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A Prognostic Model in Metastatic or Recurrent Gastric Cancer Patients with Good Performance Status Who Received First-Line Chemotherapy[1]

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Abstract

PURPOSE: Good performance status is widely known as a superior prognostic predictor. However, some patients have large survival differences despite having good performance status that are influenced by certain prognostic factors. The purpose of this study was to explore baseline host- or tumor-related factors and to establish a prognostic model for metastatic or recurrent gastric cancer patients with good performance status who received first-line chemotherapy. *METHODS:* A total of 310 metastatic or recurrent gastric cancer patients with good performance status who received first-line chemotherapy were enrolled. Prognostic significance was determined using multivariate Cox regression analysis. Incorporating all pretreatment indicators, a prognostic model was established. Overall survival outcomes were compared with different risk groups using the Kaplan-Meier method and log-rank test. *RESULTS:* In multivariate analysis, no previous gastrectomy [hazard ratio (HR) = 1.42; 95% confidence interval (CI) = 1.08-1.85], number of distant metastatic sites (HR = 1.47; 95% CI = 1.11-1.96), bone metastasis (HR = 2.20; 95% CI = 1.16–4.18), liver metastasis (HR = 1.77; 95% CI = 1.31-2.39), and an elevated neutrophil lymphocyte ratio (HR = 1.37; 95% CI = 1.04-1.79) were independent prognostic factors of overall survival. Patients were categorized into three risk groups according to their risk scores. Median survival times for the low-risk (0 point), intermediate-risk (1-3 points), and high-risk (≥4 points) groups were 19.7, 10.7 and 5.1 months, respectively ($P < .001$). *CONCLUSIONS:* A prognostic model was developed that could facilitate risk stratification for metastatic or recurrent gastric cancer patients with good performance status who received first-line chemotherapy to help clinicians choose an applicable treatment based on the estimated prognosis.

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Introduction

Gastric cancer is the second most common cause of cancer-related death in the world [1]. In China, this disease claimed approximately 297,496 lives in 2011 [2]. Although the only potential curative treatment for gastric cancer is surgery, most gastric patients are usually unable to receive curative surgical resection because of regional advanced or distant metastatic disease at the time of diagnosis. Palliative chemotherapy is still a major treatment in metastatic or recurrent gastric cancer [3,4].

However, metastatic or recurrent gastric cancer patients who receive palliative chemotherapy have varying survival outcomes. To date, several studies have reported on prognostic indicators associated with survival including host- and tumor-related factors. Some prognostic models incorporating these prognostic factors have been developed. This kind of prognostic tool can be simply used to help oncologists guide treatment plans and improve prognostic accuracy [5]. Lee et al. developed the first prognostic model for metastatic

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gastric cancer patients receiving first-line chemotherapy [6]. Then, other prognostic models were gradually reported that focused on patients treated with different specific first-line chemotherapeutic regimens, such as cisplatin based, S-1 plus cisplatin, and docetaxel and cisplatin plus fluorouracil [7–9].

Although several prognostic models have been reported, some issues still need to be resolved. For example, patients analyzed in previous models were too indiscriminate, including those patients with esophageal cancer or squamous cell carcionomas [10]. More importantly, the patient group in these prognostic models included those that had not only good performance status (PS) but also poor PS.

Eastern Cooperative Oncology Group (ECOG) PS is an important parameter which is widely used to assess responses to chemotherapy and survival [11]. A good PS (0-1) has always been considered to have a better beneficial prognostic impact than a poor PS (2-3) [6,12,13]. However, some patients have a poor prognosis despite having a good PS. In a study analyzing 148 cancer patients with a good PS, the report showed that patients had a wide range of overall survival (OS) (29-2421 days) even though they had a PS = 0 [14]. One potential explanation is that there are several variables influencing survival, for example, histopathological factors, biological behavior of the malignancy, and others. Even if it is the same host-related factor, it could have different tumor-related effects. Therefore, prognostic factors are probably different between good and poor PS patient populations. Meanwhile, some subgroup analyses of clinical trials showed that patients with a good PS belonged to mixed groups who did not show good survival outcomes. The S-1 plus cisplatin versus S-1 in random control trial in the treatment for stomach cancer and S-1 alone versus S-1 and docetaxel combination in random control trial in the treatment for stomach cancer studies found that the good PS group did not show a statistically significant survival benefit from designated chemotherapy regimens [15,16]. In other words, even though some patients had the same good PS, appropriate treatments for both good and poor PS patients should be tailored. Nevertheless, few studies have analyzed prognostic factors among cancer patients with a good PS [14,17]. To optimize treatment for this subset of patients, it will be necessary to identify prognostic factors that can stratify patients within this group.

To our knowledge, no prognostic model for metastatic gastric cancer patients with a good PS is available. The objective of this study was to explore baseline host- or tumor-related factors that may be associated with survival and establish a prognostic model for metastatic or recurrent gastric cancer patients with a good PS who received first-line chemotherapy.

Patients and methods

Patients

Between April 2007 and December 2013, 371 patients received first-line palliative chemotherapy for metastatic or recurrent gastric cancer at the First Hospital of China Medical University. The criteria for patient inclusion consisted of the following: 1) age ≥ 18 years, 2) histologically confirmed diagnosis of gastric cancer, 3) presence of evaluable disease or measurable lesions, 4) received at least one cycle of chemotherapy, 5) good PS (0-1), and 6) availability of clinicopathological data at the start of chemotherapy. Patients with esophageal cancer, squamous cell carcinomas, or gastroesophageal junction tumors were excluded from the analysis. Of the 371 patients screened, 310 patients conformed with the inclusion criteria. All patients in the study signed informed consents.

Treatment

The 5-fluorouracil (5-FU)–based chemotherapy was as follows: 1) oxaliplatin, capecitabine, or S-1 (n = 74); 2) oxaliplatin, leucovorin, and 5-FU (modified FOLFOX) (n = 56); 3) capecitabine or S-1 (n = 45); 4) capecitabine or S-1 and cisplatin (n = 21); and 5) 5-FU and cisplatin (n = 11).

The taxane-based chemotherapy was as follows: 1) docetaxel or paclitaxel, and capecitabine or S-1 (n = 83); 2) docetaxel or paclitaxel, cisplatin, and 5-fluorouracil (n = 10); 3) docetaxel and cisplatin (n = 1); and 4) docetaxel (n = 1).

Others included 1) an irinotecan-based regimen (n = 4); 2) epirubicin, 5-FU, and cisplatin (n = 3); and 3) epirubicin, oxaliplatin, and capecitabine (n = 1).

Statistical Analysis

OS was the primary end point of this study. OS was counted from the time of metastasis to the time of death or the last follow-up visit. Survival data was analyzed using the Kaplan-Meier method. Comparison of survival curves were performed using log-rank analysis. A multivariate prognostic model was performed using all variables found to be significantly associated with OS at a P value ≤ .05 in the multivariate analysis. P values < .05 were considered statistically significant, and all P values corresponded to two-sided significance tests. All statistical analyses were performed using the SPSS 17.0 software package (SPSS, Chicago, IL).

Variables included in the univariate analysis consisted of the following: sex; age; PS; previous gastrectomy; tumor location; weight loss; the number of distant metastatic sites; the presence of ascites; metastasis to liver, bone, and lung at the start of chemotherapy; white blood cell (WBC) count; absolute neutrophil count (ANC); lymphocyte (LN) count; platelet count (PLT); neutrophil/lymphocyte ratio (NLR); platelet/lymphocyte ratio (PLR); hemoglobin; total protein (TP); serum albumin (ALB); total bilirubin (TBIL); alanine aminotransferase (ALT); and alkaline phosphatase (ALP). Laboratory variables, recorded as continuous variables, were dichotomized based on the median value of each variable.

Results

Patient Characteristics

From April 2007 to December 2013, 310 patients were included in this study (Table 1). The median age was 58 years (range, 25-80 years).The percent of patients who had a PS = 0 at the time of receiving first-line chemotherapy was 19.7 (n = 61). Eighty-one percent (251 of 310) of patients had more than one distant metastatic site. Nearly half of the patients had previously received gastrectomies. There were 83 patients (26.8%) who underwent palliative gastrectomies and 66 (21.3%) who underwent radical gastrectomies. By the last follow-up date, 251 patients had died. The median time of OS was 10.6 months [95% confidence interval (CI) = 9.7-11.4] (Figure 1).

Univariate Analyses

We obtained complete information on all parameters on 296 of the 310 patients, and therefore, they were used in the prognostic analyses. In univariate analysis, statistically significant factors that adversely affected OS included no previous gastrectomy, bone and liver metastasis, number of distant organ metastasis (≥2), the presence of ascites, WBC count $>6.4*10^9$/l, ANC $>3.8*10^9$/l, PLT $>230*10^9$/l, NLR >50th percentile, and PLR >50th percentile (Table 2).