

ORIGINAL

Limited lymph node dissection in elderly patients with gastric cancer

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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, ≥ 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, ≥ 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.

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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 χ^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 |
|---------------------------|--------------------|-----------------------|---------------------|---------|
| Morbidity | | | | |
| 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 | |
| Hospital mortality | 0 | 1 | 1 | n.s. |

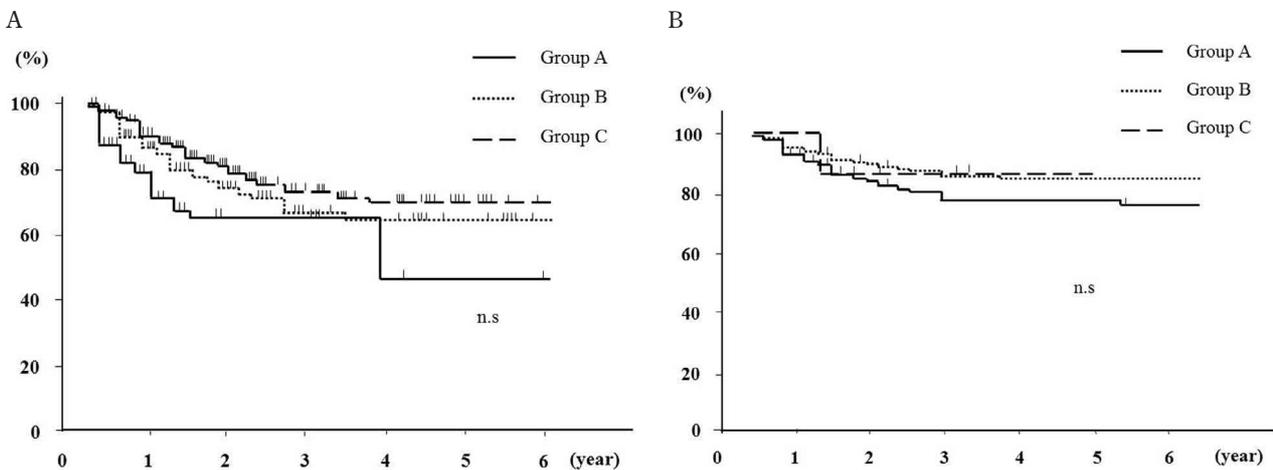


Figure 1. A : Overall survival, B : Cancer-specific survival in R0 patients

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. |

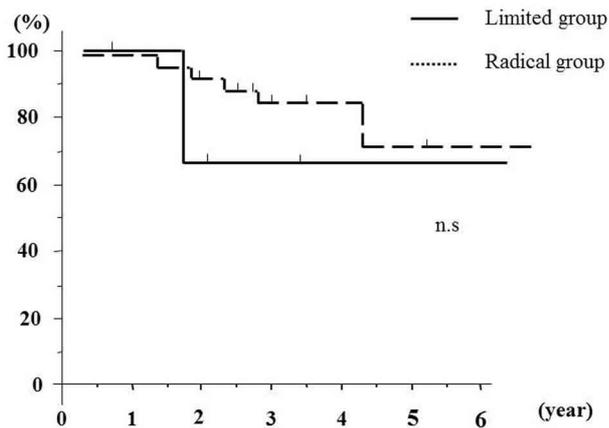


Figure 2. Cancer-specific survival in R0 patients in Group A

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.

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