A total of 461 patients who underwent gastrectomy for gastric cancer in our hospital were classi-
cancer. The aim of this study was to clarify the operative mortality and long-term survival of gastrectomy for elderly patients with gastric
Background: The frequency of comorbidities was significantly ($P < 0.05$) higher in elderly group (74.7%) than that in the control group (49.5%). No
significant difference of the postoperative complication rate was found between the elderly group (23.2%) and the control group (23.2%). Adjuvant chemotherapy was 9.5% in the elderly group, which was significantly less than 29.0% of the control group ($P < 0.05$). Stage II and III elderly patients had worse disease specific survival (DSS) than controls did. In the elderly, overall survival (OS) was significantly worse than DSS in stage I patients ($P < 0.05$).
Conclusions: The operative complication rate of elderly patients was comparable to the control group. Comorbidity and occurrence of secondary malignant disease should be followed for elderly patients at stage I. For stage II and III disease patients, a novel drug which is acceptable for the elderly is needed as a postoperative therapy.

**INTRODUCTION**

Aging progresses and opportunities of medical care for elderly patients older than 80 years are increasing with the extension of life expectancy. In particular, the increase in cancer patients is a global challenge; International Agency for Research of Cancer estimated that the number of cancer patients expect to increase from 12.8 million patients in 2010 to 26 million patients in 2030 [1]. Japan has the most aged population in the world: the proportion of patients more than 80 years old continues to increase, from 0.7% in 1963, to 4.9% in 1990, and 7.8% in 2002 [2]. The life expectancy of Japanese at 80-year-old was 8.5 years for a male and 11.4 years for a female in 2012 [3].

About one million new cases of stomach cancer were estimated to have occurred globally (989,000 cases, 7.8% of total cancer cases), making it currently the fourth most common malignancy in the world, behind cancers of the lung, breast, and colorectum. More than 70% of stomach cancer cases (714,000 cases) occur in developing countries (467,000 in men, 247,000 in women), and half of stomach cancers occur in Eastern Asia [4]. Gastric cancer is most common malignant disease in Japan. The number of new patients diagnosed with gastric cancer in 2002 was estimated to be 106,760 [5]. The proportion of elderly patients with gastric cancer is increasing [2].

Although gastrectomy for elderly patients is increasing, the surgical procedure in the elderly must be decided carefully by assessing the patient’s tolerance of surgical stress because elderly patients have declining organ capacity and the quality of life postoperatively may suffer [6]. Surgeons are concerned about the possibility of postoperative complications or hospital death when performing surgery for elderly patients with comorbidities, and often hesitate to treat these patients. It is important to consider the fact that elderly patients often have comorbidities and age-related physiological problems, such as organ dysfunction. There have been several reports of short-term outcomes of surgery in elderly patients [7–9]. However, a few reports of the evaluation of long-term outcomes including the cause of death were available. The aim of this study was to clarify the perioperative mortality and long-term survival of gastrectomy for elderly patients with gastric cancer, and to determine an appropriate postoperative treatment by assessing the long-term outcomes.

**MATERIALS AND METHODS**

**Patients**

Surgical and pathological data of 95 patients at more than 80 years-old and 366 patients at 60s years-old who had undergone gastrectomy for histologically confirmed gastric adenocarcinoma from January 2003 to

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Comorbidity

Coronary disease was assigned to patients who were diagnosed with angina or myocardial infarction and who underwent stent placement, bypass surgery, or medical therapy. Arrhythmia was assigned to patients who had taken oral anti-arrhythmia drugs. Cerebrovascular disease was assigned to patients who were diagnosed with cerebral infarction or cerebral hemorrhage. Diabetes mellitus was assigned to patients using oral hypoglycemic drugs or insulin, or to those with HbA1c ≥4.3, which are the criteria in our institution. Hypertension was assigned to patients who were taking antihypertensive drugs. Pulmonary disease was assigned to patients with a history of chronic obstructive pulmonary disease (COPD), pulmonary tuberculosis or pulmonary resection. Liver disease was assigned to patients who had viral hepatitis or liver cirrhosis. Renal disease was assigned to patients with eGFR less than 60 mL/min/1.73 m² [10].

Data

Clinicopathological features were obtained from medical records. Age, sex, comorbidity, hemoglobin, and American Society of Anesthesiology physical status classification (ASA-PS) were obtained from preoperative anesthesiology records. Tumor depth, lymph node metastasis, pathological stage, and resectability of the tumor were evaluated. Postoperative chemotherapy was defined as administration of adjuvant chemotherapy for 3 months or more. The pathological diagnosis and classification status were determined according to the 14th edition of Japanese Gastric Cancer Association [11]. The decision on the type of operation, e.g., proximal gastric resection, total gastrectomy, or distal gastrectomy depended on tumor location, infiltration depth, and histological type. Generally, all gastrectomies were combined with lymphadenectomy according to Japanese gastric cancer treatment guidelines [12]. D1 or D1+ lymph node dissection was performed for early gastric cancer, and D2 lymph node dissection was performed for advanced gastric cancer. But patients with potentially fatal comorbidities underwent limited lymph node dissections to reduce postoperative morbidity or mortality by reducing operation time and blood loss.

Short-Term Outcome

A postoperative complication was defined as grade II or more, according to the Clavien Dindo classification method [13]. The operative mortality rate was defined as death within 30 days of the operation. Hospital discharge was decided based on consideration of the following criteria: (i) no requirement for intravenous medication or nutrition, (ii) no requirement for bed side care, (iii) no clinical sign of a complication, (iv) no elevated inflammatory reaction on laboratory data, (v) tolerable pain with no or only oral analgesics, (vi) the ability to fully ambulate without assistance, (vii) oral intake of more than half of given meal without vomiting or diarrhea, and (viii) a willingness of the patient and the family to discharge home. We recommended being admitted to a care hospital if even one of these criteria does not meet though condition was stable.

Long-Term Outcome

Long-term outcome was defined as the 5-year overall survival (OS) and disease specific survival (DSS) at each stage. Cause of death was classified as recurrence, other disease and other cancer.

RESULTS

Clinicopathological Characteristics of Patients With Gastric Cancer

The clinical characteristics of both groups of patients are presented in Table I. The elderly group comprised 55 males and 40 females with a mean age of 82.8 ± 2.3. Of this group, the most common comorbidity was renal disease (42.1%), followed by hypertension (41.1%). A total of 17.9% had two comorbidities and 22.1% had three or more. More elderly patients than control had multiple comorbidities (P < 0.001). The ASA physical status of the elderly patients was 1.1% in class I, 89.5% in class II, and 9.5% in class III, which was significantly different from that of the control group (P < 0.001).

TNM stage and perioperative outcomes are shown in Table II. Of the elderly group, regarding the tumor depth, 38.9% were T1, 11.6% were T2, 9.5% were T3, and 40% were T4, which was not significantly different from the control group (P = 0.0864). In the elderly group, regarding lymph node metastasis status, 57.9% were N0, 10.5% were N1, 16.8% were N2, and 14.7% were N3, which was not significantly different from the control group.

TABLE I. Comparison of Clinicopathological Factors Between the Two Groups

| Age (years) | Elderly group (n = 95) | Control group (n = 366) | P value |
|------------|-----------------------|------------------------|---------|
| Male       | 82.8 ± 2.3            | 64.7 ± 3.0             | <0.001  |
| Female     | 89.5%                 | 71.6%                  |         |
| Comorbidities, n (%) | Present | 24 (25.3%) | 185 (50.5%) | <0.001 |
|            | Absent               | 71 (74.7%)             | 181 (49.5%) |
|            | Coronary disease     | 12 (12.6%)             | 16 (4.4%)  |
|            | Arhythmia            | 8 (8.4%)               | 9 (2.5%)   |
|            | Arrhythmia           | 44 (14.7%)             | 90 (13.2%) |
|            | Diabetes mellitus    | 7 (7.4%)               | 26 (7.1%)  |
|            | Hypertension         | 39 (14.1%)             | 100 (27.3%) |
|            | Pulmonary disease    | 14 (14.7%)             | 28 (7.7%)  |
|            | Liver disease        | 6 (6.3%)               | 14 (3.8%)  |
|            | Renal dysfunction    | 40 (42.1%)             | 61 (16.7%) |
|            | Other malignant disease | 20 (21.1%)     | 32 (8.7%)  |
| No. of comorbidities, n (%) | 0 | 24 (25.3%) | 160 (43.7%) | <0.001 |
|            | 1                    | 33 (34.7%)             | 126 (34.5%) |
|            | 2                    | 17 (17.9%)             | 53 (14.5%) |
|            | ≥3                   | 21 (22.1%)             | 27 (7.4%)  |
| ASA score, n (%) | 1 | 1 (1.1%) | 85 (23.2%) | <0.001 |
|            | 2                    | 85 (89.5%)             | 262 (71.6%) |
|            | 3                    | 9 (9.5%)               | 19 (5.2%)  |
Pathological staging results for the elderly group revealed that 45.3% were stage I, 17.9% were stage II, 21.1% were stage III, and 15.8% were stage IV, which was not significantly different from the control group ($P = 0.2577$). In the elderly group, regarding extent of resection, 82.1% were R0, 10.5% were R1, and 7.4% were R2, which was not significantly different from the control group ($P = 0.0771$). Surgical procedures performed in the elderly group included distal gastrectomy (69.5%), total gastrectomy (29.5%), and partial gastrectomy (1.1%), which was not significantly different from the control group ($P = 0.4903$). The proportion of D2 dissection was 37.9% in the elderly group and 50.3% in the control group. There was a significant difference between the groups ($P = 0.0314$). Table III shows that postoperative complications were not significantly different between the groups: 23.2% in the elderly group and 23.2% in the control group ($P = 0.9004$). Of the elderly group, by the Clavien Dindo classification system 14.7% were grade II, 7.4% were grade IIIa/IIIb, and 1.1% were grade V, which was not significantly different from the control group ($P = 0.5981$). Postoperative pneumonia occurred in 4.2% of the elderly group and in 1.6% of the control group; the incidence trended higher among the elderly, but the difference was not significant. In the elderly group, complication rate (Clavien Dindo $\geq 3$) was 13.9% in D2 dissection and 5.1% in less D2 dissection. Complication rate was higher in D2 dissection than in less D2 dissection but there was no significant difference between the groups ($P = 0.1508$). The average postoperative stay for the elderly group was 19.3 days, which was not significantly different from 20.0 days for the control group ($P = 0.6599$). Adjuvant chemotherapy was 9.5% in the elderly, which was significantly less than 29.0% of the control group ($P = 0.0012$). Mortality was one case in the elderly group and two cases in the control group. Except mortality cases, 89 patients (94.7%) in the elderly group and 356 patients (97.8%) in the control group could discharge home on foot. Five patients (5.3%) in the elderly group and eight patients (2.2%) in the control group were admitted to care hospitals. There was no significant difference of the rate ($P = 0.1043$) to discharge home between two groups (Table III).
in 5-year OS of stage I and IV patients between the elderly and control groups, but the elderly stage II and III patients had significantly poorer prognosis (Fig. 1). The stage II and III elderly patients fared worse than the corresponding controls for 5-year DSS (Fig. 2). By comparing DSS and OS of elderly patients in each stage, it can be seen that the 5-year OS of stage I patients was worse than the 5-year DSS (5-year OS/DSS; 76.2%/100%, \( P = 0.0165 \)), whereas, there was no difference between the 5-year OS and DSS for stage II, III, and IV patients (5-year OS/DSS, stage II; 17.0%/31.3%, \( P = 0.5309 \), stage III; 27.7%/32.2%, \( P = 0.9815 \), and stage IV; 15.7%/17.1%, \( P = 0.9960 \)). Survival of elderly patients in stage II and III disease who did or did not undergo adjuvant chemotherapy is shown in Figure 3. There was no significant difference in 5-year OS between both groups (\( P = 0.5244 \)).

The number of deaths was 42 in the elderly group and 87 in the control group. As shown in Figure 4, the numbers of deaths in stages I/II/III/IV were 8/9/12/13, respectively, in the elderly group and 19/11/23/34, respectively, in the control group. The rates of relapse death were 0% (for stage I), 56% (II), 92% (III), and 92% (IV) in the elderly group; in the control group, the corresponding rates were 32%, 64%, 78%, and 100%. The rates of other disease death were 75% (for stage I), 22% (II), 8% (III), and 8% (IV) in the elderly group; in the control group, the corresponding rates were 33%, 0%, 17%, and 0%. The rates of other cancer death were 25% (for stage I), 22% (II), 0% (III), and 0% (IV) in the elderly group; in the control group, the corresponding rates were 32%, 36%, 4%, and 0%. There were no significant differences in the proportion of patients who die due to recurrence, other malignant disease and other disease between the elderly group and the control group (\( P = 0.1950 \)) (Fig. 4).

**DISCUSSION**

Current Japanese gastric cancer guidelines describe the appropriate therapy for patients with gastric cancer, but there is no clear description regarding surgical treatment of the elderly [11]. In the present study, we evaluated the difference of operative mortality and long-term survival of surgical treatment for elderly patients with gastric carcinoma to determine an appropriate postoperative treatment for elderly patients. The eGFR was lower in the elderly than the control group, and more elderly patients had two or more comorbidities, especially systemic diseases such as pulmonary and cardiovascular disease. The ASA-PS was thus significantly higher in the elderly than the control group. However, there was no significant difference in the incidence of postoperative complications between the groups. These results suggest that gastrectomy can be carried out safely in patients aged 80 and older through careful monitoring of the postoperative status.

The percentage of comorbidity of 70–79 years old patients that performed gastrectomy in the same period as the current study was higher than that of control group and lower than that of the elderly. The postoperative complication rate of 70–79 years old patients was not significantly different from that of both groups (data not shown).

Many studies have shown that concomitant illness, advanced stage, prolonged operative time, excessive blood loss, and age are risk factors for the occurrence of complications after gastrectomy [14–17]. Some reported that postoperative complications are more frequent among elderly patients [6,18]. In contrast, others reported that the incidence was similar [19–21], so this topic remains controversial. Wu CW et al. [6] reported a complication rate of 25–35% in the elderly group, significantly more than in the younger group. Thomas DR et al. [18] reported that the complications after gastrectomy for elderly patients were likely to be fatal or severe compared to those in younger patients. On the other hand, Katai et al. [19] reported that gastrectomy for elderly patients was safe and feasible without surgery-related deaths. Saidi et al. [20] also reported that gastrectomy can be carried out safely in elderly patients and that the short- and long-term outcomes in elderly patients were comparable to those in younger patients. The reported short-term surgical outcomes have improved in recent studies. This safety might be due to advancements in perioperative management such as anesthesiology, intensive care, surgical techniques, and devices of...
surgical tools. In the current study, more D2 lymph node dissections in the elderly group may reduce postoperative complication. There was no significant difference in survival between D2 and less D2 dissection in stage II and stage III of the elderly group (data not shown). These results suggested that D2 dissection would be invasive for the elderly patients.

Previous report showed the incidence of postoperative pneumonia in elderly patients with gastrectomy to be 2–16% ([7–9,19,22–25]). Some reports concluded that there were no differences in postoperative pulmonary complication between elderly and younger groups [20,24–27]. However, postoperative pneumonia in these reports tended higher in elderly groups, consistent with the current results. It was reported that patients aged 85 and older were at high risk for postoperative pneumonia [7,8]. Yamada et al. [7] reported that postoperative pneumonia occurred significantly more often in patients aged 85 and older than in patients aged 75–84. Recently, performance of laparoscopic gastrectomy for early gastric cancer has been common in Asia; after short-term follow-up, this procedure was reported to be safe and feasible in the elderly [9,23,24]. Tokunaga et al. [24] reported that postoperative respiratory complications were quite low in the elderly group despite the fact that many had preoperative respiratory disease. Laparoscopy with a small incision and earlier start of postoperative walk might be useful for preventing postoperative pneumonia for elderly patients.

In this study, analysis of OS and DSS in stage II and III patients revealed a poorer prognosis for the elderly group than the control group. The reason for this may be that less adjuvant chemotherapy was used. Only nine of stage II and III patients underwent adjuvant chemotherapy of 3 months or more. In Japan, the standard treatment regimen for stage II and III in patients aged 20–80 years is surgery and adjuvant chemotherapy [28]. In this study, whether patients aged 80 and older underwent adjuvant chemotherapy depended on a discussion between the patient and attending physician. Attending physicians tended to be likely to accept the desire of patients to reject chemotherapy until their physical strength recovered sufficiently. Another reason for poor OS in stage II patients is thought to be that there are many deaths due to other disease and other cancers, and it is thought that there is a risk for developing a new cancer after surgery in the elderly. Thus, follow-up encompassing problems of the whole body, as well as cancer recurrence, is important.

To our knowledge, there is no evidence regarding postoperative chemotherapy for elderly patients aged 80 and older in Japan. A phase III clinical trial of adjuvant chemotherapy and chemotherapy for unresectable gastric cancer was performed, but patients aged 80 and over were excluded [28,29]. Aoyama et al. [30] reported that the incidences of grade III hematological and non-hematological toxicities of S-1 adjuvant chemotherapy for the elderly were <5%.
and that this regimen was safe and feasible and Tsushima et al. [31] reported that S-1 or S-1 plus cisplatin for elderly patients presented a high risk of hematological toxicities, but was feasible. However, there were only a few patients aged 80 and older in these studies. In the present study, of the elderly stage II and III patients, there was no significant difference in prognosis between the patients who underwent adjuvant chemotherapy and those who did not do. This result might be related to the fact that various kinds of chemotherapeutic regimens were performed and the period of administration were different in this study. Another reason for this result is that patient’s illness was strongly involved in decision making of undergoing or discontinuing adjuvant chemotherapy. It seems that the elderly patients, in consultation with their physicians, accepted a slightly different goal of therapy than the younger patients who are certainly understandable. They may be more interested in quality than duration of life. A large clinical trial assessing not only the safety and feasibility of adjuvant chemotherapy but also the effect for long-term outcomes in patients aged 80 and older is required.

Because this study was retrospective, we could not draw a definitive conclusion about the usefulness of D2 dissection and adjuvant chemotherapy for the elderly patients. However our results suggested that there was no benefit of D2 dissection and adjuvant chemotherapy in survival for the elderly stage II and III patients. I would advocate for a novel neoadjuvant systemic therapy in the elderly if they were known to harbor stage II or stage III gastric cancers.

In the current study, there was a significant difference between OS and DSS in the stage II, III, and IV elderly patients. Our data showed that 56% of deaths in stage II were from recurrence and 44% were due to other disease and malignant death. These results suggest that we should make an effort to not only to prevent recurrence but also to manage accompanying illness and to screen for other malignant disease. Almost all deaths of stage III elderly patients were from recurrence. Thus, we should be aware of recurrence during follow-up. However, one problem is that patients aged 80 and older often have renal dysfunction. Renal dysfunction is one of the common toxicities of S-1. Yamanaka et al. [32] reported that baseline renal impairment was a significant risk factor for grade III–IV adverse events caused by S-1 chemotherapy. Aoyama et al. [30] reported that treatment events of S-1, such as delay and dose reduction, occurred more frequently in elderly than in non-elderly patients. Thus, for the elderly, development of anti-cancer drug which has less toxicity, for example molecular target therapy, is desired. Because this study was retrospective, we could not draw a definitive conclusion about the usefulness of D2 dissection and adjuvant chemotherapy for the elderly patients. However our results suggested that there was no benefit of D2 dissection and adjuvant chemotherapy in survival for the elderly patients with stage II or stage III disease. I would advocate for a novel neoadjuvant systemic therapy in the elderly if they were known to harbor stage II or stage III gastric cancers.

In the present study, we demonstrated that there was no significant difference of the severity of complication and the rate to discharge on foot between two groups, suggesting that elderly patients could be underwent gastrectomy without falling their activity. However, the percentage (5.3%) of patients admitted to care hospitals was higher in the elderly group than those (2.2%) in the control group. One of the reasons was the requirement for intravenous nutrition or rehabilitation. In future study, therefore, it might be necessary to clarify whether the elderly patients could recover their activity to the preoperative baseline.

![Fig. 4. The cause of death according to the cancer stage.](image)
CONCLUSIONS

Gastrectomy for elderly patients was safe and the short-term outcome was satisfactory. Follow-up with attention to accompanying illness and other malignant disease of stage I elderly patients is needed. In stage II and III disease patients, a novel drug which is acceptable for the elderly is needed as a postoperative therapy.

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