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Examination of the Relationship Between Postoperative Quality of Life and Gastric Emptying Function After Pylorus-Preserving Gastrectomy and Distal Gastrectomy

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The objective of this study was to compare postoperative quality of life (QOL) of patients with early cancer of the body of the stomach who were treated with pylorus-preserving gastrectomy (PPG) and those treated with distal gastrectomy (DGR), and to evaluate the relationship between postoperative QOL and gastric emptying function (GEF). Patients with early cancer of the body of the stomach are often treated with PPG to preserve gastric function, and their QOL appears to be better after PPG than after DGR. Differences in postoperative GEF are thought to be a factor, but the relationship between GEF and postoperative QOL has not been well investigated. A total of 60 patients [23 PPG and 37 DGR (Billroth I)] completed QOL surveys [SF-36, Gastrointestinal Symptom Rating Scale (GSRS)] and underwent ^{13}C-breath tests to evaluate GEF in two groups ($\leq$12 months postoperatively and $>$12 months postoperatively). The time until the percentage of breath $^{13}CO_2$ reaches a peak during the ^{13}C-breath test (Tmax), which is an index of gastric emptying velocity, was evaluated. For the SF-36, there were no significant differences between the two procedures. For GSRS, a trend toward better scores was seen after PPG; abdominal pain and total scores at $>$12 months postoperatively were significantly better with PPG. Tmax was significantly longer for PPG patients. For each procedure, symptoms significantly worsened when Tmax was $<$21 minutes at $>$12 months after surgery. Although postoperative GEF evaluated by ^{13}C-breath tests did not affect overall QOL measured by the SF-36, it did affect disease-specific QOL measured by GSRS.

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Pylorus-preserving gastrectomy (PPG) is now widely performed to preserve gastric function in patients with early cancer of the gastric corpus. Experience has shown that patients' postoperative (PO) quality of life (QOL) is better after PPG than after distal gastrectomy (DGR). Although differences in PO gastric emptying function (GEF) are said to be a factor, the relationship between GEF and PO QOL has seldom been reported. Meanwhile, the ^{13}C-breath test[1] for GEF is noninvasive, convenient, and highly reliable for clinical evaluation of gastric emptying dysfunction.

Therefore, in this study, the ^{13}C-breath test and validated QOL index surveys were used to compare PO QOL between PPG and DGR and to evaluate the relationship with GEF. The QOL surveys, which have already been validated as being highly reliable, included the MOS 36-item Short Form Health Survey (SF-36)[2–4] for overall QOL (a comprehensive evaluation index) and the Gastrointestinal Symptom Rating Scale[5] (GSRS; a disease-specific evaluation index).

Patients and Methods

Patients

This study included 60 patients, including 23 who had a PPG and 37 who had a DGR (Billroth I) between 2008 and 2013 at our hospital and who were being followed as outpatients. The QOL surveys and ^{13}C-breath tests were performed at the same visits, and none of the patients was receiving anticancer therapy at the time of testing. None of the patients had electrolyte abnormalities or other complications that may have affected gastrointestinal tract motility. Two patients had diabetes mellitus, but both were using diet therapy only, and blood glucose was well controlled both before and after the surgery. In PPG at our hospital, the inferior pyloric artery is preserved. In addition, PPG was performed in patients in whom 3 cm or more of the remaining stomach on the anal side could be left from the pyloric ring when the incision was made grossly 3 cm away from the tumor margin, for cases of early gastric cancer of the central gastric corpus. Among patient characteristics, age in the PPG group was slightly younger, but not significantly different. Surgical invasiveness, including operative time and blood loss, did not differ between the groups (Table 1).

Methods

^{13}C-breath test

The ^{13}C-breath test (standardized method) has been well established in Japan. After ingestion of a 200-mL liquid test meal mixed with 100 mg of ^{13}C-acetate, the percentage of breath $^{13}CO_2$ was measured and analyzed during a standard 2-hour test. Breath samples were collected by blowing in a collection bag at 5-minute intervals from 0 to 20 minutes, 10-minute intervals from 20 to 60 minutes, and 15-minute intervals from 60 to 120 minutes after ingesting the liquid test meal.

Because the ^{13}C-breath test is an indirect technique, the $^{13}CO_2$ breath excretion curve that is obtained not only shows emptying function, but it also shows the overall process of gastric emptying, absorption, metabolism, and excretion. The area up to the peak mainly shows the effects of gastric emptying and absorption, and the area after the peak mainly shows the effects of metabolism and excretion (Fig. 1). For evaluation in this study, the Tmax, the parameter that is easiest to calculate, was evaluated. Tmax, which is the time to the peak of the percentage of breath $^{13}CO_2$, is an index of gastric emptying velocity. Based on Tmax data from 63 healthy volunteers at 6 institutions in Japan, the mean $\pm$ SD Tmax is 43.9 $\pm$ 10.3 minutes.[6]

Questionnaire surveys

The surveys included Japanese versions of the SF-36 version 2, a health survey questionnaire used as a comprehensive QOL index, and the GSRS, a disease-specific QOL index. The SF-36 was developed in the 1980s and is currently one of the most widely used health-related QOL scales internationally. The SF-36 is composed of 36 questions and the following 8 dimensions: physical functioning (PF), bodily pain (BP), mental health (MH), general health (GH), role limitations due to physical problems (RP), vitality (VT), role limitations due to emotional problems (RE), and social functioning (SF).

The GSRS was developed in Europe and is a disease-specific QOL index for patients with gastrointestinal symptoms. It comprises 15 questions about gastrointestinal symptoms during the preceding 1 week in 5 dimensions: reflux syndrome, abdominal pain syndrome, indigestion syndrome, diarrhea syndrome, and constipation syndrome. The mean total scores are evaluated.

Table 1 Patients' background characteristics

	PPG	DGR	*P* value
No.	23	37	
0–12 mo	11	22	NS
>12 mo	12	15	NS
Age, y (range)	59.6 (38–84)	66.5 (41–88)	0.02*
Sex, n			0.02*
Male	9	26	
Female	14	11	
Operation time, min	278 ± 19	273 ± 15	NS
Bleeding, mL	157 ± 27	127 ± 21	NS
Stage**			
IA+ IB	22	30	
IIA+ IIB	1	6	
IIIB	0	1	
Weight change, %	92.3 ± 0.8	93.1 ± 0.8	NS
Measurement time, mo	18.6 ± 4.2	17.9 ± 3.3	NS

NS, not significant ($P \geq 0.05$).

0-12 months average: 4.2 ± 0.63 months.

>12 months average: 35.2 ± 3.4 months.

*$P < 0.05$.

**Japanese classification of gastric cancer.

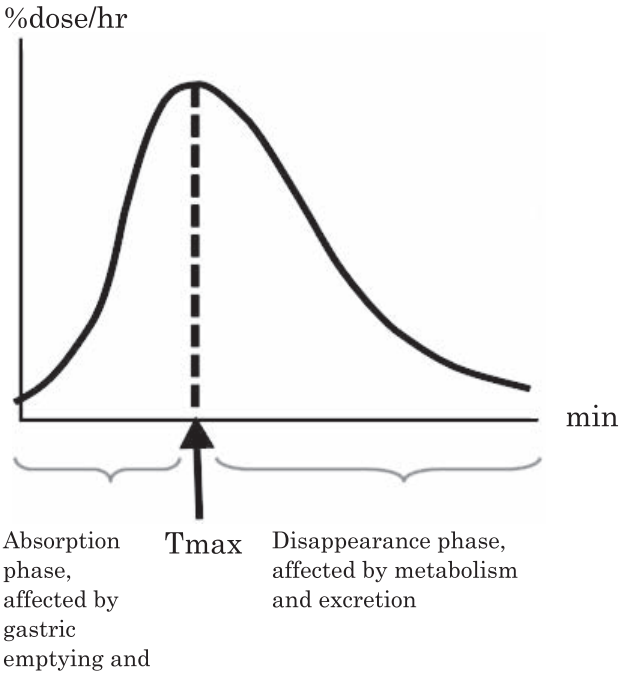

Fig. 1 Gastric emptying curve of $^{13}CO_2$.

The ^{13}C-breath test and surveys were conducted during the morning at outpatient visits after obtaining patient consent. The surveys were self-administered questionnaires. The ^{13}C-breath testing was approved by the ethics committee at our hospital.

SAS version 9 (SAS Institute, Cary, North Carolina) was used for statistical analysis. The analysis of variance procedure was used to conduct post hoc tests for multiple comparisons using the Scheffe option. In addition, Corr and Freq procedures were used for correlation coefficient calculation and the χ^2 test, as needed. A *P* value <0.05 was considered significant.

Results

The data were evaluated by type of surgical procedure and the time of the PO survey. The two survey times were up to 12 (4.2 ± 0.63) months PO and more than 12 (35.2 ± 3.4) months PO.

^{13}C-breath test

Figure 2 shows the gastric emptying curves for all patients with each procedure. The lowest curve is a control group of healthy volunteers at our hospital (4 male, 2 female; median age, 30.5 years).

The Tmax in the control group was 45.0 ± 10.5 minutes, similar to the previously mentioned data from Japan. In the DGR group, the Tmax was 18.2 ± 2.9 minutes, with significantly faster emptying than in the control group. On the other hand, in the PPG group the Tmax was 37.8 ± 3.6 minutes, significantly longer than in the DGR group. Therefore, the breath excretion curve in the PPG group was more similar to the curve in the control group.

The Tmax at 0 to 12 months PO did not differ between the PPG and DGR groups, but after 12 months PO, Tmax was significantly prolonged with PPG (Table 2).

Questionnaire surveys

SF-36

A mean score of 50 and SD of 10 were established based on Japanese standard data in 2002 for each dimension on the Japanese SF-36 version 2. A higher score for each dimension indicates better QOL, and each score can be compared to the Japanese standard of 50 points.

Although there were no significant differences between the two surgical procedures, all dimensions were improved after 12 months PO. In addition, a comparison of each procedure in each period showed that, at 0 to 12 months PO, the scores for the two dimensions of BP and GH were significantly higher (better) with PPG. On the other hand, although there were no differences in any dimensions between the two procedures after 12 months

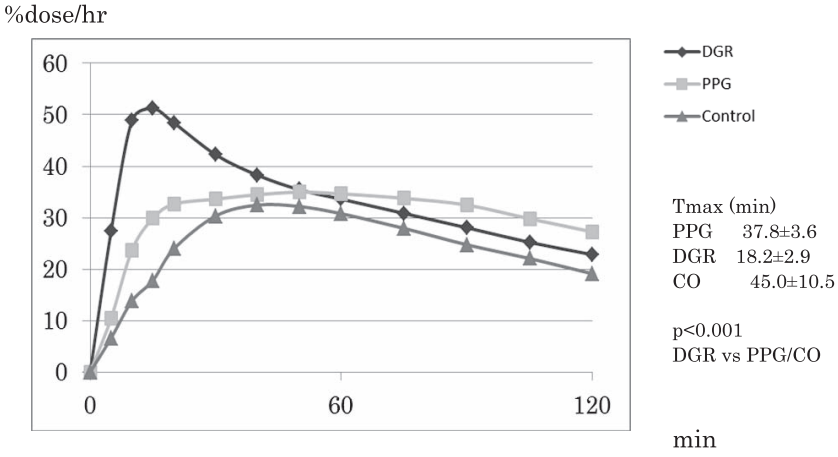

Fig. 2 Mean Tmax values for each procedure. This graph shows the mean $^{13}CO_2$ excretion curves after each surgical procedure. The lowest curve is the mean for healthy volunteer controls at our hospital.

PO, all dimension scores were thought to be good, exceeding a score of 50, in the PPG group (Table 3).

GSRS

The scores on the Japanese version of the GSRS are based on a 7-point scale ranging from 1 to 7 points as follows: 1 point indicates asymptomatic; ≥2 points indicates symptomatic; and 7 points indicates the most severe symptoms.

A comparison of dimensions with each procedure in each period showed no differences in any dimension, except diarrhea, between the surgical procedures at 0 to 12 months PO. However, in the two dimensions of abdominal pain and the total score after 12 months PO, symptoms were significantly better in the PPG group. Moreover, in the other dimensions as well, the scores tended to be lower with PPG, thus indicating a larger difference in symptoms between PPG and DGR as the time after surgery increased. The gastrointestinal symptoms were mild, as evidenced by scores of <2.5 in each dimension (Table 4).

Figure 3 shows a scatter plot of the total scores and Tmax for each surgical procedure after 12 months PO. A weak negative correlation of –0.4 ($P = 0.0384$) was seen between total score and Tmax. In addition, from a previous report that Tmax was less than 21 minutes and the total score showed significant worsening of symptoms in an investigation of cases of reconstruction after various gastric resections,[14] the relationship with total score was investigated with the same 21-minute increments as for Tmax. The results showed that the rate of scores ≥2 (indicating symptoms) was only 15.4% (2 of 13 patients) when Tmax was ≥21 minutes. However, when the Tmax was <21 minutes, this rate was 50% (8 of 16 patients). Thus, the total scores were increased with significantly worse symptoms when the Tmax was <21 minutes (χ^2 test).

Discussion

PPG is a surgical procedure that was originally reported by Maki *et al*[7] for gastric ulcers. With increased early detection rates of gastric cancer and an accumulation of clinicopathologic findings with regard to appropriate lymph node dissection, PPG is becoming established as a surgical procedure for early gastric cancer in the lower gastric corpus. PPG is also described in the Japanese Gastric Cancer Treatment Guidelines (version 3).[8] As a result, several studies have compared postoperative QOL after PPG to that after DGR.[9,10]

However, few questionnaire survey studies to date have examined the relationship between residual GEF and postoperative QOL. In the present study, the two abovementioned questionnaire surveys, which are most likely to reflect postoperative QOL, were used for subjective assessment by patients. In addition, a ^{13}C-breath test was performed to evaluate residual GEF and examine the relationship with postoperative QOL.

PPG involves gastric resection that leaves about 30 to 40 mm of the pyloric antrum from the pyloric sphincter intact. About one half of the stomach is resected. By preserving the pyloric sphincter, rapid

Table 2 Comparison of Tmax between surgical procedures at each measurement time

	PPG	DGR	*P* value
0–12 mo	29.5 ± 5.1	17.5 ± 3.6	0.06
>12 mo	45.4 ± 5.0	19.3 ± 4.4	0.0006*

*$P < 0.05$.

Table 3 Comparison of each SF-36 dimension between surgical procedures at 0-12 months and at more than 12 months postoperatively

	PPG	DGR	*P* value
0–12 mo			
PF	49.7 ± 4.0	44.7 ± 2.8	0.32
BP	52.8 ± 3.0	43.8 ± 2.1	0.021*
MH	51.3 ± 2.9	48.6 ± 2.1	0.47
GH	54.6 ± 2.5	46.4 ± 1.7	0.011*
RP	38.9 ± 5.6	39.2 ± 4.0	0.96
VT	52.6 ± 2.8	51.1 ± 2.0	0.67
RE	45.0 ± 4.6	43.4 ± 3.3	0.79
SF	44.5 ± 4.4	43.0 ± 3.1	0.78
More than 12 mo			
PF	53.7 ± 3.0	48.1 ± 2.7	0.18
BP	52.6 ± 3.2	51.5 ± 2.8	0.78
MH	55.1 ± 2.0	53.9 ± 1.8	0.67
GH	52.2 ± 2.6	50.2 ± 2.3	0.57
RP	52.0 ± 3.1	45.1 ± 2.8	0.11
VT	52.0 ± 2.3	52.9 ± 2.1	0.78
RE	50.2 ± 3.6	47.5 ± 3.2	0.58
SF	52.2 ± 3.3	48.8 ± 3.0	0.45

*$P < 0.05$.

dumping of food after eating into the duodenum is prevented, and reflux of digestive juices, such as bile, is also prevented, thus improving postoperative QOL.[11]

Tmax is the time when the percentage of breath $^{13}CO_2$ reaches a peak on the curve. The Tmax is affected by gastric emptying of food and subsequent absorption. Tmax may therefore also be thought to be closely related to pyloric function. In addition, Tmax corresponds to about 80% of the emptying time measured by the direct RI method.[12] The present study showed no differences in Tmax between the two surgical procedures at 0 to 12 months PO, but after 12 months PO, Tmax was significantly prolonged with PPG. This suggests that although pyloric function decreases early after surgery, preserving the inferior pyloric artery and nerves results in a subsequent gradual recovery of pyloric function.

Results of the SF-36 to evaluate overall QOL showed better scores in two dimensions with PPG up to 12 months PO. After 12 months PO, the scores improved to almost the standard values, without a difference between the two surgical procedures. The difference in Tmax between PPG and DGR increased after 12 months PO, but this was not thought to influence the SF-36 scores.

The most important problem that has been reported early after PPG is gastric stasis of food.[13] However, in the present study, acid reflux and dyspepsia on the GSRS, which are related to gastric stasis of food, were not worse compared with DGR.

Table 4 Comparison of each GSRS dimension between surgical procedures at 0 to 12 months and at more than 12 months PO

	PPG	DGR	*P* value
0–12 mo			
Acid-reflux	1.6 ± 0.3	1.5 ± 0.2	0.78
Abd-p	1.1 ± 0.1	1.3 ± 0.1	0.17
Dyspepsia	2.0 ± 0.2	2.0 ± 0.1	0.8
Diarrhea	1.5 ± 0.3	2.1 ± 0.2	0.049*
Constipation	2.0 ± 0.4	2.2 ± 0.2	0.67
Total score	1.6 ± 0.1	1.8 ± 0.1	0.34
More than 12 mo			
Acid-reflux	1.7 ± 0.3	2.0 ± 0.2	0.45
Abd-p	1.1 ± 0.1	1.4 ± 0.1	0.027*
Dyspepsia	1.8 ± 0.2	2.2 ± 0.2	0.07
Diarrhea	1.6 ± 0.2	2.0 ± 0.2	0.11
Constipation	2.1 ± 0.2	2.2 ± 0.1	0.54
Total score	1.6 ± 0.1	2.0 ± 0.1	0.033*

Abd-p, abdominal pain.

*$P < 0.05$.

Comparison between the surgical procedures with regard to each GSRS dimension after 12 months PO showed a trend toward lower (better) scores after PPG. In particular, the abdominal pain and total scores were significantly better with PPG. This corresponded with a wider difference in Tmax after 12 months PO, thus suggesting a relationship with recovery of pyloric function. On the other hand, the difference in diarrhea scores narrowed between the two surgical procedures after 12 months PO. Therefore, Tmax seemed to have less effect on symptoms of diarrhea.

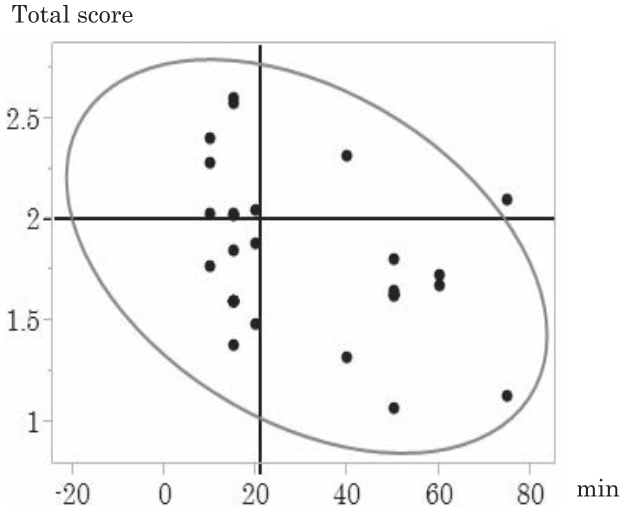

Fig. 3 GSRS (total score) – Tmax scatter plot for each surgical procedure after 12 months postoperatively.

Based on a previous report of higher symptom rates in 72 patients who underwent various types of gastrectomy when the Tmax was <21 minutes,[14] the correlation of Tmax with total scores was also investigated in the present patients after 12 months PO, and an increased rate of symptoms was found with Tmax <21 minutes. Therefore, when Tmax falls below a certain threshold value, this appears to lead to an increase in symptoms.

Conclusions

The present survey study found that SF-36 scores improved to near standard values with both PPG and DGR as the time after surgery increased. On the other hand, the differences in GSRS scores between PPG and DGR widened as the time after surgery increased. One reason for this was that the Tmax increased over time. In other words, although GEF did not seem to affect overall QOL postoperatively, GEF did affect disease-specific QOL.

This was a retrospective comparative study with a small number of patients (60 patients), and thus there is potential for bias. A prospective study would be difficult because of differences in indications, and in the future it may be necessary to conduct further investigations with a larger number of patients.

Acknowledgments

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