World J Surg (2012) 36:373–378
DOI 10.1007/s00268-011-1379-x

World Journal of Surgery

Effects of Emptying Function of Remaining Stomach on QOL in Postgastrectomy Patients

Masaru Hayami · Akiyoshi Seshimo · Kunitomo Miyake · Satoru Shimizu · Shingo Kameoka

Published online: 16 December 2011

Abstract
Background Attention has recently focused on decreased quality of life (QOL) that occurs in postgastrectomy patients. We verified how gastric emptying function affected QOL.
Methods Subjects were 72 consecutive patients after gastrectomy for cancer, including 25 after distal gastrectomy (DG), 18 after proximal gastrectomy (PG), 16 after pylorus-preserving gastrectomy (PpG), and 13 after total gastrectomy (TG). Using the ^{13}C breath test method, $^{13}CO_2$ levels in breath were measured over 2 h, and T_{max} was determined. Questionnaires (Japanese versions of the Short-Form 36 [SF-36] and Gastrointestinal Symptom Rating Scale [GSRS]) were used to analyze QOL and correlations between questionnaire results and T_{max}.
Results Mean T_{max} (min) for each procedure was 15.4 for DG, 21.1 for PG, 41.3 for PpG, and 10.4 for TG. T_{max} differed between procedures, but not between survey periods. SF-36 was not correlated with T_{max}, whereas GSRS showed a difference in diarrhea and total score between procedures, but not between survey periods. In addition, GSRS correlated with T_{max} for abdominal pain, indigestion, and total score. The total scores showed a significant symptom aggregation in patients with T_{max} less than 21 min.
Conclusions Gastrointestinal symptoms in postgastrectomy patients were associated with the function of the remaining stomach. The ^{13}C breath test is useful for objectively assessing such symptoms.

M. Hayami · A. Seshimo (✉) · K. Miyake · S. Kameoka
Second Department of Surgery, Tokyo Women's Medical University, 8-1 Kawada-cho, Shinjuku-ku, Tokyo 162-8666, Japan
e-mail: seshimo@surg2.twmu.ac.jp

S. Shimizu
Medical Research Institute, Tokyo Women's Medical University, Tokyo 162-8666, Japan

Introduction

Patients who undergo gastrectomy often suffer from postgastrectomy syndromes, resulting in a decrease in their quality of life (QOL). Gastric cancer treatments need to focus not only on curing the cancer but also on mitigation of postgastrectomy disorders, as well as improving patients' QOL. To help achieve these goals, functional preservation surgery and reconstructive surgery have been used in recent years. However, methods to evaluate patients' QOL objectively have not been established.

It has been suggested that postgastrectomy syndromes may be caused by a rapid or delayed emptying of the remaining stomach, but no reports have shown this. A ^{13}C breath test for determining gastric emptying [1] has been drawing attention as an easy, noninvasive, and reliable method to clinically assess the emptying function. We performed the ^{13}C breath test in post-gastrectomy patients and examined relationships between the residual stomach's emptying ability and patients' QOL by using two established questionnaire surveys that assess QOL: the Short-Form 36 (SF-36), which assesses overall QOL, and the Gastrointestinal Symptom Rating Scale (GSRS), which provides a disease-specific assessment of gastrointestinal symptoms.

Patients and methods

Patients

Subjects included 72 consecutive patients (43 males and 29 females) who underwent gastrectomy due to gastric cancer

(Table 1). All patients provided informed consent. The mean age was 66.8 years, and the mean total survey period was 2.4 years after surgery.

We selected patients who had undergone any one of the following procedures: distal gastrectomy (DG), proximal gastrectomy (PG), pylorus-preserving gastrectomy (PpG), or total gastrectomy (TG); the number of patients in each group was 25, 18, 16, and 13, respectively. The reconstructive techniques are described in Table 1. All patients were outpatients seen from 2008 to 2009; no patient was receiving any anticancer agent during the period of the questionnaire surveys.

^{13}C breath test

In Japan we have an established our own "standardized method" for the ^{13}C breath test [2, 3]. In our study, 200 ml of a liquid test meal containing 100 mg of ^{13}C acetate was served to a patient, and the $^{13}CO_2$ level in the breath was repeatedly measured during 2 h after the meal was ingested, instead of the 4 h recommended in the standardized method. Specifically, we collected samples of exhaled breath from each patient using a breath collection bag, at 5-min intervals during from 0–20 min, at 10-min intervals during 20–60 min, and at 15-min intervals during 60–120 min period after meal ingestion.

Table 1 Patients and background ($n = 72$)

Gender			
Male	43		
Female	29		
Age, years	66.8	10.5 (38–84)	
Postoperative period, years	2.4	3.4 (0.04–16.4)	
Procedures		Reconstructions	
Distal gastrectomy (DG)	25	Billroth-1	20
		Roux-en-Y	5
Proximal gastrectomy (PG)	18	Double tract	4
		Jejunal interposition	1
		Gastroesophageal anastomosis	13
Pylorus-preserving gastrectomy (PpG)[a]	16	Gastrogastric anastomosis	16
Total gastrectomy (TG)	13	Roux-en-Y	13
Stages (Japanese classification of gastric cancer)			
IA	46		
IB	19		
II	3		
IIIA	3		
IIIB	1		
IV	0		

[a] In our surgery department, we usually preserve the infrapyloric artery and leave 3 cm or more of the pyloric antrum in PpG

Because the ^{13}C breath test is an indirect method, a curve showing the level of $^{13}CO_2$ measured in the breath represents the overall process ranging from gastric emptying, absorption, and metabolism to excretion, rather than gastric emptying alone. On this curve, the left side of the peak mainly indicates the phases of gastric emptying and absorption, and the right side of a peak mainly indicates the phases of metabolism and excretion (Fig. 1). Among several parameters assessed, we chose T_{max}, which can be easily determined. T_{max} is the length of time before the level of $^{13}CO_2$ in the expired breath reaches a peak, representing how rapidly ^{13}C is excreted. The mean and standard deviation of T_{max} for healthy individuals have been established and are available as open data [2] in Japan. T_{max} is 43.9 ± 10.3 min, calculated based on data of 63 healthy people collected at six local facilities.

Questionnaire survey

We used the Japanese version of the SF-36 (version 2) to evaluate overall QOL and the Japanese version of the GSRS to assess disease-specific QOL.

SF-36

The SF-36 health survey questionnaire [4–7], developed in the 1980s, is one of the most widely used health-related QOL measures.

A sub-sample of persons aged 20–80 years from a Japanese population study [7] was used as a population control group for this instrument. For this control population study, 4,500 adults were interviewed in 2002 and stratified according to age (10-year intervals) and gender.

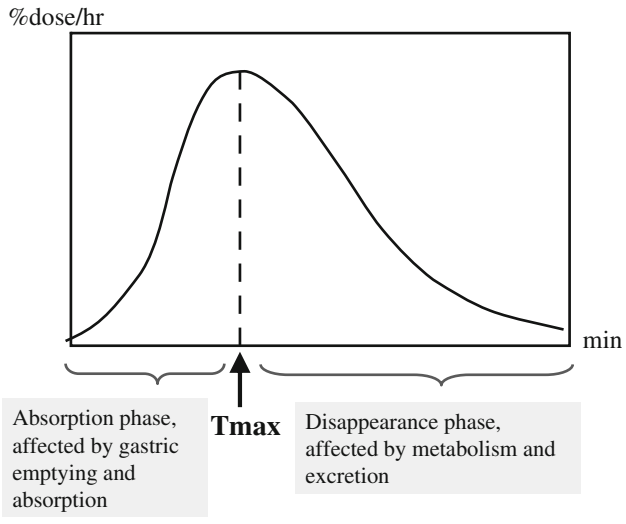

Fig. 1 Gastric emptying curve of $^{13}CO_2$. T_{max} (min): time to the peak of the abundance ratio of $^{13}CO_2$ in the expired air. Mean ± SD of 63 healthy volunteers: 43.9 ± 10.3 min (33.6–54.2 min)

Items were further grouped into the eight 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).

With the Japanese SF-36 (version 2) [7], each dimension is re-scored to have a mean of 50 and a standard deviation of 10, based on the mean established in 2002 from healthy Japanese individuals. The higher the score of a dimension relative to the Japanese mean of 50, the better the QOL for that dimension.

GSRS

The Gastrointestinal Symptom Rating Scale (GSRS) [8, 9], developed in Europe, is a disease-specific survey for patients with gastrointestinal symptoms. The Japanese version of the questionnaire was used for this study [10]. It comprises 15 items about digestive syndromes or symptoms that patients have experienced in the last week.

The GSRS items are graded on a seven-point Likert scale where 1 represents absence of troublesome symptoms and 7 represents very troublesome symptoms. The following five dimensions were identified on the basis of a factor analysis and were used in this study: abdominal pain syndrome (three items), reflux syndrome (two items), indigestion syndrome (four items), diarrhea syndrome (three items), and constipation syndrome (three items). The GSRS data are presented as syndrome scores and a total score (the mean of specific scores).

Both the ^{13}C breath test and questionnaire surveys were conducted at our hospital on patients who visited as outpatients; patients completed the questionnaire themselves. We used SAS version 9 (SAS Institute, Cary, NC) 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 chi-square test as needed. A P value ≤ 0.05 was considered statistically significant.

Results

Results were examined according to the types of procedure and the periods of survey. The entire survey period was divided into three periods: less than 6 months, 6 to less than 12 months, and 12 months or more after surgery.

^{13}C breath test

Figure 2 shows the curves describing how the level of excretion of ^{13}C into the breath changed over time. T_{max} for the control group was 40.0 ± 8.1 min, similar to the value obtained by facilities in Japan as described above. T_{max} for DG was 15.4 min, indicating rapid gastric emptying. T_{max} for PpG was 41.3 min, which was significantly longer than for the other three groups; the curve trend was similar to that of the control group. T_{max} for TG was very short that is, 10.4 min. T_{max} for PG was 21.1 min, which was longer than for TG, although differences were not significant. In terms of survey periods, T_{max} tended to become gradually longer during the third survey period (1 year or more) in all procedures except TG; however, T_{max} did not show a significant difference between these procedures. T_{max} for TG stayed constant over the survey period (Table 2).

Questionnaire survey

SF-36

The upper half of Table 3 shows the results of SF-36 s obtained from patients for each survey period. Although MH and RP decreased in the first period, they improved in later periods, demonstrating a significant difference

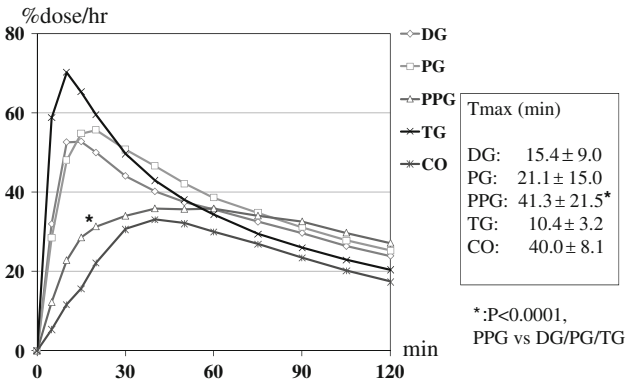

Fig. 2 Curves of T_{max} of ^{13}C breath test over time by procedure The four curves from the top represent patients with one of the four types of procedure, and the one at the bottom is that for a control group consisting of healthy individuals whose data were collected at our hospital. *DG* distal gastrectomy, *PG* proximal gastrectomy, *PpG* pylorus preserving gastrectomy, *TG* total gastrectomy

Table 2 T_{max} by procedure and survey period

	<6 months	6 months–1 year	>1 year	*P* value
T_{max} min				
DG	14.3 ± 5.4	13.0 ± 9.8	16.9 ± 10.5	0.68
PG	17.9 ± 3.9	21.3 ± 13.2	24.3 ± 22.6	0.75
PpG	31.3 ± 30.7	33.3 ± 25.2	48.3 ± 15.0	0.35
TG	12.5 ± 3.5	10.0 ± 0	10.0 ± 3.5	0.64

Table 3 Results of SF-36/GSRS questionnaires by survey period

	<6 months	6 months–1 year	>1 year	*P* value
SF-36: PF	45.6 ± 11.9	52.6 ± 4.7	51.2 ± 11.0	0.09
MH	48.2 ± 9.7	56.3 ± 7.8	53.6 ± .0	**0.02***
RP	39.0 ± 15.2	53.6 ± 5.0	49.7 ± 10.9	**0.001****
RE	46.8 ± 12.4	53.2 ± 5.8	49.9 ± 11.8	0.25
BP	47.7 ± 10.2	53.7 ± 8.0	52.3 ± 10.3	0.15
GH	49.7 ± 9.3	54.7 ± 7.1	49.7 ± 10.1	0.20
VT	51.7 ± 9.3	54.2 ± 7.0	53.1 ± 9.4	0.71
SF	44.9 ± 12.3	52.4 ± 7.9	50.7 ± 10.7	0.08
GSRS: reflux syndrome	2.0 ± 1.3	2.0 ± 0.9	1.8 ± 1.0	0.89
Abdominal pain syndrome	1.6 ± 0.9	1.4 ± 0.6	1.5 ± 0.7	0.82
Indigestion syndrome	2.3 ± 1.0	2.0 ± 0.9	2.3 ± 0.7	0.50
Diarrhea syndrome	1.8 ± 0.8	1.8 ± 0.8	2.0 ± 1.1	0.48
Constipation syndrome	2.9 ± 1.3	2.2 ± 1.2	2.5 ± 0.9	0.55
Total score	2.0 ± 0.9	1.9 ± 0.7	2.0 ± 0.6	0.77

SF-36 Short-Form 36, *GSRS* Gastrointestinal Symptom Rating Scale, *PF* physical functioning, *RP* role limitations due to physical problems, *BP* bodily pain, *GH* general health, *VT* vitality, *SF* social functioning, *RE* role limitations due to emotional problems, *MH* mental health

*<6 months versus >1 year

**<6 months versus 6 months–1 year and <6 month versus >1 year

between periods. Similar trends were found in PF and SF. All dimensions showed a small decrease in the first period, but improved and became similar to the Japanese average in later periods.

When examining the individual dimensions in connection with procedures, no significant differences were found between the four procedures in any dimension. Furthermore, no correlations were observed between T_{max} and individual dimensions (Table 4). This means that overall physical and mental QOL, as measured by the SF-36, were not associated with the procedures or with gastric emptying function as assessed by T_{max}. All dimensions decreased in the first period, but improved to a level similar to the Japanese average in later periods.

GSRS

The lower half of Table 3 shows the values of all six syndromes in each survey period. For all syndromes, no significant difference was found between survey periods. Somewhat surprisingly, none of the gastrointestinal syndromes improved over the survey periods. However, the scores of all syndromes were generally less than 3, indicating light or moderate symptoms.

When examining the GSRS symptoms with respect to the procedures, TG showed a significant aggravation in diarrhea and the GSRS total score; this was true especially when compared with PpG. By analyzing the correlations between T_{max} and the syndromes, it was revealed that T_{max} had a

Table 4 Results of SF-36/GSRS by procedure and correlations with T_{max}

	Correlation with T_{max}		Procedures				*P* value
	r	*P* value	DG	PG	PpG	TG	
SF-36: PF	0.03	0.83	49.5 ± 12.5	48.9 ± 12.6	51.6 ± 6.7	50.0 ± 8.7	0.90
MH	0.01	0.95	53.2 ± 8.1	49.0 ± 10.4	53.6 ± 9.0	55.3 ± 7.5	0.23
RP	–0.0002	0.99	47.4 ± 14.2	47.0 ± 12.6	47.5 ± 12.6	48.1 ± 10.6	0.99
RE	–0.14	0.24	50.1 ± 12.0	48.1 ± 11.8	49.1 ± 11.7	51.7 ± 8.5	0.85
BP	0.09	0.47	47.9 ± 11.9	54.2 ± 8.3	52.9 ± 8.5	52.0 ± 8.8	0.19
GH	0.09	0.46	49.4 ± 10.3	49.7 ± 11.4	54.0 ± 5.9	50.4 ± 8.6	0.45
VT	0.03	0.83	53.7 ± 7.8	49.9 ± 11.4	53.2 ± 7.4	55.0 ± 8.8	0.41
SF	–0.02	0.87	50.3 ± 10.3	50.5 ± 8.4	48.1 ± 15.2	48.0 ± 9.9	0.86
GSRS: reflux syndrome	–0.13	0.29	1.8 ± 1.0	2.3 ± 1.4	1.5 ± 0.6	2.0 ± 0.9	0.14
Abdominal pains syndrome	–0.24	**0.04**	1.5 ± 0.5	1.7 ± 1.0	1.2 ± 0.4	1.8 ± 0.8	0.09
Indigestion syndrome	–0.26	**0.03**	2.3 ± 0.6	2.2 ± 1.0	1.9 ± 0.7	2.5 ± 0.9	0.16
Diarrhea syndrome	–0.21	0.08	2.0 ± 1.1	1.8 ± 0.9	1.4 ± 0.5	2.5 ± 1.1	**0.03*****
Constipation syndrome	–0.05	0.67	2.3 ± 1.0	2.3 ± 1.4	2.2 ± 0.9	2.8 ± 1.1	0.42
Total score	–0.23	**0.05**	2.0 ± 0.6	2.1 ± 0.9	1.6 ± 0.4	2.4 ± 0.6	**0.03*****

*** TG versus PpG

significant correlation with abdominal pain, indigestion, and the total score, and a smaller T_{max} corresponded to worse symptoms. A similar trend was seen in diarrhea (Table 4).

We used a scatter chart to examine the GSRS total scores, that is, the means of all syndromes for each patient (Fig. 3). The *Y* axis represents total score values, where values of 2 or more indicate presence of a symptom and a higher value means a higher symptom severity. The *X* axis shows the values of T_{max}, where a value of 21 min was used as a threshold.

Among 55 patients with T_{max} less than 21 min, presence of symptoms was found in 31 (56.4%); among 16 patients with T_{max} of 21 min or more, presence of symptoms was only observed in 2 (12.5%). Based on the total scores, it was suggested that there was a significant aggregation of symptoms in patients with T_{max} less than 21 min. In addition, it was thought that a T_{max} value of less than 21 min was a risk factor for aggravation of gastrointestinal symptoms.

Discussion

In general, the evaluation of patients' QOL by questionnaire needs to be conducted using a combination of a comprehensive approach to assess overall QOL and a disease-specific approach to assess QOL for individual symptoms. Tyrvainen et al. [11] reported that their research on the long-term survivors after TG (median survival duration, 9 years) using the SF-36 yielded results similar to those obtained from normal healthy individuals, regardless of age, sex, tumor diameter, presence of pouch, postoperative complaints, and survey periods. Other reports, in which other comprehensive evaluation methods were used, indicate that patients' overall QOL after gastrectomy

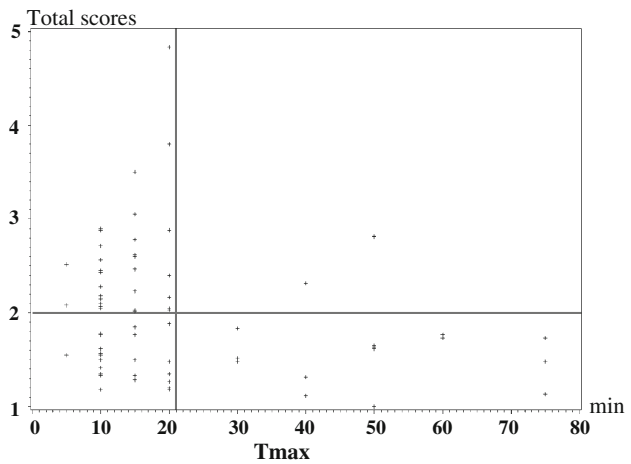

Fig. 3 GSRS (total scores) − T_{max} scatter chart. With a T_{max} value of 21 min and a total score of 2 used as thresholds, the total scores showed a significant difference in the aggregation of symptoms at the T_{max} threshold ($P = 0.002$, chi-square test)

improved to a level similar to that of normal individuals after 6 months have elapsed since gastrectomy [12, 13]. Our study also indicated that all dimensions of the SF-36 improved to levels equivalent to those of normal healthy individuals in a period of 6 months or more after surgery. T_{max} had no correlation with SF-36 dimensions.

Meanwhile, Takeichi et al. [14], in their follow-up survey of gastrointestinal symptoms, divided patients after DG into three groups: less than 5 years, from 5 years to less than 10 years, and 10 years or more after surgery. They showed that two gastrointestinal symptoms, dumping and reflux, persisted in all groups with no significant differences between these symptoms. Svedlund et al. [15] used the GSRS for up to 5 years after surgery to assess gastrointestinal symptoms of patients who underwent a gastrectomy. They reported that patients who underwent TG continued to suffer from a persistent decrease in QOL for gastrointestinal symptoms, especially indigestion and diarrhea, whereas patients who underwent surgery other than TG experienced improvement in the same symptoms. Our assessment by the GSRS also showed that gastrointestinal symptoms after TG, though moderate, did not improve much over time. Although these changes over time were not assessed based on individual patient data, a comparison of data from patient groups at different periods provides evidence that individual patients experienced similar changes over time.

It has been suggested that postgastrectomy syndromes are primarily caused by an impaired function of the remaining stomach. Conventionally, the measurement of gastric emptying by scintigraphic technique is regarded as the gold standard for clinically assessing the gastric emptying function, as it allows for a quantitative evaluation of the function and is regarded as the most reliable test. However, because this method requires a high-cost labeled compound and special equipment, and is complicated to use, it is not suitable for wide and common use [16, 17]. Recently, instead of the scintigraphic technique, many medical facilities have started using the ^{13}C breath test, which is an indirect method and is regarded as a simple, safe, and reliable. The ^{13}C breath test was first reported by Ghoos et al. [1] in 1993. Since then it has been widely used, mainly in Europe, as a clinical tool for the assessment of gastric emptying. Similarly, in Japan, since the "standardized method" of the ^{13}C breath test was proposed [2, 3], the test has become widely used in many medical facilities.

In particular, T_{max} is attracting attention as an assessment index, because it can be easily determined by actual measured values and does not require special calculation, as well as it attenuates the influence of metabolism and excretion. T_{max} in the ^{13}C breath test is supposed to correspond to the 80% excretion time in the scintigraphic technique, which is a direct method [18], and provides a high reliability. Our study used the ^{13}C breath test to track the outcomes of

patients who had undergone gastrectomy. There have been only a few reports that have verified whether the ^{13}C breath test is useful for assessing patients' QOL.

The value of T_{max} varied depending on the types of surgery performed, and was significantly lower in procedures other than PpG. In all types of surgery, T_{max} showed no significant differences between survey periods, meaning there was not much change in its value over time. Viewed in connection with the questionnaire surveys, T_{max} did not correlate with results of the SF-36. Because those results indicated an improvement in overall QOL over time, it was thought that an abnormality in gastric emptying, if any, might not have a strong effect on patients' general QOL.

In contrast, T_{max} was correlated with results of the GSRS for symptoms of abdominal pain and indigestion and the total score; none of these scores showed improvement over time. Based on the scatter chart depicting the total scores, it was revealed there was a significant aggregation of symptoms in patients with a T_{max} less than 21 min. Therefore, it was suggested that a T_{max} value of less than 21 min is a risk factor for the aggravation of patients' gastrointestinal symptoms. It is useful to perform the ^{13}C breath test from an early stage on patients who undergo a gastrectomy to predict postgastrectomy syndromes as well as evaluate the results of surgery.

Conclusions

Both a comprehensive assessment tool and a disease-specific assessment tool are needed to evaluate QOL of postgastrectomy patients. Results of the comprehensive assessment revealed that patients' QOL improved over time. In contrast, no improvement was observed over time in disease-specific assessments, suggesting that gastric dysfunction continued. The emptying function of the remaining stomach is closely related to gastrointestinal or digestive symptoms, and a value of T_{max} less than 21 min is a risk factor for aggravation of patients' gastrointestinal symptoms. The ^{13}C breath test is a useful tool for objectively assessing postoperative gastrointestinal symptoms of patients.

References

1. Ghoos YF, Maes BD, Geypens BJ et al (1993) of gastric emptying rate of solids by means of a carbon-labeled octanoic acid breath test. Gastroenterology 104:1640–1647
2. Nakada K, Aoyama N, Nakagawa M et al (2002) Report of the workshop titled "The present and the future in gastric emptying study assessed by ^{13}C breath test-with special reference to the standardization of the method" at the 44th Annual Meeting of the Japanese Smooth Muscle Society. J Smooth Muscle Res 6:J75–J91
3. Sanaka M, Nakada K (2010) Stable isotope breath tests for assessing gastric emptying: a comprehensive review. J Smooth Muscle Res 46:267–280
4. Ware JE Jr, Sherbourne CD (1992) The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 30:473–483
5. Fukuhara S, Bito S, Green J et al (1998) Translation, adaptation, and validation of the SF-36 health survey for use in Japan. J Clin Epidemiol 51:1037–1044
6. Fukuhara S, Ware JE Jr, Kosinski M et al (1998) Psychometric and clinical tests of validity of the Japanese SF-36 health survey. J Clin Epidemiol 51:1045–1053
7. Fukuhara S, Suzukamo Y (2004) Manual of SF-36 v2 Japanese version: Institute for Health Outcomes & Process Evaluation Research, Kyoto, Japan
8. Svedlund J, Sjodin I, Dotevall G (1988) GSRS—a clinical rating scale for gastrointestinal symptoms in patients with irritable bowel syndrome and peptic ulcer disease. Dig Dis Sci 33: 129–134
9. Dimenas E, Glise H, Hallerback B et al (1995) Well-being and gastrointestinal symptoms among patients referred to endoscopy owing to suspected duodenal ulcer. Scand J Gastroenterol 30: 1046–1052
10. Hongo M, Fukufara S, Green J (1999) QOL in digestive region. QOL evaluation by Japanese edition GSRS. Diagn Treat 87: 731–736
11. Tyrvainen T, Sand J, Sintonen H et al (2008) Quality of life in the long-term survivors after total gastrectomy for gastric carcinoma. J Surg Oncol 97:121–124
12. Avery K, Hughes R, McNair A et al (2010) Health-related quality of life and survival in the 2 years after surgery for gastric cancer. Eur J Surg Oncol 36:148–154
13. Wu CW, Chiou JM, Ko FS et al (2008) Quality of life after curative gastrectomy for gastric cancer in a randomised controlled trial. Br J Cancer 98:54–59
14. Takeichi A, Oguma H, Sasagawa T et al (2003) Postoperative quality of life (QOL) for patients with gastric cancer who underwent distal gastrectomy reconstructed by Billroth-I (B-I). J Tokyo Wom Med Univ 73:450–456
15. Svedlund J, Sullivan M, Liedman B et al (1999) Long term consequences of gastrectomy for patient's quality of life. The impact of reconstructive techniques. Am J Gastroenterol 94: 438–445
16. Heading RC, Tothill P, McLoughlin GP et al (1976) Gastric emptying rate measurement in man. A double isotope scanning technique for simultaneous study of liquid and solid components of a meal. Gastroenterology 71:45–50
17. Hanyu N, Nakada K, Aoki T (1999) Measurement of gastric emptying by scintigraphic technique. Gastroenterology 28: 220–227
18. Kawasaki N, Nakada K, Nakayoshi T et al (2006) The significance of T_{max} by gastric emptying study using ^{13}C-breath test, Comparison with direct method. Dig Absorpt 29:23–25