

## ORIGINAL

# Limited lymph node dissection in elderly patients with gastric cancer

Kozo Yoshikawa, Mitsuo Shimada, Jun Higashijima, Toshihiro Nakao, Masaaki Nishi, Hideya Kashiwara, and Chie Takasu

*The Department of Surgery, the University of Tokushima, Japan 770-8503 Kuramoto-cho Tokushima, Japan*

**Abstract : Background :** The number of elderly patients with gastric cancer is continuing to increase along with the life expectancy of the general population. The purpose of this study was to investigate both the impact of age on postoperative outcome and the effect of limited lymph node dissection for elderly patients. **Methods :** Patients were classified into the following three groups : Group A,  $\geq 80$  years old ( $n=44$ ) ; Group B, 70-80 years old ( $n=139$ ) ; Group C,  $< 70$  years old ( $n=219$ ). Postoperative complication and survival rates were compared between the three groups **Results :** Limited lymph node dissection was performed significantly more frequently in Group A. In terms of surgery-related complications, no significant difference was seen between groups. In terms of general related complications, the complication rate increased with age, from 4% in Group C to 13% in Group B and 14% in Group A ( $p < 0.05$  each). Although limited lymph node dissection was frequently performed in Group A, cancer-specific survival showed no significant difference in R0 patients. **Conclusions :** Limited lymph node dissection for gastric cancer did not affect the cancer-specific survival in elderly patients. *J. Med. Invest.* 63 : 91-95, February, 2016

**Keywords :** Cancer specific survival, Limited lymph node dissection

## INTRODUCTION

The number of elderly patients with gastric cancer is continuing to increase (1), and opportunities to treat aged patients with gastric cancer are becoming more frequent (2). Elderly patients show an increased incidence of comorbidities such as pulmonary, cardiovascular, and renal disease (1). The optimal surgical approach for these patients remains controversial because of the operative risks (2). Complete tumor removal is essential to treat gastric cancer, and because morbidity and mortality rates after D2 surgery are 20.9% and 0.8%, respectively (3), and the procedure is safe to perform, D2 gastrectomy is the standard surgical procedure in Japan. On the other hand, several randomized clinical trials have indicated that dissection is associated with a significantly higher postoperative risk (4). D2 resection for elderly patients thus remains controversial. The purposes of this study were to investigate the effects of age on postoperative outcome and the utility of limited lymph node dissection for elderly patients.

## PATIENTS AND METHODS

### Patients

From January 2001 to December 2009, a total of 402 patients underwent gastrectomy for gastric cancer at the University of Tokushima. Patients were classified into the following three groups : Group A,  $\geq 80$  years old ( $n=44$ ) ; Group B, 70-80 years old ( $n=139$ ) ; and Group C,  $< 70$  years old ( $n=219$ ). Regarding prognoses, data for all patients was checked from the medical records, and overall survival (OS) and disease-free survival rates were analyzed based on follow-up data as of August 2014.

Received for publication November 16, 2015 ; accepted December 24, 2015.

Address correspondence and reprint requests to Kozo Yoshikawa MD Ph.D FACS, The Department of Surgery, the University of Tokushima 3-18-15 Kuramoto-cho Tokushima Japan and FAX : +81-88-631-9698.

## METHODS

The three groups were examined and compared in terms of sex, stage, operative procedures, approach methods, and pathological features. Postoperative surgical complications included anastomotic leakage, pancreatic fistula, postoperative bleeding, and wound infection. Postoperative general complications included cardiac, respiratory, and renal disorders occurring within 30 days after surgery. Complications were verified and graded according to the Clavien-Dindo classification. In this study, complications were defined as those higher than grade 3a. Hospital mortality was defined as postoperative death within 30 day of surgery.

### Limited lymph node dissection

According to the Japanese guidelines, D2 dissection is the standard procedure for advanced gastric cancer, while D1+ dissection is used for early gastric cancer. In this study, limited lymph node dissection was defined as dissection that did not reach adequate lymph node dissection.

### Statistical analyses

The unpaired Student's t-test, the  $\chi^2$  test for categorical variables, and Mann-Whitney's U test for continuous variables, were performed. Continuous variables are expressed as mean  $\pm$  standard deviation (SD). JMP 8 software (SAS Institute, Cary, NC) was used for all statistical analyses.

## RESULTS

### Patient characteristics

No significant differences were seen in sex, stage, or histologic type. However, patients with preoperative complications were more frequently observed in older groups (Groups A and B) than in the younger group (Table 1).

**Table 1.** Patient characteristics and surgical procedures and extent of lymph node dissection

	Group A (80<) n=44	Group B (70-80) n=139	Group C (< 70) n=219	p value
Gender				
Male	31	104	153	n.s.
Female	13	35	66	
Stage				
I+II	26	85	138	n.s.
III+IV	18	54	81	
Histologic type				
Differentiated	28	90	134	n.s.
Undifferentiated	16	49	85	
Pre-operative complication	18	21	22	p< 0.05
Cardiovascular	4	3	6	
Hypertention	6	4	6	
Diabetes	1	6	4	
Pulmonary	7	7	3	
Renal	1	1	2	
Brain infarction	1	2	2	
Surgical Procedure				
Total	17	56	81	n.s.
Distal	22	67	116	
Other	5	16	22	
Approach				
Open	30	95	138	n.s.
Lap	14	44	81	
Curability				
R0	35	106	175	n.s.
R1, 2	9	33	44	
Lymph node dissection				
Radical	16	121	191	p< 0.05
Limited	28	18	28	
Operation time (min)	204	233	215	n.s.
Blood loss (ml)	188	156	192	n.s.

#### *Surgical procedure and lymph node dissection*

No significant differences in operative procedure, curability, blood loss, or operation time were seen in groups. However, limited lymph node dissection was performed significantly more frequently in Group A (63%) than in Groups B (13%) or C (13%;  $p < 0.05$  each) because of pre-operative complication (Table 1).

#### *Post-operative complications*

In terms of surgery-related complication, no significant difference was identified in three groups. However, in terms of general related complications, the complication rate increased with age (Group A, 14%; Group B, 13%; Group C, 4%;  $p < 0.05$  each) (Table 2). Hospital mortality means death during hospital stay.

#### *Survival analysis*

OS tended to be lower in Group A, but no significant difference was found (Fig. 1A). Even though limited lymph node dissection was more frequently performed in Group A, cancer-specific survival showed no significant difference in R0 patients (Fig. 1B). Follow up duration was from 60 month to 168 month.

#### *Survival analysis in elderly patients*

To investigate the effects of lymph node dissection in elderly patients, cancer-specific survival was compared between limited

and radical lymph node dissection in R0 patients. A comparison of patient characteristics in Group A between limited and radical lymph node dissection is shown in Table 3. In the limited lymph node dissection subgroup, patients with preoperative complication were observed significantly more frequently. Cancer-specific survival showed no significant difference between groups (Fig. 2).

## DISCUSSION

Due to increased life expectancy, the number of elderly patients with gastric carcinoma is continuing to increase (5). In Japan, 20% of gastric cancer patients are now over 80 years old (3). In general, surgeons are hesitant to perform extended gastrectomy, because the frequency of operative complications is higher in the elderly (6). While opportunities to treat aged patients with gastric cancer are increasing, the optimal surgical approach to elderly patients remains problematic because of the operative risks associated with extended surgery (2). Our hospital is a general hospital located in a rural region, and elderly patients with various complications are abundant at our hospital. This study therefore investigated post-operative complications and the survival rate of elderly patients with gastric cancer.

Previous studies have indicated that the incidence of differentiated cancer (well or moderately differentiated adenocarcinoma) is

Table 2. Postoperative complications

	Group A (80<) n=44	Group B (70-80) n=139	Group C (<70) n=219	p value
<b>Morbidity</b>				
Surgical (Total)	6	26	36	n.s.
Anastomotic leakage	1	1	1	
Pancreatic fistula	1	3	5	
Intraabdominal abscess	0	3	4	
Intraabdominal Bleeding	2	2	6	
Stasis	2	9	13	
General (Total)	6	18	10	p< 0.05
Respiratory	1	6	3	
Cardiovascular	1	0	2	
Renal	1	0	0	
Other	3	12	5	
<b>Hospital mortality</b>	0	1	1	n.s.

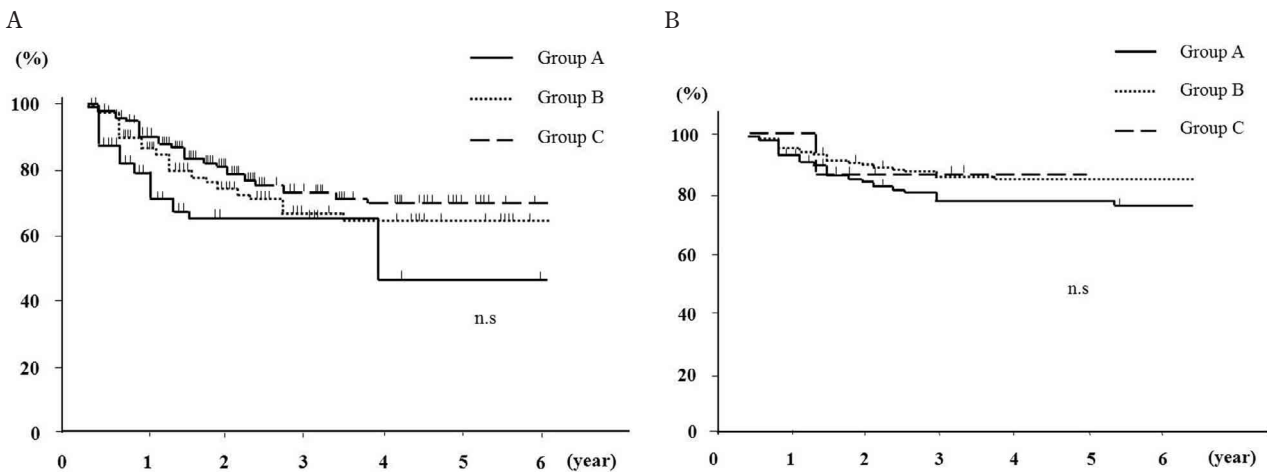


Figure 1. A : Overall survival, B : Cancer-specific survival in R0 patients

significantly higher in elderly patients, and older patients show more advanced disease and expansive growth pattern of the tumor without scirrhus changes (7, 8). However, the present study found no significant difference in pathological features (9).

Surgery for gastric cancer in elderly patients is a high-risk option (3), and the rate of severe complications after gastrectomy is high in elderly patients. Surgery for gastric cancer in elderly patients is therefore risky (3). Careful preoperative evaluation and limited surgeries can reduce the risk of postoperative complications in elderly patients, although complications can prove fatal if they occur. The potential for aggravation of surgical complications in elderly patients therefore requires special attention.

Advanced age has been identified as an independent predictor of morbidity, mortality, and prolonged hospital stay in patients undergoing non-cardiac surgery. In contrast, the most important preoperative risk factor for poor postoperative outcome was not chronological age, but the sum of co-morbidities (10). Chronological age alone is not a sufficient reason to withhold curative or palliative treatment from an elderly gastric cancer patient (11, 12).

Patients with heart disease, high TNM stage, long operation time, multi-organ resection, chronic liver disease, hypertension, and excessive blood loss are at higher risk of morbidity and mortality in radical surgery for gastric cancer (13, 14). In this study, as

elder patients received limited lymph node dissection, operation time tended to be shorter than in younger patients.

Although survival is the essential aim of surgical treatment, extended resection sometimes reduces the subsequent quality of life (14). Extended lymph node dissection has been recommended on the basis of studies of lymphatic flow and the nodal spread of cancer cells. Some authors have recommended extended dissection in elderly patients (14). As morbidity and mortality rates in patients without preoperative surgical risk factors were comparable to those in the control group, such patients represent good candidates for extended surgery (15).

On the other hand, age has been considered the most significant factor for postoperative morbidity. As a result, various studies have shown that limited surgery reduces operative complication without compromising oncological outcomes in elderly patients. Several series of D1 lymph node dissection in patients presenting with small gastric cancer at low risk of nodal metastasis showed curability rates exceeding 80%. In addition, D1 can reduce the hospital stay and rates of postoperative complications, anastomotic leakage, reoperation, and 30-day mortality (16).

Extent of surgery should be carefully considered for elderly patients. Total gastrectomy and extended nodal dissection are both associated with high operative mortality and 90-day mortality rates

Table 3. Comparison of radical and limited lymph node dissection in Group A

	Limited group n=20	Radical group n=15	p value
Sex			
Male	14	9	n.s.
Female	6	6	
Pre-operative complication			
+	16	2	p< 0.05
-	4	13	
Approach			
Open	13	9	n.s.
Lap	7	6	
Operative procedure			
Total	4	5	n.s.
Distal	12	8	
Other	4	2	
Sentinel navigation			
+	4	0	n.s.
-	16	15	
Stage			
I	14	8	n.s.
II	2	3	
III	4	4	
Histologic type			
Differentiated	11	3	p< 0.05
Undifferentiated	9	12	
Lymph node metastasis			
+	6	7	n.s.
-	14	8	
Operation time	198	214	n.s.
Blood loss	153	210	n.s.

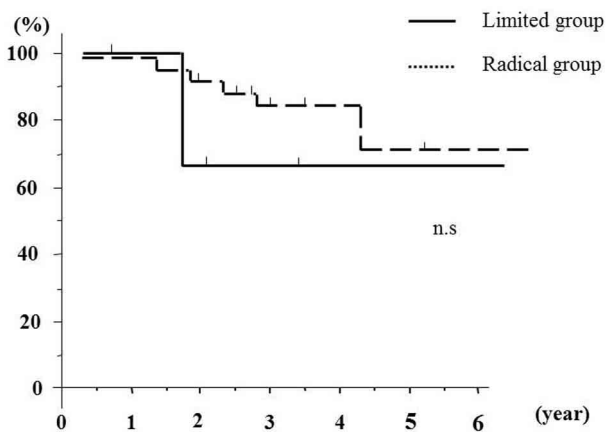


Figure 2. Cancer-specific survival in R0 patients in Group A

in the elderly, particularly in those with preoperative morbidity. The relative risk ratio for morbidity and mortality is significantly higher than that for D2 dissection, age older than 70 years, splenectomy and pancreatectomy. No significant difference in morbidity and mortality rates was seen between D1 and D2 lymph node dissection. Furthermore, no difference was found in 5-year OS (4, 17). At the same time, radical surgery is able to be performed safely in elderly patients, with mortality and morbidity rates similar

to those of young patients (8). R0 resection with at least limited lymph node dissection should be considered as the treatment of choice for elderly patients with gastric cancer (9). As such limited surgery is not necessarily sufficient for the treatment of the gastric cancer itself (18), informed consent is crucial.

## CONCLUSION

Limited lymph node dissection for gastric cancer did not affect cancer-specific survival in elderly patients.

## CONFLICT OF INTEREST STATEMENT

Drs. Kozo Yoshikawa, Mitsuo Shimada, Jun Higashijima, Toshihiro Nakao, Masaaki Nishi, Hideya Kashihara, Chie Takasu, Shohei Eto have no conflicts of interest or financial ties to disclose.

## REFERENCE

1. Biondi A, Cananzi FC, Persiani R, Papa V, Degiuli M, Doglietto GB, D'Ugo D : The road to curative surgery in gastric cancer treatment : a different path in the elderly? J Am Coll Surg 215 : 858-867, 2012
2. Jeong O, Park YK, Ryu SY, 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
3. Hayashi T, Yoshikawa T, Aoyama T, Ogata T, Cho H, Tsuburaya A : Severity of complications after gastrectomy in elderly patients with gastric cancer. *World J Surg* 36 : 2139-2145, 2012
  4. Jiang L, Yang KH, Chen Y, Guan QL, Zhao P, Tian JH, Wang Q : Systematic review and meta-analysis of the effectiveness and safety of extended lymphadenectomy in patients with resectable gastric cancer. *Br J Surg* 10 : 595-604, 2014
  5. Orsenigo E, Tomajer V, Palo SD, Carlucci M, Vignali A, Tamburini A, Staudacher C : Impact of age on postoperative outcomes in 1118 gastric cancer patients undergoing surgical treatment. *Gastric Cancer* 10 : 39-44, 2007
  6. Hwang SH, Park do J, Jee YS, Kim HH, Lee HJ, Yang HK, Lee KU : Risk factors for operative complications in elderly patients during laparoscopy-assisted gastrectomy. *J Am Coll Surg* 208 : 186-192, 2009
  7. Saidi RF, Bell JL, Dudrick PS : Surgical resection for gastric cancer in elderly patients : is there a difference in outcome? *J Surg Res* 118 : 15-20, 2004
  8. Kitamura K, Yamaguchi T, Taniguchi H, Hagiwara A, Yamane T, Sawai K, Takahashi T : Clinicopathological characteristics of gastric cancer in the elderly. *Br J Cancer* 73 : 798-802, 1996
  9. Takeshita H, Ichikawa D, Komatsu S, Kubota T, Okamoto K, Shiozaki A, Fujiwara H, Otsuji E : Surgical outcomes of gastrectomy for elderly patients with gastric cancer. *World J Surg* 37 : 2891-2898, 2013
  10. Takeshita H, Ichikawa D, Komatsu S, Kubota T, Okamoto K, Shiozaki A, Fujiwara H, Otsuji E : Surgical outcomes of gastrectomy for elderly patients with gastric cancer. *World J Surg* 37 : 2891-2898, 2013
  11. Gretschel S, Estevez-Schwarz L, Hünerbein M, Schneider U, Schlag PM : Gastric cancer surgery in elderly patients. *World J Surg* 30 : 1468-1474, 2006
  12. Saif MW, Makrilia N, Zalonis A, Merikas M, Syrigos K : Gastric cancer in the elderly : an overview. *Eur J Surg Oncol* 36 : 709-717, 2010
  13. Jeong SH, Ahn HS, Yoo MW, Cho JJ, Lee HJ, Kim HH, Lee KU, Yang HK : Increased morbidity rates in patients with heart disease or chronic liver disease following radical gastric surgery. *J Surg Oncol* 101 : 200-204, 2010
  14. Eguchi T, Takahashi Y, Ikarashi M, Kasahara M, Fujii M : Is extended lymph node dissection necessary for gastric cancer in elderly patients? *Eur J Surg* 166 : 949-953, 2000
  15. Katai H, Sasako M, Sano T, Maruyama K : The outcome of surgical treatment for gastric carcinoma in the elderly. *Jpn J Clin Oncol* 28 : 112-115, 1998
  16. Memon MA, Subramanya MS, Khan S, Hossain MB, Osland E, Memon B : Meta-analysis of D1 versus D2 gastrectomy for gastric adenocarcinoma. *Ann Surg* 253 : 900-911, 2011
  17. Degiuli M, Sasako M, Ponti A, Vendrame A, Tomatis M, Mazza C, Borasi L, Capussotti L, Fronda G, Morino M : Randomized clinical trial comparing survival after D1 or D2 gastrectomy for gastric cancer. *Br J Surg* 101 : 23-31, 2014
  18. Ariake K, Ueno T, Takahashi M, Goto S, Sato S, Akada M, Naito H : E-PASS comprehensive risk score is a good predictor of postsurgical mortality from comorbid disease in elderly gastric cancer patients. *J Surg Oncol* 109 : 586-592, 2014
  19. Takama T, Okano K, Kondo A, Akamoto S, Fujiwara M, Usuki H, Suzuki Y : Predictors of postoperative complications in elderly and oldest old patients with gastric cancer. *Gastric Cancer* 18 : 653-661, 2015
  20. Tokunaga M, Tanizawa Y, Bando E, Kawamura T, Terashima M : Poor survival rate in patients with postoperative intra-abdominal infectious complications following curative gastrectomy for gastric cancer. *Ann Surg Oncol* 20 : 1575-1583, 2013