Adjuvant chemotherapy for gastric cancer in elderly patients has same benefits as in younger patients

ABSTRACT

Objective: The age-adjusted mortality rate due to gastric cancer was reported to increase with age. This study aims to investigate the results of adjuvant chemotherapy in patients aged 65 years or older comparing with younger patients and focusing on its impact on survival.

Materials and Methods: A total of 406 patients with nonmetastatic gastric cancer that consisted of 283 patients younger than 65 years (range: 23–64 years) and 123 patients 65 years of age or older (range: 65–75 years) were retrospectively evaluated. Categorical and continuous variables were summarized using the descriptive statistics and compared with Chi-square and Mann–Whitney U-tests, respectively. Cancer-specific survival rates were estimated by the Kaplan–Meier method.

Results: Median age at diagnosis was 58 years (range: 23–75 years). There was no significant difference in gender, tumor localization in the stomach (cardia/noncardia), tumor histology, perineural invasion, lymphovascular invasion, histopathological characteristics of the tumor, and tumor stage between groups. No significant difference was detected in survival between groups. The median survivals were 20.8 months (range: 17–24.6) in patients younger than 65 years and 19.5 months (range: 14.8–24.1) in patients 65 years of age or older (P = 0.9).

Conclusions: We showed that adjuvant chemotherapy in elderly patients with gastric cancer has same effectiveness as nonelderly patients. However, further well-designated prospective studies are needed to confirm these findings.

KEY WORDS: Adjuvant treatment, elderly and nonelderly patients, gastric cancer, survival

INTRODUCTION

The incidence and mortality rates for most cancers have been decreasing in the United States and in other developed western countries. However, cancer is still responsible for more deaths than heart disease in patients aged 85 years or younger. Cancer in older people has become an increasingly common problem due to the prolonged life expectancy of the general population. The overall gastric cancer incidence and mortality rates have been decreasing worldwide, but despite the recent decline, gastric cancer remains the fourth most common cancer and the second leading cause of cancer-related mortality. Moreover, the incidence of gastric cancer increases with age, especially in the United States, and most gastric cancer patients in Japan are older. The age-adjusted mortality rate of gastric cancer was reported to increase with age. As the world population has been aging, gastric cancer in the elderly will become an increasing clinical challenge. However, the elderly are less likely to receive the recommended treatment because of their shorter life expectancy, higher incidence of comorbidities, and a higher risk of complications. Thus, the effectiveness of postoperative chemotherapy for patients 65 years of age or older should be carefully assessed to avoid overtreatment or under treatment. However, there are limited data available.

In this study, we aimed to investigate the results of adjuvant chemotherapy in patients aged 65 years or older comparing with younger patients and focusing on its impact on survival.

Cite this article as: Karaca M, Tural D, Kocoglu H, Selcukbiricik F, Bilgetekin I, Özet A. Adjuvant chemotherapy for gastric cancer in elderly patients has same benefits as in younger patients. J Can Res Ther 2018;14:593-6.
MATERIALS AND METHODS

Patients

The study included gastric cancer patients treated at a tertiary hospital in Turkey between 2000 and 2015. Cancer in each patient was coded according to the International Classification of Diseases for Oncology[12]. The cases were retrospectively evaluated and divided into two groups based on age: Group 1 consisted of 123 patients aged 65 years or older (range: 65–75 years) at the time of treatment, and Group 2 was composed of 283 patients younger than 65 years (range: 23–64 years). Patients whose tumors were histologically confirmed as adenocarcinoma and whose survival data available were included in the study. Patients whose tumors were identified as other than adenocarcinoma were excluded from the study.

In nonmetastatic patients, the protracted 5-fluorouracil (5-FU) infusion chemotherapy regimen was used concurrently with postoperative radiotherapy (RT). Five cycles of adjuvant bolus 5-FU (425 mg/m^2/day) and leucovorin (20 mg/m^2/day) as Mayo regimen were administered on treatment days 1–5 every 28 days to these patients after surgery. Bolus 5-FU and leucovorin were administered on treatment days 1 to 4 every 28 days concurrently with postoperative RT during the second and third cycles of the planned five-cycle adjuvant chemotherapy. RT was administered (range: 45 to 50.4 Gy) to the tumor bed and draining lymph nodes in cases with 2- to 3-cm margins.

Patients with positive surgical margins, incomplete chemoradiotherapy, poor performance status (Eastern Cooperative Oncology Group (ECOG) >2), inadequate renal and hepatic functions, and other second primary cancers were excluded from the study. Adjuvant chemotherapy was administered to stage IB, II, and III patients. Patients older than 75 years were not included in this study.

Statistical analysis

Categorical and continuous variables were summarized using the descriptive statistics (e.g., median, range, frequency, and percentage) and compared with Chi-square and Mann–Whitney U-tests, respectively. Cancer-specific survival rates were estimated by the Kaplan–Meier method and cancer relative survival was calculated from the date of diagnosis until death. All analyzes were performed using the SPSS 15.0 (SPSS Inc., Chicago, IL, USA) software. The statistical level of significance was defined as \( P < 0.05 \).

RESULTS

The hospital-based registry included 406 cases of gastric adenocarcinoma who received adjuvant chemotherapy between 2000 and 2015. Median age at diagnosis was 58 years (range: 23–75 years). There was no significant difference in gender, tumor localization in the stomach (cardia/noncardia), tumor histology, perineural invasion, lymphovascular invasion, and tumor stage between Groups 1 and 2. There was no statistical difference between two groups in regard to histopathological characteristics. Details of demographic and histologic factors are shown in Table 1.

There was no statically significant survival difference between patients aged 65–75 years and patients younger than 65 years. In this study, median survival in patients aged 65–75 years and patients younger than 65 years were 20.8 months (range: 17–24.6) and 19.5 months (14.8–24.1), respectively \( (P = 0.9) \) [Figure 1].

| Table 1: Clinicopathological features of all patients |
| Variable | Patients <65 years | Patients aged 65-75 years | \( P \) |
| --- | --- | --- | --- |
| Gender | 283 (70) | 123 (30) | 0.8 |
| Male | 193 (68) | 85 (69) | 0.8 |
| Female | 90 (32) | 38 (31) | 0.8 |
| ECOG P2 | 123 (44) | 53 (43) | 0.7 |
| 0 | 160 (56) | 70 (57) | 0.7 |
| 1 | 123 (44) | 53 (43) | 0.7 |
| Stomach localization | 232 (82) | 94 (76) | 0.2 |
| Proximal | 51 (18) | 29 (24) | 0.2 |
| Distant | 76 (27) | 30 (24) | 0.5 |
| Lymphovascular invasion | 141 (50) | 68 (56) | 0.5 |
| Absent | 66 (23) | 25 (20) | 0.5 |
| Present | 81 (29) | 28 (23) | 0.4 |
| Unknown | 135 (48) | 69 (56) | 0.4 |
| Perineural invasion | 67 (23) | 26 (21) | 0.4 |
| Absent | 14 (5) | 11 (9) | 0.13 |
| Present | 15 (5) | 11 (9) | 0.13 |
| Unknown | 241 (85) | 93 (76) | 0.13 |
| Stage | 13 (5) | 8 (6) | 0.13 |

ECOG=Eastern Cooperative Oncology Group

Figure 1: Overall survival of patients aged 65–75 years and younger than 65 years with adjuvant chemotherapy (median survivals in patients aged 65–75 years and patients younger than 65 years were 20.8 months [17–24.6] and 19.5 months [14.8–24.1], respectively \( (P = 0.9) \) [Figure 1].

[Downloaded free from http://www.cancerjournal.net on Monday, November 12, 2018, IP: 88.255.99.39]
DISCUSSION

In current study, we evaluated that whether or not adjuvant chemotherapy is effective in older patients. In literature, there is no sufficient knowledge about this issue. Therefore, it is important to determine which optimal management is suitable for elderly patients. In current study, we demonstrated that there was no significant difference in gender, tumor localization in the stomach (cardia/noncardia), tumor histology, perineural invasion, lymphovascular invasion, and tumor stage between groups. Furthermore, there was no statically significant survival difference between patients aged 65–75 years and patients younger than 65 years. Median survival in patients aged 65–75 years and patients younger than 65 years were 20.8 months (range; 17–24.6) and 19.5 months (14.8–24.1), respectively ($P = 0.9$). Therefore, we demonstrated that adjuvant chemotherapy in elderly patients has same effectiveness as in the young patients.

Jin et al.[13] investigated the use of adjuvant chemotherapy for gastric cancer after D2 gastrectomy in the elderly and they evaluated its impact on survival. They retrospectively evaluated 360 patients aged 65 years or older with nonmetastatic gastric cancer in a single institution. This study showed the survival benefits of adjuvant fluoropyrimidine-based chemotherapy among the elderly patients. However, limitation of that study was being retrospective design. Further well-designated prospective studies are needed to confirm these findings.

The Intergroup trial SWOG 9008/INT-0116[14] showed the effect of surgery plus postoperative chemoradiation on the survival in patients with resectable gastric cancer. Median age at diagnosis was 60 years (range: 25–87 years) for chemoradiation group, and older age was not an exclusion criteria in this study. MAGIC[15] trial assessed whether or not addition of perioperative chemotherapy to surgery improves outcome among patients with potentially gastric cancer. In perioperative chemotherapy group median age was 62 years (range: 29–85 years). Patients were excluded if they had previously received cytotoxic chemotherapy or RT, uncontrolled cardiac disease, or creatinine clearance of 60 ml/min or less. However, older age was not an exclusion criteria in this study. CLASSIC trial[16] evaluated postoperative chemotherapy after curative gastric resection with D2 dissection in patients with gastric cancer. Eligible patients were ambulatory; aged 18 years or older; histologically confirmed, and achieved R0 resection. Patients were included only if they had a Karnofsky performance status of 70% or more. Patients who had chemotherapy, immunotherapy, or RT for gastric cancer were excluded. Patients had to have adequate renal function, hepatic function, and hematological function.

However, all those studies did not evaluate the subgroup of elderly patients, and there is no available information whether or not adjuvant chemotherapy in elderly patients has same effectiveness as nonelderly patients. The elderly patients are less likely to receive adjuvant therapy even if the treatments are known to be effective and tolerable. There may be various reasons of this result. Older patients may have more comorbid diseases; they might be less tolerant to chemotherapy, and they may prefer to undergo less treatment in their relatively limited lifetime.[17,18]

Although, Tural et al. demonstrated that patients aged 70 years or older with gastric cancer were treated less frequently with adjuvant chemotherapy when compared nonelderly patients with gastric cancer.[19] Furthermore, Saito et al.[20] suggested that chemotherapy was carried out more frequently in nonelderly than in elderly patients.

In current study, we demonstrated that adjuvant chemotherapy in patients aged 65–75 years has same benefits as in patients younger than 65 years. However, there are some limitations in our study. We retrospectively evaluated patient records, and this may cause same bias on our outcome data. Also, there is no available information about patients’ comorbid disease. However, we evaluated ECOG performance status, and this variable was similar in each group.

CONCLUSION

We demonstrated that adjuvant chemotherapy in elderly patients with gastric cancer had same effectiveness as nonelderly patients. However, further well-designated prospective studies are needed to confirm these findings.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Parkin DM, Pisani P, Ferlay J. Estimates of the worldwide incidence of eighteen major cancers in 1985. Int J Cancer 1993;54:594-606.
2. Parkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000. The global picture. Eur J Cancer 2001;37 Suppl 8:S4-66.
3. Parkin DM. International variation. Oncogene 2004;23:6329-40.
4. Botterweck AA, Schouten LJ, Volovics A, Dorant E, van Den Brandt PA. Trends in incidence of adenocarcinoma of the oesophagus and gastric cardia in ten European countries. Int J Epidemiol 2000;29:645-54.
5. Devesa SS, Blot WJ, Fraumeni JF Jr. Changing patterns in the incidence of esophageal and gastric carcinoma in the United States. Cancer 1998;83:2049-53.
6. Siegel R, Ward E, Brawley O, Jemal A. Cancer statistics, 2011: The impact of eliminating socioeconomic and racial disparities on premature cancer deaths. CA Cancer J Clin 2011;61:212-36.
7. Jemal A, Center MM, DeSantis C, Ward EM. Global patterns of cancer incidence and mortality rates and trends. Cancer Epidemiol Biomarkers Prev 2010;19:1899-907.
8. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. CA Cancer J Clin 2010;60:277-300.
9. Hayat MJ, Howlader N, Reichman ME, Edwards BK. Cancer statistics, trends, and multiple primary cancer analyses from the Surveillance,
Karaca, et al.: Adjuvant chemotherapy in elderly

1. Epidemiology, and End Results (SEER) Program. Oncologist 2007;12:20-37.
2. Saif MW, Makrilia N, Zalonis A, Merikas M, Syrigos K. Gastric cancer in the elderly: An overview. Eur J Surg Oncol 2010;36:709-17.
3. Goodwin JS, Hunt WC, Samet JM. Determinants of cancer therapy in elderly patients. Cancer 1993;72:594-601.
4. Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin LD, Parkin DM, et al. International Classification of Diseases for Oncology. 3rd ed. Geneva: World Health Organization; 2000.
5. Jin Y, Qiu MZ, Wang DS, Zhang DS, Ren C, Bai L, et al. Adjuvant chemotherapy for elderly patients with gastric cancer after D2 gastrectomy. PLoS One 2013;8:e53149.
6. Macdonald JS, Smalley SR, Benedetti J, Hundahl SA, Estes NC, Stemmermann GN, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med 2001;345:725-30.
7. Cunningham D, Allum WH, Stenning SP, Thompson JN, Van de Velde CJ, Nicolson M, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med 2006;355:11-20.
8. Bang YJ, Kim YW, Yang HK, Chung HC, Park YK, Lee KH, et al. Adjuvant capecitabine and oxaliplatin for gastric cancer after D2 gastrectomy (CLASSIC): A phase 3 open-label, randomised controlled trial. Lancet 2012;379:315-21.
9. Sakuramoto S, Yamashita K, Watanabe M. Newly emerging standard chemotherapies for gastric cancer and clinical potential in elderly patients. World J Gastrointest Oncol 2009;1:47-54.
10. Dudeja V, Habermann EB, Zhong W, Tuttle TM, Vickers SM, Jensen EH, et al. Guideline recommended gastric cancer care in the elderly: Insights into the applicability of cancer trials to real world. Ann Surg Oncol 2011;18:26-33.
11. Tural D, Selçukbiricik F, Serdengeçti S, Büyükünal E. A comparison of patient characteristics, prognosis, treatment modalities, and survival according to age group in gastric cancer patients. World J Surg Oncol 2012;10:234.
12. Saito H, Osaki T, Murakami D, Sakamoto T, Kanaji S, Tatebe S, et al. Effect of age on prognosis in patients with gastric cancer. ANZ J Surg 2006;76:438-61.