreatic adenocarcinoma from 2014 to 2016, DGE rate was reported to be significantly increased in NAT cases (15.2% *vs.* 8.3%, P=0.04) (14).

Centralization in specialized institution and refinement of the surgical technique in the last few decades have significantly decreased mortality rate of PD and already made it a safe procedure. However, management of postoperative complications with associated socioeconomic burden still warrant further clinical research.

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Footnote

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