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Pylorus-preserving gastrectomy for early gastric cancer

Ke-kang SUN *et al*. Pylorus-preserving gastrectomy

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Abstract

Pylorus-preserving gastrectomy has been widely accepted as a function-preserving gastrectomy for middle-third early gastric cancer with a distal tumor border at least 4 cm proximal to the pylorus. The procedure essentially preserves the function of the pyloric sphincter, which requires to preserve the upper third of the stomach and a pyloric cuff at least 2.5 cm. The suprapyloric and infrapyloric vessels are usually preserved, as are the hepatic and pyloric branches of the vagus nerve. Compared with distal gastrectomy, pylorus-preserving gastrectomy has significant advantages in preventing dumping syndrome, body weight loss and bile reflux gastritis. The postoperative complications after pylorus-preserving gastrectomy have reached an acceptable level. Pylorus-preserving gastrectomy can be considered a safe, effective, and superior choice in early gastric cancer, and is expected to be extensively performed in the future.

Key Words: Gastric cancer; Pylorus-preserving gastrectomy; Oncological safety; Gastric stasis

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Core Tip: Pylorus-preserving gastrectomy has been widely accepted as a function-preserving gastrectomy for middle-third early gastric cancer. The procedure requires to preserve the upper third of the stomach and a pyloric cuff at least 2.5 cm. The hepatic and pyloric branches of the vagus nerve are usually preserved. Pylorus-preserving gastrectomy has significant advantages in preventing dumping syndrome, body weight loss and bile reflux gastritis.

INTRODUCTION

Pylorus-preserving gastrectomy (PPG) was initially proposed for treating gastric ulcers in 1967 [1]. It has since been regularly performed as a function-preserving gastrectomy for early gastric cancer (EGC) in Japan and South Korea [2], which embodies the pursuit of "precision medicine". In its development over 60 years, PPG has gradually reached a consensus on lymph node dissection, the length of the pyloric cuff, and preservation of the vagus nerve and pyloric vessels. PPG is acceptable with favorable outcomes for the middle portion EGC. This article reviewed the development history, indications, oncological safety, complications, and functional benefits of PPG.

Historical development

As early as the end of the 19th century, surgeons have tried to perform gastrectomy with the preservation of the gastric antrum and pylorus to reduce the complications of bile gastric reflux and dumping syndrome. Segmental gastrectomy (SG) was first reported in gastric ulcers treatment in 1897 [3]. However, SG was abandoned in the 1920s because of postoperative complications such as anastomotic stenosis, ulcer recurrence, and delayed gastric emptying (DGE) [4, 5]. Subsequently, Wangensteen recommended the supplementing pyloroplasty to promote gastric drainage, but this exactly offset the merits of preserving the pylorus [6]. Maki *et al* [1] first described the detailed surgical procedures of PPG in 1967, and reported long-term satisfactory results in gastric ulcer treatment in 1992 [7]. However, the development of internal medicine has greatly changed the therapeutic strategy of peptic ulcer, and PPG has gradually faded

out of gastric ulcers treatment. In 1991, Kodama *et al* [8] first proposed PPG for treating EGC. At this late hour, PPG has been recommended as a treatment route for middle-third early gastric cancer with a distal tumor border at least 4 cm proximal to the pylorus [9]. Nunobe *et al* [10] reported that to retain the functions of the gastric antrum and pylorus, the length of the preserved gastric antrum should be at least 2.5 cm. Since most T1aN0M0 cases undergo endoscopic mucosal resection, the indications of PPG are mainly T1aN0M0 cases which are not suitable for endoscopic resection and T1bN0M0 cases. It can also be considered as an additive surgery after endoscopic resection [9].

Lymph node dissection

Preservation of pyloric function during PPG procedure depends on the pyloric antrum blood flow and nerve preservation, which result in the incomplete dissection of No.5 and No.6 Lymph nodes. In recent years, the regularity of lymph node metastasis with the middle portion EGC has provided a theoretical basis for PPG. In 1991, Kodama *et al* [8] investigated the lymphatic drainage pathways in middle-third gastric cancer by the subserosal injection of activated carbon particles on the lesser and greater curvatures of the stomach. The results showed that the lymph flowed mostly from the lesser curvature to the No.3 and No.7 Lymph nodes, with few drainaging to the No.5 nodes, while drainage from the greater curvature included the No.4d and No.6 Lymph nodes. 154 patients undergoing subtotal gastrectomy for middle-third EGC were analyzed and the result showed no involvement of the No.5 and No.6 Lymph nodes in 82 cases with mucosal invasion, while No.6 node involvement was only confirmed in 4.2% (3/72) patients with submucosal invasion. Another cohort study of 701 cases found metastasis rates of 0% and 0.4% for the No.5 and No.6 nodes, respectively, and involvement of No.12a and No.11p was negligible in middle-body EGC. Therefore, the authors proposed that PPG is safe for middle-third EGC, as well as for high and moderately differentiated T2 gastric cancer below 4 cm in diameter. In 2013, Shinohara *et al* [12] investigated the embryology and topographic anatomy of the infrapyloric lymph region and divided No.6 Lymph nodes into 3 subgroups, namely 6a, 6v and 6i. No.6a is separated from No. 6i by the infrapyloric artery and the initial branch of the right

gastroepiploic artery. The involvement No.6i lymph node is extremely rare, which provides an important theoretical basis for selective dissection of No.6 Lymph nodes in PPG. Similarly, to retain the hepatic and pyloric branches of the vagus nerve, No.5 and No.12a lymph nodes are routinely preserved. Additionally, metastasis to the left suprapancreatic lymph nodes is extremely rare, so that dissection of the No.11p node is not required in PPG. Therefore, the dissection of No.1, 3, 4sb, 4d, 6a, 6v, 7, 8a, 9 Lymph nodes is required in PPG procedure [9]. (Figure 1)

Anastomosis method

Both extracorporeal and intracorporeal anastomosis can be performed in PPG. The extracorporeal anastomosis was attached from the middle incision in the upper abdomen with the anastomosis site lying directly beneath [13, 14]. This allowed the surgeons to palpate the margin before transection of the stomach, avoiding insufficient resection margin or excessive resection. The handsewn anastomosis can be intermittent or continuous suture, and a continuous suture does not increase the risk of anastomotic stenosis. More recently, total laparoscopic gastrectomy was gradually performed, and there are many methods for intracorporeal anastomosis [15]. Yang *et al* [16] performed a layer-to-layer manual anastomosis of the anterior and posterior walls using two double-needle barbed sutures intracorporeal. Alternatively, suture of the posterior side with a linear stapler and handsewn suture on the front side was performed. Intracorporeal delta-shaped gastrogastrostomy with a linear stapler was a relatively simple method during laparoscopic PPG, but it requires the sacrifice of part of the gastric antrum. Additionally, the antrum and proximal remnant stomach twist partially around the anastomosis, and the lesser curvature side was not used for anastomosis [15]. A retrospective analysis showed no significant difference in proximal margin, the number of lymph nodes, surgical complication and postoperative hospital stay between intracorporeal and extracorporeal anastomosis [17]. Ohashi *et al* [18] reported the "piercing method" to perform intracorporeal end-to-end anastomosis with a linear stapler, but this method is cumbersome and time-consuming. Similarly, overlap anastomosis also requires the sacrifice of a certain length of the gastric antrum.

Interruption of the annular muscle may affect the function of the gastric antrum. Therefore, extracorporeal anastomosis is still performed by hand suture in many institutions.

Oncological safety

The concerns surrounding the oncological safety of PPG come from two aspects: the limited dissection of the No.5 and No.6i lymph nodes and the resection margins of the stomach. Since PPG meets the requirement of a 2-cm margin, and the frozen section diagnosis can also determine the tumor resection margin during the operation. Therefore, the concerns mainly come from incomplete lymph node dissection. According to a database of 305 patients with middle-third EGC, the rate of No.5 Lymph node metastasis was 0.2%; meanwhile, a 98% overall 5-year survival and 0% cancer-specific mortality was reported after PPG [19]. Jiang *et al* [14] reported an overall 3-year survival rate of 97.8 % and disease-specific 3-year survival rate of 99.3 % in 188 patients received PPG. These results were consistent with previous reports on the mortality after distal gastrectomy (DG) for EGC. A multicenter cohort analysis involving 1004 EGC patients (502 PPG and 502 DG) showed that the 5-year overall survival rate was 98.4% for PPG and 96.6% for DG, and no significant differences in either overall survival or relapse-free survival between the two groups [20]. Another systematic review evaluated the pathological and oncological outcomes betwwen PPG and DG in 4500 EGC patients. The results showed fewer lymph nodes harvested, shorter proximal and distal margins in the PPG group, and there was no significant difference in overall survival or relapse-free survival [21]. Thus, the oncological safety of PPG was comparable to that of DG in EGC patients. In addition, due to the accuracy of preoperative staging, some patients with preoperative diagnosis of T1 showed T2 or deeper invasion [22]. Whether such patients require additive surgery is another question to be concerned. Takahashi *et al* [23] reported that 6.4% of the patients had postoperative pT2 or deeper after PPG in 897 patients; nevertheless, no higher recurrence rate was observed in these patients. It has been reported that patients with a preoperative staging of T1 but postoperative pT2 had a better prognosis and less occurrence of lymph node metastases in comparison with

patients preoperatively diagnosed as T2 [24]. Although several retrospective studies have reported acceptable long-term survival outcomes for PPG [14, 19, 20, 25, 27], it has not been confirmed by prospective clinical studies. It is hoped that the ongoing multicenter randomized controlled trial KLASS-04 will settle the question of the advantages of PPG to DG in terms of oncological safety and functional benefits.

Postoperative complication

The core technology of PPG is the functional preservation of the pylorus, and it can theoretically prevent postoperative dumping syndrome and alkaline reflux. Recent studies have shown that compared with DG, PPG can maintain body weight and better postoperative nutritional status [25, 27, 28]. Terayama M *et al* [29] compared postoperative skeletal muscle index between PPG and DG in in old EGC patients, and the result showed a great advantage in maintaining the postoperative skeletal muscle mass after PPG. Moreover, the retention of the hepatic branches could also reduce the occurrence of cholestasis and gallbladder stones. Nevertheless, PPG is also associated with non-negligible postoperative complications, namely DGE, gastric stasis or gastroparesis. Therefore, to benefit patients with PPG, it is necessary to understand the mechanisms responsible for postoperative DGE and find the preventive methods. It is acknowledged that the normal pyloric function is largely dependent on the length of the pyloric cuff, together with the retention of circulation and nerve supply to the pyloric antrum. In the early years of PPG, surgeons focused on the retention of the vagus nerve and, at that time, the preservation of the pyloric and hepatic branches was strictly required. With the continuous deepening of research, people realized that the blood flow of the pyloric cuff was another important factor in the functional preservation of the pylorus. Kiyokawa *et al* [30] found that the preservation the infrapyloric vein significantly reduced the incidence of DGE after PPG, which may be effective to reduce pyloric edema. The appropriate length of the pyloric cuff is another important factor affecting postoperative complications. Nakane *et al* [31] demonstrated that 2.5 cm was superior in terms of some postoperative complications and weight recovery compared with 1.5 cm. However, Morita *et al* [32] found that the occurrence of gastric stasis did not differ

between cuff length 3.0 cm and over 3.0 cm. The Postgastrectomy Syndrome Assessment Study (PGSAS) after PPG revealed that the dimensions of the proximal gastric remnant and hand-sewn anastomosis also played a significant part in postoperative symptoms and quality of life [33]. In terms of patient eligibility, a retrospective study found that age (≥ 61 years), diabetes, and postoperative intra-abdominal infection were risk factors for DGE [23]. High body mass index was identified as another risk factor for gastric stasis after PPG [22]. The patients with the presence of hiatal hernia and dietary complications would predispose to reflux esophagitis after PPG [34, 35].

CONCLUSION

Pylorus-preserving gastrectomy has been widely accepted as a function-preserving gastrectomy for middle-third early gastric cancer. Compared with distal gastrectomy, pylorus-preserving gastrectomy has significant advantages in preventing dumping syndrome, body weight loss and bile reflux gastritis. The postoperative complications after pylorus-preserving gastrectomy have reached an acceptable level. The preservation of pyloric function has complicated the technicalities of PPG and suggested the potential risks associated with incomplete lymph node dissection. The precise determination of functional benefits, oncological safety, technique standardization and the clarification of complications have not been strictly addressed. It is also not fully understood whether patients benefit from PPG if they suffer gastric stasis, or whether PPG for EGC increases the risk of secondary gastric cancer.

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