Operative Risk Factors in Gastric Cancer Surgery for Elderly Patients

Su Han Seo, Hoon Hur, Chang Wook An, Xian Yi, June Young Kim, Sang-Uk Han, and Yong Kwan Cho

Department of Surgery, Ajou University School of Medicine, Suwon, National Police Hospital, Seoul, Korea

Purpose: Gastric cancer surgery is a common operation in East Asia, such as Korea and Japan, and there has been a significant increase in the need for this procedure due to the aging population. As a result, surgery for the treatment of gastric cancer for elderly patients is expected to increase. This study examined the effect of old age on gastric cancer surgery, and analyzed the operative risk factors for elderly patients.

Materials and Methods: From November 2008 to August 2010, 590 patients, who underwent a curative resection for gastric cancers, were enrolled. Patients who underwent palliative or emergency surgery were excluded. A retrospective analysis of the correlation between surgical outcomes and age was performed. The elderly were defined as patients who were over the age of 65 years.

Results: The mean age of all patients was 58.3 years, and complications occurred in 87 cases (14.7%). The most common complication was wound infection and severe complications requiring surgical, endoscopic, or radiologic intervention developed in 52 cases (8.8%). The rate of complications increased with increasing age of the patients. Univariate analysis revealed age, comorbidity, extent of resection, operation time, and combined resection to be associated with surgical complications. In particular, age over 75 years old, operation time, and comorbidity were predictive factors in multivariate analysis. In the elderly, only comorbidity was associated with surgical complications.

Conclusions: The patients’ age is the most important factor for predicting surgical complications. Surgeons should pay an attention to the performance of gastric cancer surgery on elderly patients. In particular, it must be performed carefully for elderly patients with a comorbidity.

Key Words: Stomach neoplasms, Risk factors, Gastrectomy, Aged

Introduction

Gastric cancer is the most common malignancy in Korea, and the second cause of malignancy–related death in the world.(1) The only method proven to increase survival of gastric cancer patients is curative resection of the primary tumor and proper range of lymph nodes. The conventional surgical modality is the subtotal or total gastrectomy and extended lymph node dissection, as well as combined resection of adherent organs, as occasion demands, under open laparotomy.(2,3) However, surgical treatment has recently been developed considering the improvement of quality of life (QoL) and early recovery after surgery. In Korea, the rate of postoperative complication after gastric cancer surgery has been reported as 10.5% to 14.7%. In several clinical researches, the elderly has been presented as one of the factors related to complication for evaluation the risk factors of gastric cancer surgery.(6,7)

The elderly are the fastest growing part of the entire population in Korea. According to the annual report of the Korea National Statistical Office in 2007, the proportion of elderly over 65 years old was 9.9%, the so called ‘aging society’ defined by the World Health Organization.(8) Therefore, the proportion of elderly in patients diagnosed with gastric cancer who undergo gastric cancer surgery...
is expected to increase. The elderly have a functional diminution of reserve capacity, and show high incidence of comorbidity. These may lead to reduced ability of older patients to tolerate surgical stress, including gastric cancer surgery. The other feature of elderly patients is less social and economical support and greater burden from additional fees associated with postoperative complication. For physicians, clinical practices for the elderly should be performed with caution in order to minimize postoperative complications, and awareness of risk factors for complication in elderly patients is important.

In this study, we aimed to determine factors for prediction of complications after gastric cancer surgery through retrospective review of patients who have undergone gastric cancer surgery in a single institution in Korea during a period of 2 years.

Materials and Methods

We reviewed clinical information, operation and progress records, and pathologic results of 590 patients who were diagnosed with gastric cancer and who underwent curative gastrectomy with proper lymph node dissection from November 2008 to August 2010 in Ajou University Hospital, Suwon, Korea. All patients were diagnosed with adenocarcinoma by gastrofiberscopic biopsy, and patients with clinically early disease underwent minimally invasive surgery including a laparoscopic or robotic approach. Total or subtotal gastrectomy was performed considering the location of the tumor in order to secure a resection margin with free from tumor, and lymph nodes of over D1+beta lesions were dissected according to the classification suggested by the Japanese Gastric Cancer Association.(9) The combined resection was deemed to completely remove the adherent organs, including distal pancreas or spleen, invaded by tumor or for treatment of other diseases, like gall stones and other malignancy.

During the postoperative period, all patients were managed with a common clinical pathway. Prophylactic antibiotics were injected during two postoperative days, and patients were supplied with a soft diet from the fifth postoperative day. Patients were recommended for discharge from the hospital two days after ingestion of a soft diet without intolerance. Events causing an increase in the length of hospital stay or delay of the dietary schedule during hospital periods were defined as postoperative complications.

We defined patients over 65 years old as the elderly. We analyzed the correlation between clinicopathologic results, including patients’ age and postoperative complications. In addition, subgroup analysis for the elderly was performed for determination of risk factors for postoperative complication.

Statistical Package for the Social Sciences ver. 13.0 (SPSS Inc., Chicago, IL, USA) was used for performance of statistical analysis. Univariate analysis was performed using Pearson’s chi-square test, and multivariate analysis was carried out using binary multiple linear regressions analysis. P-value of <0.05 was considered statistically significant.

Results

Mean age of patients was 58.3 year olds. When the age of patients was classified into 5 years, the number of patients from 60 to 65 years old was most frequent (Fig. 1). In our study, of a total of 590 patients, 203 (34.4%) patients were proved to be elderly. And the number of patients over 75 years old was 42 (7.1%).

345 patients (58.4%) had one and over comorbidity, and 142 patients (24.1%) had two and more. Most common comorbidity was hypertension (190 patients), and diabetics (84 patients) and heart disease (52 patients) were also common. The rate of patients with comorbidity was increased into 76.4% in the elderly (≥65 years old).

Table 1. Distribution of major postoperative complications and mortality of a total of 87 cases (14.7%)

| Complication          | N  | %   |
|-----------------------|----|-----|
| Total complication    | 87 | 14.7%|
| Wound infection       | 21 |     |
| Postoperative ileus   | 16 |     |
| Bleeding              | 14 |     |
| Pulmonary complication| 9  |     |
| Mortality             | 4  | 0.7%|
Postoperative complications occurred in 87 patients (14.7%); the most common was wound problems, including seroma, infection, and dehiscence. In addition, sixteen patients had postoperative prolonged ileus, fourteen had bleeding from intraabdominal or intraluminal, and nine had pneumonia as frequent complications (Table 1). Severe complications occurred in 52 patients (8.8%) who should be managed with radiologic, endoscopic intervention or surgical procedures under general anesthesia. Postoperative mortality occurred in 4 patients (0.67%).

We evaluated the correlation between complications and clinical factors. Patients’ age (P=0.024), comorbidity (P=0.011), and the extension of resection (P=0.008) and operation time (P=0.008), and combined resection (P=0.010) were significantly associated with postoperative complication (Table 2). Specifically, when patients’ ages were divided into three groups, increasing age showed a significant association with complications (below 65, from 66 to 75, above 76).

In multivariate analysis for determination of factors for prediction of postoperative complications, age over 75 years (OR=2.353, P=0.023), operation time (OR=1.923, P=0.008), and comorbidity (OR=1.674, P=0.034) were found to be pertinent (Table 3). In addition, we performed subgroup analysis of 204 patients over the age of 65. One hundred fifty five patients had comorbidity, and complication occurred in 27.7% of elderly patients with comorbidity. As a result, comorbidity was only factor related to postoperative complication in univariate (P=0.031) and multivariate analysis (OR=2.683, P=0.038) (Table 4, 5). Meanwhile, operative time was

### Table 2. Correlation between clinical factors and complication

| Variables             | N  | Complication cases (%) | P-value |
|-----------------------|----|------------------------|---------|
| **Age**               |    |                        |         |
| <65                   | 387| 59 (15.2)              | 0.024   |
| ≥65, <75              | 161| 33 (20.5)              |         |
| ≥75                   | 42 | 13 (31.0)              |         |
| **Gender**            |    |                        | 0.592   |
| Male                  | 420| 77 (18.3)              |         |
| Female                | 170| 28 (16.5)              |         |
| **BMI (kg/m²)**       |    |                        | 0.581   |
| <25                   | 417| 75 (18.0)              |         |
| ≥25                   | 168| 27 (16.1)              |         |
| **Comorbidity**       |    |                        | 0.011   |
| Yes                   | 345| 73 (21.2)              |         |
| None                  | 245| 32 (13.1)              |         |
| **Resection**         |    |                        | 0.006   |
| Total gastrectomy     | 108| 29 (26.9)              |         |
| Partial gastrectomy   | 482| 76 (15.8)              |         |
| **Approach**          |    |                        | 0.091   |
| Conventional          | 310| 63 (20.3)              |         |
| Minimal invasive      | 280| 42 (15.0)              |         |
| **Op time (min)**     |    |                        | 0.008   |
| <180                  | 226| 28 (12.4)              |         |
| ≥180                  | 357| 75 (21.0)              |         |
| **Combined resection**|    |                        | 0.010   |
| Yes                   | 73 | 21 (28.8)              |         |
| None                  | 514| 84 (16.3)              |         |
| **LN dissection**     |    |                        | 0.172   |
| D1 (α or β)           | 335| 53 (15.8)              |         |
| D2                    | 253| 51 (20.2)              |         |

BMI = body mass index; Op = operation; LN = lymph node.

### Table 3. Multivariable analysis for risk factors of postoperative complication

| Variables             | P-value | Odd ratio | 95% CI  |
|-----------------------|---------|-----------|---------|
| **Age**               |         |           |         |
| ≥65, <65 vs. <75      | 0.442   | 1.219     | 0.736–2.017 |
| <65 vs. ≥75           | 0.023   | 2.353     | 1.125–4.920 |
| **Op time**           |         |           |         |
| <180 minutes vs. ≥180 minutes | 0.008 | 1.923 | 1.184–3.123 |
| **Comorbidity**       |         |           |         |
| None vs. yes          | 0.034   | 1.674     | 1.038–2.699 |
| **Combined operation**|         |           |         |
| None vs. yes          | 0.057   | 1.770     | 0.984–3.185 |

CI = confidence interval; Op = operation.

### Table 4. Correlation between clinic-operative factors and complication in elderly patients (≥ 65 years old)

| Variables             | n   | Complication case (%) | P-value |
|-----------------------|-----|-----------------------|---------|
| **Age**               |     |                       |         |
| <75                   | 161 | 36 (22.4)             | 0.311   |
| ≥75                   | 42  | 13 (31.0)             |         |
| **Gender**            |     |                       | 0.961   |
| Male                  | 155 | 37 (23.9)             |         |
| Female                | 48  | 11 (25.0)             |         |
| **BMI**               |     |                       | 0.478   |
| <25                   | 138 | 34 (24.6)             |         |
| ≥25                   | 60  | 12 (20.0)             |         |
| **Comorbidity**       |     |                       | 0.031   |
| Yes                   | 155 | 43 (27.7)             |         |
| None                  | 48  | 6 (12.5)              |         |
| **Resection**         |     |                       | 0.073   |
| Total gastrectomy     | 33  | 12 (36.4)             |         |
| Partial gastrectomy   | 170 | 37 (21.8)             |         |
| **Approach**          |     |                       | 0.465   |
| Conventional          | 113 | 31 (27.4)             |         |
| Minimal invasive      | 90  | 168 (17.8)            |         |
| **Op time**           |     |                       | 0.177   |
| <180                  | 83  | 16 (19.3)             |         |
| ≥180                  | 116 | 32 (27.6)             |         |
| **Combined resection**|     |                       | 0.096   |
| Yes                   | 36  | 12 (33.3)             |         |
| None                  | 166 | 34 (20.5)             |         |
| **LN dissection**     |     |                       | 0.709   |
| D1 (α or β)           | 121 | 30 (24.8)             |         |
| D2                    | 80  | 18 (22.5)             |         |

BMI = body mass index; Op = operation; LN = lymph node.
Operative Risk Factors in Gastric Cancer Surgery for Elderly Patients

Table 5. Comparison of predicting factors for postoperative complication between subgroups according to age

| Variables       | <65 years old | ≥65 years old |
|-----------------|---------------|--------------|
| Op time         |               |              |
| <180 minutes vs | 0.012         | 0.038        |
| ≥180 minutes    | 2.32          | 2.683        |
| Comorbidity     |               |              |
| None vs. yes    | 1.204~4.470   | 1.054~6.833  |
| Combined op     | 0.074         | 0.931~4.735  |

CI = confidence interval; Op = operation.

Discussion

The elderly is known in various surgical fields as a risk factor for postoperative complication, due to loss of physical function. We confirmed the results though analysis of the records of patients who underwent gastric cancer surgery in a single center during a period of two years. In addition, we obtained additional information in which the comorbidity was only risk factor for complication in the elderly patients.

Although the definition of an elderly patient varies according the social and economic situation, most developed and developing countries have defined the elderly as those aged 65 years because of the decreased role in the community and society. On the other hand, being elderly is medically defined in accordance with the functional loss of major organs and decreased ability of recovery from severe stress, like trauma. In particular, several clinical research studies have reported that patients who were at least 75 years old showed a higher frequency of comorbidity and severe loss of physical function; therefore, the definition of “young elderly” is over the age of 65 and “old elderly” as over the age of 75 years. We assumed that increased complication after gastric cancer surgery may also be effected by increased age, because it requires surgical resection of an extensive range and reconstruction in the upper abdomen. In the present study, we analyzed the correlation between postoperative complications and clinical factors, including the patient’s age, which was divided by age 65 and 75 years. As a result, age over 75 years was found to be a strongest predicting factor for postoperative complication in gastric cancer surgery.

Several studies have reported on increased postoperative morbidity and mortality in the elderly. Researchers have suggested that a reduced range of surgery and minimally invasive treatment, like endoscopic therapy, could be applied for elderly patients as an alternative method for replacement of standard surgery. However, the number of elderly patients requiring gastric cancer surgery would increase, and we cannot avoid standard surgery in all elderly patients. Therefore, evaluation of surgical risk for elderly patients and determination of which elderly patients might be suitable for limited surgery or minimally invasive treatment is important. In subgroup analysis of only elderly patients, comorbidity was found to be a higher risk factor than being an elderly patient.

In our study, we confirmed that the biological age of patients considering the organic function was more informative for postoperative complication after gastric cancer surgery than physical age. Hypertension, diabetic mellitus, and pulmonary problems were major comorbidities in our study, and 58.4% of all patients had one or more types of comorbidity. The proportion of patients with comorbidity was increased to 76.4% in elderly patients over the age of 65. Meanwhile comorbidity was not a predicting factor for postoperative complication in patients under 65 years; it was the only factor for patients over 65 years. This means that comorbidity can have a greater effect on complication in elderly patients. To date, several studies have reported on the effect of comorbidity on gastric cancer surgery; Kim et al. reported that comorbidity was significantly related to postoperative complication after laparoscopic surgery for gastric cancer in a multicenter study of 1,237 patients. However, no study has been conducted for analysis of the effect of comorbidity on increasing age in postoperative complication with a focus on all types of gastric cancer surgery.

In the present study, 280 (47.5%) of a total of 590 patients underwent minimally invasive surgery (MIS) by the laparoscopic or robotic approach. Although recent indication for MIS was early disease of gastric cancer, it is expected that its indication will be expanded due to the increasing number of cases of early disease and development of technique and instruments. Regarding MIS for the elderly, there has been controversy regarding whether this
procedure has a positive or negative effect on surgical outcome of elderly patients.(16) Patients who underwent MIS in our study showed a relatively lower complication rate than the open procedure; however, the difference was not statistically significant in elderly patients, as well as all patients. Therefore, the efficacy of MIS for elderly patients could not be confirmative from data presented in our study.

Development of treatment for gastric cancer has followed with reducing the range of surgery as well as maintaining oncologic safety.(22) According to this principle, endoscopic resection for early gastric cancer, and partial gastric resection with limited lymph node dissection using sentinel lymph node navigation has been developed. The absolute indication of endoscopic resection was mucosal cancer under 2 cm considering metastasis to the perigastric lymph node(23); however, this indication has recently been extended by the effect of precise preoperative diagnosis and development of endoscopic technique.(24,25) The definite advantage of endoscopic treatment is that general anesthesia is not required. Therefore, the extended indication of endoscopic treatment could be primarily applied for elderly patients who are highly expected to have postoperative complication related to anesthesia, in spite of the possibility of incomplete tumor resection and not confirmative lymph node status. Another option for prevention of postoperative complication is partial gastrectomy with limited lymph node dissection under sentinel node navigation.(26,27) Although this procedure did not provide confirmative results for application to clinical practice, future studies will provide researchers with additional clues.

The three surgeons in the present study have experience in performance of more than 80 gastric cancer surgeries per year, and 400 surgeries for gastric cancer patients per year have been performed in the institution. Our result in view of the complication rate is similar with the rate, 10.5~14.7%, from large scale studies conducted in Korea.(5,28) Therefore, our result may be generally acceptable in other institutions. Our study had the limitation that long term follow-up for evaluation of survival after cancer surgery was not performed. The benefit of limited surgery or endoscopic treatment for elderly patients did not reach a conclusion.

As a result, the most important factor for prediction of postoperative complication after gastric cancer surgery is patient’s age, and specific precautions for elderly patients are required. In particular, the authors suggest that the surgeon performing gastric cancer surgery should consider limited surgery or endoscopic treatment for elderly patients with comorbidity, if the disease status is applicable.

References

1. Stewart BW, Kleihues P. World cancer report. Lyon: IARC Press, 2003.
2. Okamura T, Tsujitani S, Korenaga D, Haraguchi M, Baba H, Hiramoto Y, et al. Lymphadenectomy for cure in patients with early gastric cancer and lymph node metastasis. Am J Surg 1988;155:476-480.
3. Fukagawa T, Sasako M, Mann GB, Sano T, Katai H, Maruyama K, et al. Immunohistochemically detected micrometastases of the lymph nodes in patients with gastric carcinoma. Cancer 2001;92:753-760.
4. Kim HH, Hyung WJ, Cho GS, Kim MC, Han SU, Kim W, et al. Morbidity and mortality of laparoscopic gastrectomy versus open gastrectomy for gastric cancer: an interim report--a phase III multicenter, prospective, randomized Trial (KLASS Trial). Ann Surg 2010;251:417-420.
5. Park DJ, Lee HJ, Kim HH, Yang HK, Lee KU, Choe KJ. Predictors of operative morbidity and mortality in gastric cancer surgery. Br J Surg 2005;92:1099-1102.
6. Wu CW, Lo SS, Shen KH, Hsieh MC, Lui WY, P'eng FK. Surgical mortality, survival, and quality of life after resection for gastric cancer in the elderly. World J Surg 2000;24:465-472.
7. Otsuji E, Fujiyama J, Takagi T, Ito T, Kuriy Y, Toma A, et al. Results of total gastrectomy with extended lymphadenectomy for gastric cancer in elderly patients. J Surg Oncol 2005;91:232-236.
8. http://kosis.kr/ Accessed May 1, 2011.
9. Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma - 2nd English edition -. Gastric Cancer 1998;1:10-24.
10. Randel J, German T, Ewing D. The ageing and development report: poverty, independence and the world’s older people. London: Earthscan Publications Ltd., 1999.
11. Neugarten BL, Moore JW, Lowe JC. Age norms, age constraints, and adult socialization. AJS 1965;70:710-717.
12. Hazzard WR. Burton JR. Health problems in the elderly. In: Braunwald E, Isselbacher KJ, Petersdorf RG, eds. Harrison’s principles of internal medicine, 11th ed. New York: McGraw-Hill, 1987:450-451
13. Williams EI. Health checks for people aged 75 years and older. In: Pathy MSJ, ed. Principles and practice of geriatric medicine. New York: John Wiley & Sons, 1998.
14. Katai H, Sasaki M, Sano T, Fukagawa T. Gastric cancer sur-
surgery in the elderly without operative mortality. Surg Oncol 2004;13:235-238.
15. Winslet MC, Mohsen YM, Powell J, Allum WH, Fielding JW. The influence of age on the surgical management of carcinoma of the stomach. Eur J Surg Oncol 1996;22:220-224.
16. Kunisaki C, Akiyama H, Nomura M, Matsuda G, Otsuka Y, Ono HA, et al. Comparison of surgical outcomes of gastric cancer in elderly and middle-aged patients. Am J Surg 2006;191:216-224.
17. Rim IG, Yu HC, Yang DH, Hwang YH. A study of the factors related to the frequency of postoperative complications for gastric cancer. J Korean Surg Soc 1997;53:341-352.
18. Sørensen LT, Hemmingsen U, Kallehave F, Wille-Jørgensen P, Kjaergaard J, Møller LN, et al. Risk factors for tissue and wound complications in gastrointestinal surgery. Ann Surg 2005;241:654-658.
19. Matsuda K, Hotta T, Takifuji K, Yokoyama S, Higashiguchi T, Tominaga T, et al. Long-term comorbidity of diabetes mellitus is a risk factor for perineal wound complications after an abdominoperineal resection. Langenbecks Arch Surg 2009;394:65-70.
20. Kim W, Song KY, Lee HJ, Han SU, Hyung WJ, Cho GS. The impact of comorbidity on surgical outcomes in laparoscopy-assisted distal gastrectomy: a retrospective analysis of multicenter results. Ann Surg 2008;248:793-799.
21. Kitagawa Y, Kitano S, Kubota T, Kumai K, Otani Y, Saikawa Y, et al. Minimally invasive surgery for gastric cancer--toward a confluence of two major streams: a review. Gastric Cancer 2005;8:103-110.
22. An JY, Cheong J, Hyung WJ, Noh SH. Recent evolution of surgical treatment for gastric cancer in Korea. J Gastric Cancer 2011;11:1-6.
23. Yamao T, Shirao K, Ono H, Kondo H, Saito D, Yamaguchi H, et al. Risk factors for lymph node metastasis from intramucosal gastric carcinoma. Cancer 1996;77:602-606.
24. Yokoi C, Gotoda T, Hamanaka H, Oda I. Endoscopic submucosal dissection allows curative resection of locally recurrent early gastric cancer after prior endoscopic mucosal resection. Gastrointest Endosc 2006;64:212-218.
25. Gotoda T. Endoscopic resection of early gastric cancer. Gastric Cancer 2007;10:1-11.
26. Ishii K, Kinami S, Funaki K, Fujita H, Ninomiya I, Fushida S, et al. Detection of sentinel and non-sentinel lymph node micrometastases by complete serial sectioning and immunohistochemical analysis for gastric cancer. J Exp Clin Cancer Res 2008;27:7.
27. Lee SE, Lee JH, Ryu KW, Cho SJ, Lee JY, Kim CG, et al. Sentinel node mapping and skip metastases in patients with early gastric cancer. Ann Surg Oncol 2009;16:603-608.
28. Sano T, Sasako M, Yamamoto S, Nashimoto A, Kurita A, Hiratsuka M, et al. Gastric cancer surgery: morbidity and mortality results from a prospective randomized controlled trial comparing D2 and extended para-aortic lymphadenectomy--Japan Clinical Oncology Group study 9501. J Clin Oncol 2004;22:2767-2773.