

Local recurrence following total or subtotal gastrectomy for adenocarcinoma of the antrum

Ali Marashi, Mehrdad Moghimi, Mohammad Taghi Salehian, Habib Ollah Peirovi, Faezeh Sodagari

Department of surgery, Taleghani hospital, Shahid Beheshti University, M.C., Tehran, Iran

ABSTRACT

Aim: This study aimed to compare the recurrence rate, mortality, and morbidity of curative resection of distal adenocarcinoma of the stomach between total gastrectomy (TG) and subtotal gastrectomy (STG).

Background: The choice between TG and STG for adenocarcinoma of the lower third of the stomach is still a matter of debate and controversy among surgeons.

Patients and methods: Hospital records of 66 patients with distal adenocarcinoma of stomach, which had undergone even-total or subtotal gastrectomy between October 2001 and February 2006 in Taleghani hospital, Iran were reviewed retrospectively. Demographic data and clinicopathological factors were recorded. Post-operative outcomes including mortality, morbidity and tumor recurrence were assessed. Univariate analyses using Fisher's exact test, the Student t-test, and the Pearson χ^2 test were used. *P* values less than 0.05 were considered statistically significant.

Results: Recurrence rate was higher in STG than TG (61% vs. 23%, RR=2.68, 95% CI=1.37-5.24, *P*=0.002). The mean time interval between gastrectomy and tumor recurrence was not different between TG and STG (19.75±5.1 vs. 18.0±7.8 months, *P*=0.507). Tumor size >5 cm (*P*=0.004), diffuse type (*P*=0.034), poor differentiation (*P*=0.001) and serosal invasion (*P*=0.012) were found to be significantly related to tumor recurrence in patients who had undergone gastrectomy.

Conclusion: Subtotal and total gastrectomy techniques have similar surgical outcome and postoperative complication rate; however, STG is associated with a more than twofold increase in local recurrence risk.

Keywords: *Stomach Neoplasms, Gastrectomy, Postoperative Complications, Neoplasm recurrence.*

(Gastroenterology and Hepatology From Bed to Bench 2008;1(3):133-138).

INTRODUCTION

Gastric adenocarcinoma is the most common fatal cancer in Iran according to a cancer surveillance study performed by the Ministry of Health of Iran (1). Gastric adenocarcinoma constitutes 90-95% of all gastric malignancies and is a major health problem not only in Iran but also in many other countries (2-5).

Radical surgery offers the only possibility for cure in patients with gastric cancer (6, 7); however, it is often challenging because of the extent of the operation and the frailty of the patient. The extent of resection required has been the subject of considerable debate (8-12). Total gastrectomy (TG) and subtotal gastrectomy (STG) both have been applied for the treatment of gastric cancer for more than one century (13), but because of the higher rates of post-operative mortality and morbidity reported

Received: 15 March 2008 Accepted: 23 June 2008

Reprint or Correspondence: Mehrdad Moghimi, MD.

Department of surgery, Taleghani hospital, Shahid Beheshti University, M.C., Tehran, Iran

E-mail: drmoghimi@yahoo.com

for TG, STG is routinely used and is becoming widely accepted for distal gastric cancers.

In addition, better quality of life outcomes are reported in STG treated patients. However, STG is known to have higher rates of local tumor recurrence comparing to TG. On the other hand, results of large well designed randomized trials comparing total versus subtotal gastrectomy indicate that TG and STG do not show a significant difference in mortality, morbidity and long-term survival results (14, 15). The choice between TG and STG for adenocarcinoma of the lower third of the stomach remains a matter of debate and controversy among surgeons worldwide. Some surgeons believe that for disease in the proximal half of the stomach, the time-honored treatment is total gastrectomy and tumors in the pyloric canal, antrum or on the lesser curve in the body of the stomach can be treated by subtotal gastrectomy (12).

Most surgeons in the United States perform total gastrectomy (if required for negative margins), esophagogastrectomy for tumors of the cardia and gastroesophageal junction, and subtotal gastrectomy for tumors of the distal stomach (16-18). Besides, in many European centers, TG is still the treatment of choice for advanced cancers of the antrum, especially those of the diffuse type according to the Lauren's classification (19-22). Nowadays in Iran, the choice of surgical procedure (TG or STG) is still based on the preference of the surgeons. The side effects of gastrectomy, total gastrectomy in particular, are considerable and include post-operative weight loss, anorexia, diarrhea, and other metabolic and nutritional changes (5).

Gastric adenocarcinoma carries a particularly poor prognosis. Even though the initial operative treatment is considered to be potentially curative, more than half of these patients develop a recurrent tumor. Prospective studies have shown the liver and peritoneum to be the most commonly affected sites of recurrence. Thus, when local recurrence and distant metastases are developed,

any kind of curative or palliative treatment becomes necessary (23).

Identification of the factors associated with the recurrence of tumor in patients who have undergone gastrectomy can lead to strategies to prevent the recurrence and even to predict it. In order to establish guidelines in treatment of gastric distal adenocarcinomas, it is necessary to evaluate short-term and long-term outcomes of these two surgical procedures.

The aim of this study was to compare the outcome and recurrence rate of curative resection of distal adenocarcinoma of the stomach between two surgical modalities: TG and STG.

PATIENTS and METHODS

Hospital records of all patients with early distal adenocarcinoma of stomach that had undergone either total or subtotal gastrectomy between October 2001 and February 2006 in Taleghani Hospital, Iran were reviewed retrospectively.

Patients were considered eligible only if the surgery was not a palliative treatment and nonmetastatic adenocarcinoma was restricted to the antrum. Records were not reviewed for patients with linitis plastica, gastric lymphoma, abdominal metastasis, ascites, superficial gastric carcinoma, microscopic lymph node involvement in cardioesophageal junction or splenopancreatic field, cardiac failure, renal failure, uncontrolled diabetes mellitus, arthritis, obesity (20% more than normal body weight), recent myocardial infarction, and liver cirrhosis. The antrum was defined by the anatomic limits of the pylorus and a transverse line drawn at the junction of the vertical and horizontal segments of the lesser curvature.

Demographic data such as age, gender, clinical factors including lymph node involvement (≤ 15 or > 15 nodes), tumor grading (well, moderate, and poorly differentiated), depth of tumor invasion, tumor size, tumor type according to the Lauren classification (diffused or intestinal), and the

Table 1- Main post-operative results of the patients subdivided according to the type of surgery

	Total gastrectomy (n=35)	Subtotal gastrectomy (n=31)	P value
Length of hospital stay (days)*	14.71 ±2.9	15.19 ±2.0	0.44
Hospital readmission [†]	8 (22.9)	16 (51.6)	0.02
Time to readmission, months*	20.50 ±4.9	17.19 ± 4.8	0.13
Second surgery [†]	5 (14.3)	11 (35.5)	0.04
Tumor recurrence, No (%)	8 (22.9)	19 (61.3)	0.002
Time to recurrence (months)*	19.75±5.1	18.0±7.8	0.51
Death [†]	3 (8.6)	8 (25.8)	0.06

*Mean ± standard deviation

[†] Number (%)

presence of any underlying diseases were recorded. Data regarding the operation including type of surgery (total or subtotal gastrectomy), post-operation complications (fever, nausea and vomiting, wound infection, pneumonia, myocardial infarction, dyspnea, muscle cramps), and length of hospital stay (LOS) was obtained.

Any hospital readmission, second surgery, tumor recurrence or death was assessed and recorded during follow-up period. Time to recurrence or death was assigned as the duration between the date of surgery and the date of recurrence or death for any cause.

As the patients had been followed post-operatively through the outpatient clinic regularly, follow-up data were obtained from patients' records and patients' health status was evaluated using telephone contacts if needed.

Statistical analysis was performed using the Statistical Package for Social Sciences, version 15 for Windows™ (SPSS® Inc., Chicago, IL). Continuous variables were summarized as mean ± standard deviation and categorical variables as numbers (percent). The relationship between clinicopathological factors and tumor recurrence was evaluated by univariate analysis using the student t-test, the Pearson χ^2 test and Fisher's exact test if needed. The statistical differences were two-tailed and considered to be significant at *P* value less than 0.05.

RESULTS

In this study 66 patients (41 men and 24 women) who aged from 38 to 74 (60.68 ± 6.8) years were investigated. Twenty six (39%) patients had an underlying disease at the time of surgery and forty seven (71%) had more than 15 involved lymph nodes. Subserosal penetration was found in 14 patients and the rest had serosal invasion which was the measure of depth of tumor invasion. Tumor size was less than 5 cm in 16 patients. Histological type was intestinal in 16 (24.2%) and diffuse in 50 (75.8%) patients.

Among these patients 35 (53%) had undergone total gastrectomy and 31 (47%) had subtotal gastrectomy. The length of hospital stay did not differ significantly between two groups (Table 1); however, a second surgery was more likely to be needed in STG group. Moreover, twenty three post-operation complications occurred in TG group and 21 in STG. Fever and nausea and vomiting were observed more frequent in both TG and STG (Table 2).

Hospital readmission rate was significantly higher in STG group than in patients of TG group (*P*= 0.015) with dysphagia as the most frequent cause of readmission in both groups. But mean time to hospital readmission was not significantly different between TG and STG groups (Table 1).

The second surgery was performed more frequently in STG patients mostly for tumor resection and also as a palliative surgery (Table 1).

Table 2- Distribution of post-operative complications

	Total gastrectomy (n=35)	Subtotal gastrectomy (n=31)
Fever	8	6
Nausea and vomiting	5	5
Wound infection	3	2
Pneumonia	2	3
Myocardial infarction	3	1
Dyspnea	1	3
Muscle cramps	1	1
Total	23	21

Table 3- Clinicopathological prognostic factors of recurrence

	Recurrence (n=29)	No Recurrence (n=37)	P-value
Gender			0.10
Male	21 (72.4) *	20 (54)	
Female	8 (27.6)	17(46)	
Lymph node involvement			0.48
>15	21 (72.4)	26 (70.2)	
≤15	8 (27.6)	11 (29.8)	
Tumor grading			<0.001
Well differentiated	2 (6.8)	17 (45.9)	
Mod. differentiated	5 (17.2)	20 (54.1)	
Poor. differentiated	22 (76)	0(0)	
Depth of tumor invasion			0.01
Subserosal	2 (6.9)	12 (32.4)	
Serosal invasion	27 (93.1)	25 (67.6)	
Tumor size			0.004
>5 cm	27 (93.1)	23 (62.1)	
>15 cm	2 (6.9)	14 (37.9)	
Tumor type			0.03
Diffuse	27 (93.1)	14 (37.8)	
Intestinal	2 (6.9)	23 (62.2)	
Underlying Disease	12 (41.3)	14 (37.8)	0.48

*Number (%)

Recurrence of tumor was found in 8 patients of TG group and in 19 patients of STG group. The Pearson χ^2 test showed a significantly higher

recurrence rate in STG (RR=2.68, 95% CI: 1.37-5.24, P=0.002). However, the mean interval between primary gastrectomy operation and tumor recurrence was not different between two groups (Table 1).

Tumor size >5 cm, diffuse type, poor differentiation and serosal invasion were found to be significantly related to tumor recurrence in patients who had undergone gastrectomy (Table 3).

During the follow-up period, 3 patients died in TG (1 myocardial infarction, 1 hepatic failure and 1 widespread metastasis) and 8 patients in STG group (3 abdominal metastases, 2 hepatic metastases, 1 myocardial infarction, and 1 widespread metastasis). The incidence rate of death was not significantly different in these two groups (P=0.061)

DISCUSSION

This retrospective study of existing data mainly focused on the impact of two different surgical procedures (total or subtotal gastrectomy) on short- and long-term outcomes in patients with distal adenocarcinoma of stomach.

In our results, TG did not increase post-operative hospital stay, mortality and even morbidity in comparison with STG. Hospital readmission was higher in STG group and consequently a greater number of second surgeries were needed in these patients. A significantly higher incidence of tumor recurrence was observed in STG method which made STG associated with a more than two-fold increase in local recurrence risk.

No significant difference was observed in mortality between the two resection procedures, in contrast with some studies that found a higher incidence of mortality following total gastrectomy (24, 25). Gastrectomy is traditionally known as a major procedure with a high mortality risk and

total gastrectomy is generally considered at least twice as dangerous as distal gastrectomy (23, 26, 27), although there are some exceptions to this rule that are consistent with our results (14).

The retrospective nature of this study made it difficult to draw a conclusion about exact survival rates and the predicting factors of survival in patients with early gastric adenocarcinoma of the antrum.

Selecting the resection procedure is still based on the surgeon's decision according the clinicopathological factors and to some extent the patient's preference. Higher rates of recurrence following STG should be considered in selecting this procedure.

In conclusion, subtotal and total gastrectomies have a similar postoperative complication rate and surgical outcome, but STG is associated with a more than twofold increase in local recurrence risk and hospital readmission. In addition to subtotal gasterctomy, tumor size >5 cm, diffuse type, poor differentiation and serosal invasion are significantly related to the tumor recurrence in patients who undergo gastrectomy.

REFERENCES

- Iranian Ministry of Health and Medical Education. Death in four provinces of Iran; 2000.
- De Vries AC, Kuipers EJ. Epidemiology of premalignant gastric lesions: implications for the development of screening and surveillance strategies. *Helicobacter* 2007;12 Suppl 2:S22-31.
- Goh KL. Changing trends in gastrointestinal disease in the Asia-Pacific region. *J Dig Dis* 2007;8:179-85.
- Matsuzaka M, Fukuda S, Takahashi I, Shimaya S, Oyama T, Yaegaki M, et al. The decreasing burden of gastric cancer in Japan. *Tohoku J Exp Med* 2007;212:207-19.
- Tsugane S, Sasazuki S. Diet and the risk of gastric cancer: review of epidemiological evidence. *Gastric Cancer* 2007;10:75-83.
- Scurtu R, Groza N, Otel O, Goia A, Funariu G. Quality of life in patients with esophagejejunal anastomosis after total gastrectomy for cancer. *Rom J Gastroenterol* 2005;14:367-72.
- Liedman B. Symptoms after total gastrectomy on food intake, body composition, bone metabolism, and quality of life in gastric cancer patients—is reconstruction with a reservoir worthwhile? *Nutrition* 1999;15:677-82.
- Fuchs C, Mayer R. Gastric carcinoma. *N Engl J Med* 1995;333:32-39.
- De MG, Verlato G, Roviello F, Di LA, Marrelli D, Morgagni P, et al. Subtotal versus total gastrectomy for T3 adenocarcinoma of the antrum. *Gastric Cancer* 2003;6:237-42.
- Roukos D, Schmidt-Mathiesen A, Encke A. Adenocarcinoma of the gastric antrum: does D2 total gastrectomy with splenectomy improve prognosis compared to D1 subtotal gastrectomy? A long-term survival analysis with emphasis on Lauren classification. *Surg Oncol* 1995;4:323-32.
- Cenitagoya GF, Bergh CK, Klinger-Roitman J. A prospective study of gastric cancer. 'Real' 5-year survival rates and mortality rates in a country with high incidence. *Dig Surg* 1998;15:317-22.
- Robertson CS, Chung SC, Woods SD, Griffin SM, Raimes SA, Lau JT, et al. A prospective randomized trial comparing R1 subtotal gastrectomy with R3 total gastrectomy for antral cancer. *Ann Surg* 1994;220:176-82.
- Schlatter C. Uber Ernährung und Verdauung nach vollstandiger Entfernung des Magens und Osophagejejunostomie beim Menschen. *Brun's Beitrage Klin Chir* 1887;19:757-76.
- Bozzetti F, Marubini E, Bonfanti G, Miceli R, Piano C, Crose N, et al. Total versus subtotal gastrectomy: surgical morbidity and mortality rates in a multicenter Italian randomized trial. The Italian Gastrointestinal Tumor Study Group. *Ann Surg* 1997;226: 613-20.
- Bozzetti F, Marubini E, Bonfanti G, Miceli R, Piano C, Gennari L. Subtotal versus total gastrectomy for gastric cancer: five-year survival rates in a multicenter randomized Italian trial. Italian Gastrointestinal Tumor Study Group. *Ann Surg* 1999;230:170-78.
- Lau MK, Le AT, El-Serag HB. Non-cardia gastric cancer remains important and deadly in the United States: secular trends in incidence and survival. *Am J Gastroenterol* 2006;101:2485-92.
- Le A, Berger D, Lau M, El-Serag HB. Secular trends in the use, quality, and outcomes of gastrectomy

for noncardia gastric cancer in the United States. *Ann Surg Oncol* 2007;14:2519-27.

18. Smith JK, McPhee JT, Hill JS, Whalen GF, Sullivan ME, Litwin DE, et al. National outcomes after gastric resection for neoplasm. *Arch Surg* 2007;142:387-93.

19. Siewert JR, Botcher K, Roder JD, Bush R, Hermanek P, Meyer HJ. Prognostic relevance of systematic lymph node dissection in gastric carcinoma. German Gastric Carcinoma Study Group. *Br J Surg* 1993; 80:1015-18.

20. Roukos D, Paraschou P, Lorenz M. Distal gastric cancer and extensive surgery: a new evaluation method based on the study of the status of residual lymph nodes after limited surgery. *Ann Surg Oncol* 2000;7:719-26.

21. Piso P, Werner U, Lang H, Mirena P, Klempnauer J. Proximal versus distal gastric carcinoma-what are the differences? *Ann Surg Oncol* 2000;7:520-25.

22. Hansson LE, Ekstrom AM, Bergstrom R, Nyren O. Surgery for stomach cancer in a defined Swedish population: current practices and operative results. Swedish Gastric Cancer Study Group. *Eur J Surg* 2000;166:787-95.

23. McCulloch P, Ward J, Tekkis PP. Mortality and morbidity in gastro-oesophageal cancer surgery: initial results of ASCOT multicentre prospective cohort study. *BMJ* 2003;327:1192-97.

24. Adashek K, Sanger J, Longmire WP. Cancer of the stomach: review of consecutive ten-year intervals. *Ann Surg* 1979;189:6-10.

25. White RR, Mackie JA, Fitts WT. An analysis of twenty years' experience with operations for carcinoma of the stomach. *Ann Surg* 1975;181:611-15.

26. Bittner R, Butters M, Ulrich M, Uppenbrink S, Beger HG. Total gastrectomy. Updated operative mortality and long-term survival with particular reference to patients older than 70 years of age. *Ann Surg* 1996; 224: 37-42.

27. Wu CW, Hsieh MC, Lo SS, Wang LS, Hsu WH, Lui WY, et al. Morbidity and mortality after radical gastrectomy for patients with carcinoma of the stomach. *J Am Coll Surg* 1995;181:26-32.

28. Svedlund J, Sullivan M, Liedman B, Lundell L, Sjödin I. Quality of life after gastrectomy for gastric carcinoma: controlled study of reconstructive procedures. *World J Surg* 1997;21:422-33.