

Survival Benefit of Pylorus-Preserving Gastrectomy in Early Gastric Cancer

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- BACKGROUND:** Pylorus-preserving gastrectomy (PPG) is performed in some patients for the treatment of early gastric cancer. The aim of this study was to investigate longterm survival for patients having PPG with extensive lymph node dissection, except for the suprapyloric nodes, for early gastric cancer.
- STUDY DESIGN:** From January 1995 to December 2006, 305 patients underwent PPG if they met the following criteria: cT1 (mucosa or submucosa), cN0 gastric cancer in the middle body of the stomach. Overall 5-year survival, cancer-related mortality, and freedom from recurrence were assessed retrospectively.
- RESULTS:** The median followup period was 61 months (range 27 to 144 months). Seven patients died, and the overall 5-year survival probability was 98%. Gastric cancer-related mortality was 0% and none of the patients had evidence of tumor recurrence. The accuracy of the preoperative diagnosis of T1 gastric cancer using endoscopy or endoscopic ultrasonography was 95.7%.
- CONCLUSIONS:** PPG may provide a longterm survival benefit for patients with clinically diagnosed T1 (mucosa or submucosa), cN0 gastric cancer in the middle body of the stomach, only when the accuracy of preoperative diagnosis can be assured. (J Am Coll Surg 2009;209:297–301. © 2009 by the American College of Surgeons)

Pylorus-preserving gastrectomy (PPG) is performed in some patients to treat early gastric cancer^{1–3} as a function-preserving surgical procedure to maintain a better quality of postoperative life. By preserving pyloric function, PPG has many advantages over conventional distal gastrectomy with Billroth I reconstruction, particularly in the prevention of postgastrectomy disorders, such as dumping syndrome and alkaline reflux.⁴ Although PPG preserves gastric function, patients occasionally have a feeling of gastric fullness after food intake in the early postoperative period and some manifest longterm retention of food in the residual stomach.^{2,5} To prevent this gastric stasis, both the right gastric artery and the pyloric branch of the vagal nerve to the pyloric cuff are preserved³; consequently, the procedure does not involve dissection of the suprapyloric lymph nodes.

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The proportion of T1 (mucosal or submucosal) gastric cancers is approximately 50% in Japan and Korea. A survival rate < 90% has been demonstrated for patients with T1 (mucosal or submucosal) gastric cancer after radical surgery with complete removal of the first- and second-tier lymph nodes.^{6,7}

Our indication for PPG was cancer located in the middle one-third of the stomach, with a maximum diameter < 5 cm, and intramucosal or submucosal carcinoma without lymph node metastasis (cT1, cN0). Since 1990, we have been performing PPG with second-tier lymph node clearance, except for suprapyloric lymph nodes, and we routinely perform pickup sampling of these lymph nodes. These procedures should be sufficient for the curative treatment of early gastric cancer because the metastatic rate of suprapyloric nodes in 3,646 cases of T1 (mucosal or submucosal) cancer located in the middle body of the stomach was found to be only 0.2% in a previous retrospective survey.⁸ But the longterm outcomes of PPG for T1 (mucosal or submucosal) gastric cancer are rarely reported.

In this study, to investigate longterm survival of PPG with extensive lymph node dissection (but not the suprapyloric lymph nodes) in patients with T1 (mucosal or submucosal) gastric cancer, followup data from 305 PPG procedures were analyzed.

METHODS

From January 1995 to December 2006, we performed 3,975 potentially curative gastrectomies. Among these cases, 1,953 patients with clinically diagnosed early gastric cancer underwent surgical intervention with curative intent in the Department of Gastrointestinal Surgery at The Cancer Institute Hospital, Tokyo, Japan. Of these patients, 305 met our indications for PPG and underwent the procedure. Only 3 of 1,953 patients (0.2%) were suspected of having lymph node swelling of the peripyloric area on the basis of a preoperative CT scan, and no patients were found to have lymph node metastasis by intraoperative frozen section diagnosis. So, only three patients were excluded from PPG because of suspected lymph node metastasis of the peripyloric area. All tumors were histologically confirmed as adenocarcinomas and were clinically diagnosed as mucosal or submucosal gastric cancer without lymph node metastasis (cT1, cN0). Clinical classification of tumor depth (cT) and nodal involvement (cN) was determined by pre- and intraoperative evaluation, including barium radiography, upper gastrointestinal tract endoscopy, abdominal ultrasonography, CT, or endoscopic ultrasonography. Intraoperative cN classifications were made by routine intraoperative frozen section diagnosis of lymph nodes from the dissected stomach specimen. PPG was indicated if the cancer was located in the middle one-third of the stomach, had a maximum diameter <5 cm, was located >5 cm proximal to the pyloric ring, and was intramucosal or submucosal carcinoma without lymph node metastasis (cT1, cN0). PPG was not indicated in patients with cardiac (greater than New York Heart Association II), pulmonary (greater than Hugh-Jones II), hepatic (Child classes B and C), or renal insufficiency.

Procedures of pylorus-preserving gastrectomy

Lymph node stations correspond to specific lymph node tiers, as classified by the Japanese Classification of Gastric Cancer (JCGC).⁹ Dissection of first-tier nodes and preferred lymph nodes along the left gastric (station 7), common hepatic (station 8), and celiac (station 9) arteries is defined as a modified D2 dissection. We performed modified D2 lymph node dissection in our PPG procedures; the supraduodenal lymph node (station 5) was used for pickup sampling only, and both the right gastric artery and vein were preserved up to the first branch of the stomach wall with lymph node sampling (station 5) (Fig. 1). The remaining PPG procedures were the same as described previously.¹⁰

Clinical data

The following data were obtained from medical charts: age, gender, median followup period, Lauren's histologic type, maximum cancer diameter, depth of cancer invasion, nodal status (TNM), and the number of lymph nodes retrieved.

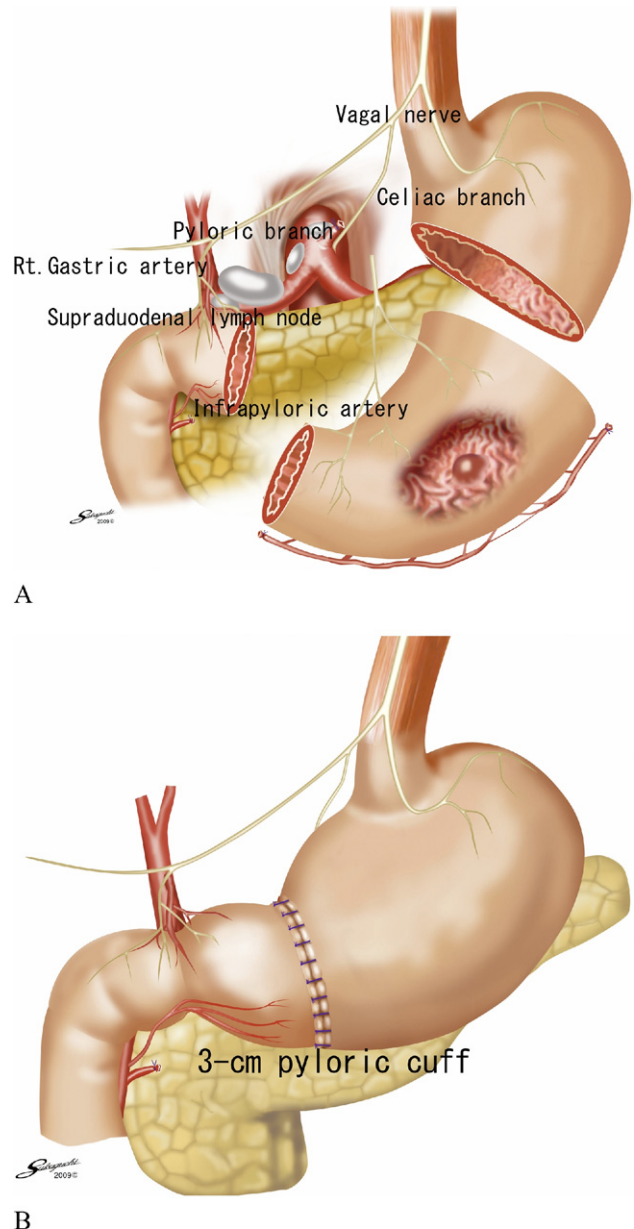


Figure 1. Surgical procedure of pylorus-preserving gastrectomy (PPG). (A) We performed modified D2 lymph node dissection in our PPG procedures; the supraduodenal lymph node (station 5) was used for pickup sampling only and both the right gastric artery and vein were preserved. The infrapyloric artery was preserved in this step to maintain the blood supply to the remaining pyloric cuff. Both the pyloric and celiac branches of the vagal nerve were preserved. (B) The distal part of the stomach was resected while retaining a 3-cm pyloric cuff. The proximal portion of the stomach was then resected just proximal to Demel's line (between the right and left gastroepiploic artery). Reprinted with permission of the artist.

All resected stomachs were opened immediately after the operation. Dissected lymph nodes were divided according to their anatomic distribution and numbering of the re-

gional lymph nodes was based on the system of the Japanese Classification of Gastric Cancer.⁹ Retrieved lymph nodes at each nodal point were counted to compare procedures with respect to the quality of lymph node dissection. Depth of wall invasion, number of lymph nodes harvested, and presence or absence of lymph node metastases were determined histologically on formalin-fixed, hematoxylin and eosin-stained sections. The degree of lymph node metastases, according to the TNM classification system (6th edition), was also examined.

Postoperative surveillance

All patients were followed according to an established protocol in our hospital, which includes medical history, physical examination, and laboratory studies, such as determination of serum carcinoembryonic antigen (CEA), carbohydrate antigen 19–9 (CA 19–9), and α -fetoprotein (AFP) levels 1 and 3 months after operation, and then every 6 months. At each visit, symptoms were recorded; CT was performed every 6 months and gastroscopy was performed each year.

Vital statistics of all patients were confirmed using data from either followup charts or the city registry. Overall survival was calculated by the Kaplan-Meier method using Sigma Plot for Windows (Systat Software Inc). Information about patients who were free of tumor recurrence and, when appropriate, the cause of death, was also recorded.

RESULTS

Patient characteristics

The patients' clinical histories are given in Table 1. Median patient age was 57 years (range 27 to 82 years), with 58% of patients being men. The clinicopathologic characteristics of the stomach tumors were determined and included Lauren's histologic type (intestinal, 39%; diffuse-mixed, 61%), maximum cancer diameter (2.3 ± 2.0 cm), and histologic depth of tumor invasion (T1 [mucosa], 65%; T1 [submucosa], 31%; T2a, 2.5%; T2b, 1%; and T3, 0.5%). In this series, the accuracy of the preoperative diagnosis of T1 gastric cancer by endoscopy or endoscopic ultrasonography was 95.7%. Nodal status (TNM classification) was found to be pN0 in 91% of patients, pN1 in 8.5% of patients, and pN2 in 0.5% of patients. The mean number of lymph nodes retrieved was 33.4 ± 12.8 (Table 1). Approximately 45% of patients were operated on laparoscopically because we have been performing laparoscopy-assisted PPG since 2004. The mean operation time in all patients was 213 ± 73 minutes and estimated blood loss was 152 ± 36 mL. The most frequent complication was gastric stasis after operation. But the rate of stasis was only 3%. Common bile duct stones developed in one patient postoperatively, caused by fallen gallbladder stones that

Table 1. Background of Patients Undergoing Pylorus-Preserving Gastrectomy

Characteristic	Data
n	305
Age, y	
Median	57
Range	27–82
Gender	
Male	176 (58)
Female	129 (42)
Lauren's histologic type	
Intestinal	119 (39)
Diffuse-mixed	186 (61)
Maximum cancer diameter, cm	2.3 ± 2.0
Tumor invasion	
T1 (mucosa)	198 (65)
T1 (submucosa)	94 (31)
T2a	8 (2.5)
T2b	3 (1)
T3	2 (0.5)
Nodal status (TNM)	
pN0	278 (91)
pN1	25 (8.5)
pN2	2 (0.5)
Lymph nodes retrieved, n	33.4 ± 12.8
Type of approach (laparoscopic/open), n	94/211
Operation time, min	213 ± 73
Estimated blood loss, mL	152 ± 36
Postoperative complications	18 (6)
Wound infection	3 (1)
Stasis	9 (3)
Pancreatic leak	3 (1)
Common bile duct stone	1 (0.3)
Myelosuppression	1 (0.3)
Pulmonary embolism	1 (0.3)
Postoperative hospital stay, d	11 ± 0.7

Where appropriate, data are given as mean \pm SD or as number of patients with percentages given in parentheses.

were not detected preoperatively. In addition, one patient showed myelosuppression after PPG, probably from a viral infection. Mean postoperative hospital stay was 11.0 ± 0.7 days.

Followup

All patients were compliant with the proposed postoperative surveillance protocol in the Cancer Institute Hospital. The median followup period for the entire series was 61 months (range 22 to 144 months; Table 2).

Survival

In terms of surveillance of the survival of these patients, the vital status of 201 patients (66%) was confirmed by insti-

Table 2. Tumor Recurrence and Survival

Variable	Data
Overall 5-y survival probability, %	98
Gastric cancer-related mortality, n (%)	0 (0)
Tumor recurrence, n (%)	0 (0)
Cause of death, n	
Perioperative mortality	0
Other cancer	3
Other	3
Unknown	1
Median followup, mo	61
Range	22–144

tutional followup; information about the remaining 104 patients (34%) was obtained from the city registry. Overall 5-year survival probability was 98% during the followup period. In all, seven patients died (Table 2). Perioperative mortality was 0%, three patients died from a cancer other than stomach cancer, three patients died from other diseases, and the cause of death was unknown in one patient. So, gastric cancer-related mortality was 0%. No patients had evidence of tumor recurrence.

DISCUSSION

This study is a large retrospective study that demonstrates excellent longterm survival after PPG with extensive lymph node dissection for gastric cancer. Overall 5-year survival was 98% and there were no gastric cancer-related deaths and no evidence of tumor recurrence in any of the patients. The 5-year survival rate for early gastric cancer after gastrectomy with radical lymph node dissection has been reported to range from 93% to 98%.^{6,7} Recently, Morita and colleagues¹¹ provided the first report of the overall 5-year survival rate for 611 T1 gastric cancer patients after PPG (96.3%) and concluded that PPG should be recommended as the standard procedure for early gastric cancer in the middle one-third of the stomach. But there is some debate as to whether the indications for PPG should always be applied for early gastric cancer and whether the prognosis of conventional distal gastrectomy is better than that of PPG in these patients.¹² Our results of a 98% overall 5-year survival and 0% gastric cancer-related deaths are clearly in line with previous reports on the mortality of early gastric cancer. Indeed, based on this rate of overall 5-year survival (98%) and that reported by Morita and associates (96.3%),¹¹ PPG may be indicated for clinically diagnosed T1 gastric cancer without suprapyloric lymph node dissection if the accuracy of the diagnosis of T1 gastric cancer can be assured.

Our indication for PPG was cancer located in the middle one-third of the stomach, with a maximum diameter

<5 cm, and intramucosal or submucosal carcinoma without lymph node metastasis (cT1, cN0). We have no strict criteria about age or body mass index, and, in this series, 15.0% of patients were older than 70 years of age and 19.3% had a body mass index >25 kg/m².

Modified D2 lymph node dissection for submucosal gastric cancer is considered sufficient for the curative treatment of gastric cancer.^{13,14} One of the pitfalls of PPG for gastric cancer is considered to be the lack of suprapyloric lymph node dissection,^{14,15} with intention to preserve the right gastric artery and the pyloric branch of the vagal nerve to maintain pyloric blood flow and motility,¹⁶⁻¹⁹ reducing the likelihood of postoperative gastric stasis.³ Complete clearance of lymph nodes that are at risk of metastasizing is considered necessary in a curative approach to gastric cancer, so many have advocated strict and limited indications for PPG.¹⁶⁻¹⁹ These authors argued that the suprapyloric lymph nodes are classified as first-tier nodes in the case of cancer in the middle one-third of the stomach, and preservation of the right gastric artery results in incomplete D1 lymph node dissection.²⁰ Some investigators have defined the indications for PPG on the basis of the incidence of lymph node metastasis in resected specimens obtained after conventional distal gastrectomy.^{21,22} Although a rate of metastases of suprapyloric lymph nodes of 4% was found in these series, 29% to 34% of patients were diagnosed with T2–T3 gastric cancer and the lower rate of diagnostic accuracy may be the reason for the higher incidence of metastases compared with our retrospective survey. In our retrospective survey, the rate of metastases of suprapyloric nodes in 3,646 cases of T1 (mucosal or submucosal) cancer located in middle of the body of the stomach was only 0.2%.⁸ In this study, a final diagnosis of the depth of invasion revealed that only 4% of patients were T2 or T3. So, the possibility of metastasis of the suprapyloric lymph nodes in this study should, theoretically, be lower than that reported for the other series. So we believe that patients who are diagnosed clinically as T1N0 could be candidates for PPG without suprapyloric lymph node dissection, if the preoperative diagnosis of T1N0 is accurate.

PPG prevents postprandial symptoms such as dumping syndrome and alkaline reflux,⁴ but delayed gastric retention from aberrant pyloric function can occur during the early postoperative period. In this study, only 9 of 305 patients (3%) were found to have gastric stasis, which was defined if the patient exhibited symptoms such as upper abdominal distension and remnant stomach fullness on x-ray, or if the patient required starvation for longer than 24 hours. These data are comparable with those of our previous study, which showed that the PPG procedure was associated with less postoperative stasis and adequate

lymph node retrieval. But more precise surveillance about the postoperative quality of life after PPG is required.

In conclusion, in a dedicated high-volume cancer center with accurate preoperative diagnosis of early gastric cancer, we have shown that PPG may result in a longterm survival benefit for patients diagnosed with cT1 (mucosa or submucosa), cN0 gastric cancer in the middle of the body of the stomach.

Author Contributions

Study conception and design: Hiki

Acquisition of data: Hiki, Fukunaga, Ohyama, Tokunaga

Analysis and interpretation of data: Hiki, Sano

Drafting of manuscript: Hiki

Critical revision: Sano, Yamaguchi

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