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Original Research

The prevalence and clinical significance of postgastrectomy anemia in patients with early-stage gastric cancer: A retrospective cohort study

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ABSTRACT

Background: This study explored the cumulative incidence of anemia after gastrectomy in patients with early-stage gastric cancer and evaluated the relationship between postgastrectomy anemia and nutritional factors during long-term follow-up.

Methods: The medical records of patients with stage I gastric cancer who underwent curative gastrectomy between January 2006 and December 2013 were reviewed retrospectively. Hematologic parameters like hemoglobin, iron, ferritin, and vitamin B_{12} level were obtained prior to and after surgery with other nutritional parameters such as total protein, albumin, total cholesterol, triglyceride, calcium, and phosphate. Postoperative follow-up was conducted at 6 months after surgery and then annually for 5 years.

Results: Among 566 patients who did not have anemia preoperatively, 240 (42.4%) experienced anemia at least once during the 5 years after gastrectomy. These 240 patients (the anemia group) showed lower preoperative levels of hemoglobin, iron, ferritin, and triglyceride than those of the patients who did not experience anemia (the normal group). Total gastrectomy, advanced T stage, and lymph node metastasis were significantly more common in the anemia group compared with the normal group. During long-term follow-up, the anemia group showed significantly lower serum levels of nutritional markers, especially triglycerides, compared with the normal group. The overall survival rate was significantly lower in the anemia group than in the normal group.

Conclusions: Anemia was common among gastric cancer patients after gastrectomy. Total gastrectomy and advanced T stage were identified as independent risk factors for postgastrectomy anemia. In addition, anemia might be associated with nutritional problems and a poor prognosis. Thus, regular monitoring and appropriate management of postgastrectomy anemia are important for early-stage gastric cancer patients with a long life expectancy.

1. Introduction

Gastric cancer is common in East Asia, such as Korea, Japan, and China, although its global prevalence is gradually decreasing [1]. The survival rate and life expectancy of gastric cancer patients are increasing with improvements in the early detection of gastric cancer by regular endoscopic screening [2]. Early gastric cancer shows a 5-year survival rate > 90% with surgery alone and no chemotherapy, although advanced gastric cancer still shows a high mortality rate [3]. Considering this improvement in the survival rate among gastric cancer patients after gastrectomy, maintaining a high quality of life after surgery has become more important.

Anemia is one of the most common metabolic disorders after gastrectomy, which is caused by deficiencies in iron, vitamin B_{12}, and folic acid. Postgastrectomy anemia is caused by various mechanisms including changes in the gastrointestinal tract by surgery, decreased levels of digestive enzymes such as gastric juice, and altered binding of several other enzymes during metabolism [4,5]. In previously reported studies, old age, female sex, and total gastrectomy (TG) were found to be risk factors for postgastrectomy anemia. However, these studies were performed a small number of patients, non-regular follow-up schedules, vague definitions of anemia, and insufficient biochemical markers of anemia [6–10]. Moreover, the majority of these studies included advanced gastric cancer patients, and it was difficult to exclude the effects of cancer progression or chemotherapy when evaluating the effects of anemia on patients after gastrectomy.

The aim of this study was to investigate the incidence of postgastrectomy anemia and the associated factors in patients who

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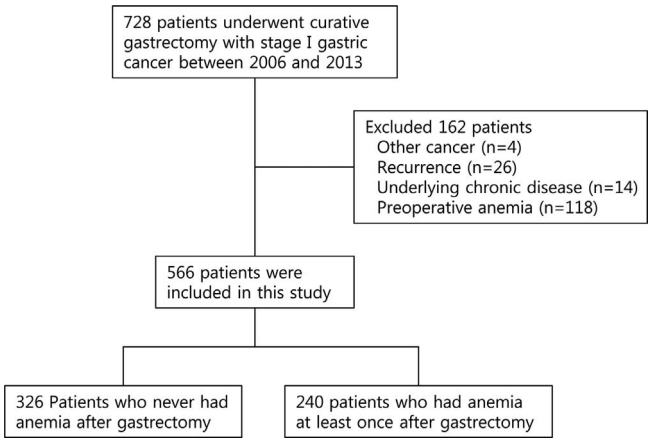

Fig. 1. Flow diagram of the patient selection for this study.

underwent curative gastrectomy without chemotherapy for early-stage gastric cancer. In addition, we explored the impact of postgastrectomy anemia on the nutritional status and survival of patients based on long-term observation.

2. Methods

2.1. Study population

Using a prospectively maintained gastric cancer database in our institution, 728 patients who underwent curative gastrectomy for stage IA or IB gastric cancer between January 2006 and December 2013 were identified. Pathologic staging of the patients was performed according to the seventh edition of the American Joint Committee on Cancer (AJCC) Tumor-Node-Metastasis (TNM) classification [11]. Fig. 1 shows a flow diagram of the study population. Among 728 patients, 162 were excluded from this study because of another malignancy (n = 4), recurrence during the follow-up period (n = 26), other underlying chronic diseases that can cause anemia (n = 14), or preoperative anemia (n = 118), as defined by the World Health Organization (WHO) criteria were excluded. All patients underwent standard subtotal gastrectomy (STG) or TG with lymph node dissection via either a laparoscopic or open approach. No patient in the study population received preoperative iron or vitamin B_{12} replacement therapy. Complete data were available for 554, 521, 420, 279, 184, and 115 patients at the 6-month and 1-, 2-, 3-, 4-, and 5-year follow-ups, respectively. This study was approved by the Institutional Review Board of our institution (No. VC14RISI0107), and it has been reported in line with the STROCSS criteria [12].

2.2. Data collection and follow-up

Data related to patient's clinicopathological characteristics including age, sex, body mass index (BMI), medical history, surgical procedures, TNM stage, and postoperative outcomes were collected retrospectively based on their medical records. The blood test included other nutritional parameters such as total protein, albumin, total cholesterol, triglyceride, calcium, and phosphate levels, as well as hematologic parameters, such as hemoglobin, iron, ferritin, and vitamin B_{12} levels, in both preoperative and postoperative examinations. Postoperative follow-up was conducted at 6 months after surgery and then annually for 5 years. The follow-up program consisted of history taking, physical examination, imaging studies, endoscopic examination, and blood tests. The mean follow-up period was 67 (range, 27–122) months.

2.3. Definition of anemia and the treatment protocol

Anemia was defined as a hemoglobin level < 12 g/dL in women and < 13 g/dL in men according to the WHO criteria. Iron deficiency was defined as a ferritin level < 10 ng/mL. Vitamin B_{12} deficiency was defined as a serum level < 200 pg/mL. Iron deficiency anemia was defined as anemia with concomitant iron deficiency. The incidence of postgastrectomy anemia was measured as the cumulative incidence over 5 years after gastrectomy. After the diagnosis of iron deficiency anemia was confirmed, patients were treated with oral iron supplements (ferrous sulfate 256 mg, twice a day) for 12 weeks or until the hemoglobin level was normalized. No patient in the study population received a transfusion during the follow-up period.

2.4. Statistical analysis

Continuous variables were presented as means with standard deviations or standard errors and categorical data as numbers with percentages. To compare the baseline characteristics of the patients with postgastrectomy anemia, independent *t*-test or chi-squared tests were used for univariate comparisons. Kaplan-Meier survival analysis was used to determine the cumulative incidence rate of anemia over 5 years, as well as the overall survival and disease-free survival rates. Univariate and age- and sex-adjusted multivariate Cox models were presented to examine the different variables and 5-year cumulative incidence of anemia. The linear mixed model was used to compare the nutrition status according to postgastrectomy anemia. A P value < 0.05 was considered statistically significant. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

3. Results

3.1. Comparison of clinicopathologic characteristics according to the incidence of postgastrectomy anemia

The patient's clinicopathologic characteristics are shown in Table 1. Of the total patients, 240 experienced anemia at least once after gastrectomy (the anemia group), while the remaining 326 never experienced anemia during the follow-up period (the normal group). Age, sex, histologic subtypes and preoperative BMI were not significantly different between the two groups according to the incidence of postgastrectomy anemia. TG with Roux-en-Y reconstruction (R-Y TG), proximal tumor location, T2 stage, and lymph node metastasis were significantly more common in the anemia group compared with the normal group. Preoperative hemoglobin, iron, and ferritin levels were significantly lower in the anemia group than in the normal group. The overall survival rate was significantly different between the two groups and was higher in the normal group compared with the anemia group.

3.2. Cumulative incidence of postgastrectomy anemia

The cumulative incidence of anemia steadily increased postoperatively. We observed incidences of 1.4% at 6 months and 7.1%, 18.4%, 27.0%, 32.0%, and 42.4% at 1, 2, 3, 4, and 5 years after surgery, respectively. Fig. 2 showed a comparison of the incidences of postgastrectomy anemia according to sex and operation type. Although the incidence of postgastrectomy anemia tended to be higher in women than men, the difference was not significant (HR = 1.26; 95% CI = 0.96–1.65; P = 0.055) (Fig. 2A). The incidence of anemia was significantly higher after R-Y TG than after Billroth-I STG (B-I STG) (HR = 1.77; 95% CI = 1.28–2.45; P = 0.001) (Fig. 2B). However, there was no significant difference in the incidence of anemia between B-I STG and Billroth-II STG (B-II STG) (HR = 1.33; 95% CI = 0.99–1.80; P = 0.061).