

Assessment of Surgical Treatment and Postoperative Nutrition in Gastric Cancer Patients Older than 80 Years

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Abstract. *Background:* A gastrectomy for gastric cancer is sometimes required in patients older than 80 years due to the continuously increasing age of society. However, if a gastrectomy worsens the postoperative quality of life and daily activity in elderly patients because of poor nutrition, the procedure may not always be a useful treatment strategy. *Patients and Methods:* Clinicopathological data of patients with gastric cancer who underwent a gastrectomy at our Department between 1998 and 2008 (N=471) were collected and analyzed. The results of treatment for patients older than 80 years (N=41) were analyzed and compared against those of patients younger than 80 years (N=430). *Results:* Patients older than 80 years had a higher frequency of preoperative co-morbidities than patients younger than 80 years. However, there was no statistical difference in postoperative complications regarding nutrition between the two groups. *Conclusion:* Older age is not a determinant of poor nutrition following gastrectomy. Gastrectomy for gastric cancer is, therefore, a useful treatment strategy, regardless of ageing.

The population is ageing throughout the world (1, 2). As a consequence, the age of patients with gastric cancer is also increasing, with more than 40% of patients in Japan being over 70 years of age (3). We have previously reported the clinicopathological features and prognosis of gastric cancer in 344 patients older than 70 years who underwent gastrectomy between 1965 and 1990. This finding demonstrated that the frequency of surgical treatment increased with survival of elderly patients with gastric cancer (4). However, mean life expectancy in Japan has increased

to 79.3 years for males and 86.1 years for females (5). The age of gastric cancer patients has also been increasing gradually at our Department. Treatment strategies are, therefore, now required for gastric cancer patients over 80 years of age. The aim of the present study was to elucidate whether treatment strategies for patients with gastric cancer older than 80 years are comparable with patients younger than 80 years with regard to complications, postoperative nutrition, survival rate, and clinical outcome.

Patients and Methods

A total of 471 patients with gastric adenocarcinoma underwent gastrectomy at the Department of Surgery and Science, Kyushu University Hospital between 1998 and 2008. Forty-one patients (8.7%) were older than 80 years. The clinicopathological features of the patients were reviewed using hospital records, followed by a comparison of data of patients either younger or older than 80 yr. Informed consent was obtained from each patient.

The surgical specimens were examined pathologically and scored according to the TNM classification of the International Union Against Cancer (UICC) (6). The preoperative physical status prior to gastrectomy was scored according to the American Society of Anesthesiologists Physical Status (ASA-PS) (7).

All patients were followed-up for intervals ranging from 3 to 12 months. These follow-up visits included physical examination, blood analysis, and a combination of imaging examinations such as computed tomography. The median follow-up period in the study was 30 (range=1.5-130) months.

All values such as operative time, estimated blood loss, postoperative hospital stay, blood test results, and degree of weight loss were expressed as the mean±standard deviation (SD). The comparisons between the two study groups were carried out using Fisher's exact test. Survival rates were calculated using the Kaplan-Meier method. The level of significance was set at $p<0.05$.

Results

Patients' characteristics. The characteristics of patients are shown in Table I. The median age of patients older or younger than 80 years was 82.1 and 61.9 years, respectively. There were no significant differences in sex distribution

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Key Words: Gastrectomy, elderly patients, nutrition.

Table I. Patients' characteristics.

Factor	Under 79 years (n=430)	Over 80 years (n=41)	p-Value
Age (years)	61.9±11.1	82.1±2.6	<0.0001
Gender			
Male/Female	293/137	22/19	ns
ASA-PS			
<2	414 (96.3)	38 (92.7)	ns
>3	16 (3.7)	3 (7.3)	
Histology			
Differentiated	214 (49.8)	24 (58.5)	ns
Not differentiated	216 (50.2)	17 (41.5)	
Depth of invasion			
T1	219 (50.9)	19 (46.3)	ns
T2	125 (29.1)	18 (43.9)	
T3,4	86 (20.0)	4 (9.7)	
Lymphatic involvement			
N0	260 (60.5)	28 (68.3)	ns
N1	93 (21.6)	10 (24.4)	
N2	52 (12.1)	2 (4.9)	
N3	25 (5.8)	1 (2.4)	
Stage			
I	270 (62.8)	28 (68.3)	ns
II	49 (11.4)	7 (17.1)	
III	49 (11.4)	4 (9.7)	
IV	62 (14.4)	2 (4.9)	

between the two groups. The majority of patients were categorized as ASA-PS 0-2. Histologically, the depth of tumor invasion, lymphatic involvement, and pathological stage were not different in the two groups.

Preoperative co-morbidities. Preoperative co-morbidities were more likely to be observed (61.0%) in patients older than 80 years compared to those under 80 years of age (Table II). In particular, anemia, cardiovascular dysfunction, and renal dysfunction were more frequently observed in patients older than 80 years, whereas there was no significant difference in other morbidities such as diabetes mellitus, liver, and respiratory dysfunction.

Surgical procedures and postoperative complications. There was no statistical difference in surgical procedures between the two groups (Table III). Operation time, volume of blood loss, and period of postoperative hospital stay also showed no statistical differences. No operation-related death occurred in either group. Postoperative complications were observed in 4 cases (9.8%) in patients older than 80 years. This frequency was not significantly different than that observed in patients younger than 80 years (12.8%). Cardiovascular dysfunction and delirium was also observed in patients older than 80 years Other postoperative complications included acute colitis and mild paralytic obstruction.

Table II. Preoperative co-morbidities.

Factor	Under 79 years (n=430)	Over 80 years (n=41)	p-Value
Anemia	48 (11.2)	10 (24.4)	<0.05
Cardiovascular dysfunction	56 (13.0)	9 (21.9)	<0.05
Respiratory dysfunction	16 (3.7)	4 (9.8)	ns
Liver dysfunction	27 (6.3)	1 (2.4)	ns
Renal dysfunction	24 (5.6)	11 (26.8)	<0.05
Diabetes mellitus	27 (6.3)	3 (7.3)	ns

Table III. Surgical procedures and postoperative complications.

Factor	Under 79 years (n=430)	Over 80 years (n=41)	p-Value
Procedures			
Methods (%)			
Distal gastrectomy	227 (52.8)	27 (65.9)	ns
Total gastrectomy	200 (46.5)	13 (31.7)	
Others	3 (0.7)	1 (2.4)	
Laparoscopic or open (%)			
Laparoscopic	44 (10.2)	4 (9.8)	ns
Open	386 (89.8)	37 (90.2)	
LN's dissection			
<D2	203 (47.2)	23 (56.1)	ns
>D2	227 (52.8)	18 (43.9)	
Curability (%)			
Curative; R0	299 (69.5)	32 (78.1)	ns
Non-curative; R>1	131 (30.5)	9 (21.9)	
Operation time (min)	248.2±103.0	220.4±52.6	ns
Blood loss (g)	504.3±458.5	431.2±307.1	ns
Hospital stay (day)	22.3±36.9	19.9±10.0	ns
Complications			
Surgery Related (%)			
Pancreatic-related abscess	11 (2.6)	0	ns
Anastomotic leakage	7 (1.5)	0	ns
Bleeding	2 (0.4)	0	ns
Others	12 (2.8)	1 (2.4)	ns
Non-surgery related (%)			
Pneumonia	1 (0.2)	0	ns
Cardiovascular dysfunction	0	1 (2.4)	ns
Delirium	10 (2.3)	1 (2.4)	ns
Others	8 (1.9)	2 (4.9)	ns
Total (complications)	55 (12.8)	4 (9.8)	ns

Postoperative nutritional assessment. A total of 336 patients who were followed-up as outpatients over a one-year period had a postoperative nutritional assessment. The degree of weight loss after gastrectomy was selected as an indicator of postoperative nutrition. One year after gastrectomy, mean weight loss was not statistically different in the two groups (≥80 years, 6.8 kg; <80 years, 6.0 kg) (Table IV). Variations in the levels of serum total protein and albumin, and hemoglobin

Table IV. Postoperative nutritional assessment one year after gastrectomy.

Factor	Under 79 years (n=310)	Over 80 years (n=26)	p-Value
Weight (kg)	-6.0±7.4	-6.8±5.3	ns
Hemoglobin (g/dL)	-0.6±2.1	-0.6±1.7	ns
Total protein (g/dL)	-0.1±0.7	-0.2±0.6	ns
Albumin (g/dL)	-0.1±0.5	-0.0±0.4	ns

Table V. Adjuvant chemotherapy for advanced cases.

Status	Under 79 years (n=167)	Over 80 years (n=13)	p-Value
Not performed	54 (32.3)	9 (69.2)	<0.01
Performed	113 (67.6)	4 (30.8)	

Table VI. Reasons why adjuvant chemotherapy was not performed in patients older than 80 years.

Reasons	Cases (n=9)
Rejected by patient or family, due to ageing	6 (66.7)
Co-morbidities	3 (33.3)

level were also assessed as postoperative nutritional indicators one year after gastrectomy. These levels showed no significant difference between the two groups. There was also no significant difference in these serum chemistry values at 3 or 5 years after gastrectomy (data not shown).

Postoperative adjuvant chemotherapy. Only four patients older than 80 years had postoperative adjuvant chemotherapy and received either UFT (oral tegafur and uracil) or S-1 (oral fluoropyrimidine). Two of these cases did not complete the course of chemotherapy because of tumor progression or severe appetite loss. Nine of the patients older than 80 years were adaptation cases for adjuvant chemotherapy, although this was not carried-out because of severe co-morbidities or the patient or their family declined the treatment (Tables V and VI).

Survival. Twelve of 41 (29.3%) patients older than 80 years died during the follow-up period. The median follow-up period was 28.3 months. Five of the deaths (12.2%) were associated with progression or recurrence of the gastric cancer. In contrast, 67 (15.6%) of the 430 patients younger than 80 years died of gastric cancer. The overall survival

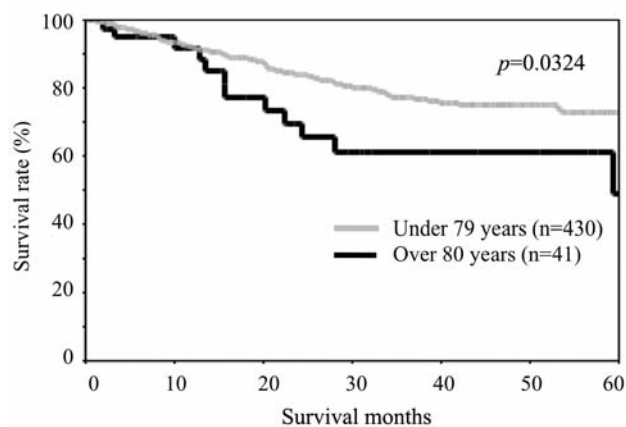


Figure 1. Overall survival in patients younger than 80 years (gray line) or older than 80 years (black line).

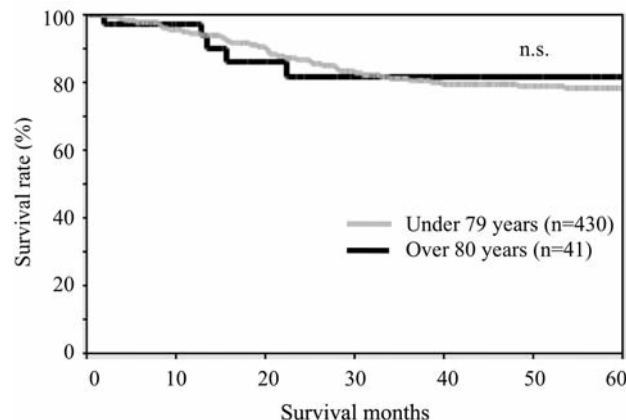


Figure 2. Cumulative survival in patients younger than 80 years (gray line) or older than 80 years (black line).

rates were 48.8% and 72.9% in patients older or younger than 80 years, respectively ($p=0.0324$) (Figure 1). In contrast, the cumulative 5-year survival rate of patients in the over 80 and under 80 years age groups was 81.8% and 78.2%, respectively. This difference was not statistically significant ($p=0.963$) (Figure 2).

Discussion

The incidence of gastric cancer in Japan is considerably higher than in other countries. An ageing society has an increased number of elderly people with various diseases such as gastric cancer (8). Although gastrectomies in elderly patients are since long been performed, recent improvements in surgical procedures and perioperative management have changed the environment for elderly patients with gastric cancer (9, 10).

Our study showed no difference between the over-80 and under-80 age groups in ASA-PS classification. This finding suggests that patients older than 80 years who had a gastrectomy may be selected because of their natural better performance status (11). However, gastrectomy is not indicated for patients older than 80 years if they have poor performance status. The number of patients older than 80 years categorized as stage IV was less than in the under-80 years age group, whereas there was no difference in the other stages. Gastrectomy for stage IV patients is performed as palliative surgery, but is not indicated for these patients. Gastrectomy is also not indicated in patients older than 80 years classified as IV because of their performance status (12, 13). Performing gastrectomy for ageing patients, with an advanced stage may worsen postoperative quality of life, especially in patients older than 80 years (14).

Weight and appetite loss is not rare in patients after a gastrectomy (15, 16) but may not necessarily reflect differences in age. Despite ageing, there was no difference in the degree of weight loss compared to younger patients. If weight loss and poor nutrition is observed considerably more frequently in patients older than 80 years, a gastrectomy should not be recommended. Because weight loss and poor nutrition induce poor quality of life (17), these factors may also result in a poor prognosis after gastrectomy, especially in patients older than 80 years. The cumulative survival rates demonstrate that there was no difference between the over 80 years and under 80 years age groups in death caused by gastric cancer. This finding indicates that gastrectomy improves prognosis for ageing gastric cancer patients, and that gastrectomy may not necessarily lead to a deterioration in quality of life.

In general, adjuvant chemotherapy in gastric cancer patients reduces the recurrence rate after a gastrectomy (18-21). However for ageing patients, chemotherapy is not usually safe, because of side-effects or co-morbidities (22-24). In particular, it is not uncommon for patients older than 80 years to die from any other causes. While postoperative adjuvant chemotherapy is recommended for advanced cases because it reduces the risk of recurrence, not all patients agree to undergo this therapy. Patients and their family tend to worry about side-effects and worsening of co-morbidities, especially in ageing patients. The usefulness of adjuvant chemotherapy to improve prognosis in patients older than 80 years needs to be examined in a larger number of cases.

Conclusion

The present study showed that gastrectomy and adjuvant chemotherapy for patients older than 80 years is a safe treatment strategy. There was no significant difference observed in the degree of weight loss and worsening of nutrition caused by gastrectomy in patients younger or older than 80 years.

References

- 1 Siegel R, Naishadham D and Jemal A: Cancer statics, 2012. *CA Cancer J Clin* 62: 10-29, 2012.
- 2 Eray F, Ren JS, Masuyer E and Ferlay J: *Int J Cancer* 132: 1133-1145, 2013.
- 3 Current status of gastric cancer screening in Japan 2004, Tokyo. Ministry of Health, Labour and Welfare, 2010.
- 4 Maehara Y, Oshiro T, Oiwa H, Oda S, Baba H, Akazawa K and Sugimachi K: Gastric carcinoma in patients over 70 years of age. *Br J Surg* 82: 102-105, 1995.
- 5 Abridged life table for Japan 2008, Tokyo. Statistics and Information Department, Minister's Secretariat, Ministry of Health, Labour and Welfare, 2010.
- 6 Sobin LH, Gospodarowicz MK and Wittekind C: TNM classification of malignant tumors. 7th ed. Oxford: Wiley; 2010.
- 7 Wolters U, Wolf T, Stültzer H and Schröder T: ASA classification and perioperative variables as predictors of postoperative outcome. *Br J Anaesth* 77: 217-222, 1996.
- 8 Age-specific cancer incidence rate, 2004. Center for Cancer Control and Information Services, National Cancer Center, Japan 2010.
- 9 Shojania KG, Duncan BW, McDonald KM, Wachter RM and Markowitz AJ: Making health care safer: a critical analysis of patient safety practices. *Evid Rep Technol Assess* i-x, 1-668, 2001.
- 10 Jeong O, Park YK, Ryu SY and Kim YJ: Effect of Age on Surgical Outcomes of Extended Gastrectomy With D2 Lymph Node Dissection in Gastric Carcinoma: Prospective Cohort Study. *Ann Surg Oncol* 17: 1589-1596, 2010.
- 11 Turrentine FE, Wang H, Simpson VB and Jones RS: Surgical risk factors, morbidity, and mortality in elderly patients. *J Am Coll Surg* 203: 865-877, 2006.
- 12 Kahlke V, Bestmann B, Schmid A, Doniec JM, Küchler T and Kremer B: Palliation of metastatic gastric cancer: impact of preoperative symptoms and the type of operation on surgical and quality of life. *World J Surg* 28: 369-375, 2004.
- 13 Huang KH, Wu CW, Fang WL, Chen JH, Lo SS, Wang RF and Li AF: Palliative resection in noncurative gastric cancer patients. *World J Surg* 34: 1015-1021, 2010.
- 14 Martella B, Millitello C, Spirch S, Bruttocao A, Nistri R, De Rossi A, Barbon B and Terranova O: Palliative surgery for gastric cancer in elderly patients. *Acta Biomed* 76(Suppl 1): 49-51, 2005.
- 15 Marano L, Porfidia R, Pezzella M, Grassis M, Petrillo M, Esposito G, Braccio B, Gallo P, Boccardi V, Cosenza A, Izzo G and Di Martino N: Clinical and immunological impact of early postoperative enteral immunonutrition after total gastrectomy in gastric cancer patients: a prospective randomized study. *Ann Surg Oncol* 20: 3912-3918, 2013.
- 16 Malmström M, Ivarsson B, Johansson J, Klefsgård R: Long-term experiences after oesophagectomy/gastrectomy for cancer – a focus group study. *Int J Nurs Stud* 50: 44-52, 2013.
- 17 Amarantos E, Martinez A and Dwyer J: Nutrition and quality of life in older adults. *J Gerontol A Biol Sci Med Sci* 56: 54-64, 2001.
- 18 Jackson C, Cunningham D, Oliveira. ESMO Guidelines Working Group: Gastric cancer: ESMO clinical recommendations for diagnosis, treatment and follow-up. *Ann Oncol* 20: 34-36, 2009.
- 19 Liu TS, Wang Y, Chen SY and Sun YH: An updated meta-analysis of adjuvant chemotherapy after curative resection for gastric cancer. *Eur J Surg Oncol* 34: 1208-1216, 2008.

- 20 GASTRIC GROUP, Paoletti X, Oba K, Burzykowski T, Michiels S, Ohashi Y, Pignon JP, Rougier P, Sakamoto J, Sargent D, Sasako M, Van Cutsem E and Buyse M: Benefit of adjuvant chemotherapy for resectable gastric cancer: a meta-analysis. *JAMA* 303: 1729-1737, 2010.
- 21 Sakuramoto S, Sasako M, Yamaguchi T, Kinoshita T, Fujii M, Nashimoto A, Nakajima T, Ohashi Y, Imamura H, Higashino M, Yamamura Y, Kurita A, ACTS-GC Group: Adjuvant chemotherapy for gastric cancer with S-1, an oral fluoropyrimidine. *N Engl J Med* 357: 1810-1820, 2007.
- 22 Repetto L: Greater risks of chemotherapy toxicity in elderly patients with cancer. *J Support Oncol* 1: 18-24, 2003.
- 23 Laurent M, Pailland E, Tournigand C, Caillet P, Le Thuaut A, Lagrange JL, Beauchet O, Vincent H, Carvahlo-Verlinde M, Culine S, Bastuji-Garin S, Canoui-Poitrine F; ELCAPA Study Group: Assessment of social cancer treatment feasibility in older patients: a prospective cohort study. *Oncologist* 19: 275-282, 2014.
- 24 Gillison TL and Chatta GS: Cancer chemotherapy in the elderly patient. *Oncology* 24: 76-85, 2010.

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