



Original research

Anemia after gastrectomy in long-term survivors of gastric cancer: A retrospective cohort study



Ji-Hye Jun ^a, Jung Eun Yoo ^a, Jung Ah Lee ^a, Young Sik Kim ^a, Sung Sunwoo ^{a,*},
Bum Soo Kim ^b, Jeong-Hwan Yook ^b

^a Department of Family Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea

^b Department of Surgery, University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea

HIGHLIGHTS

- Gastric cancer is the second most common malignancy in Korea.
- Anemia is frequently observed after gastrectomy, and caused by iron deficiency, vitamin B12 deficiency, or both.
- The incidence of anemia is steadily increased and the 5-year cumulative incidence of anemia was almost 40%.
- Female patients and those who had received total gastrectomy showed an increased risk of anemia.
- A high postoperative body mass index was associated with a decreased risk of anemia.

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ABSTRACT

Introduction: The prevalence of gastric cancer in Korea is increasing, and anemia is one of the most common complications of a gastrectomy. The purpose of this study was to estimate the incidence of anemia and assess its associated factors in long-term gastric cancer survivors.

Methods: This study was a retrospective cohort study of gastric cancer patients who visited a single medical center from January 2009 to December 2014 in Korea. We included 385 patients who survived for at least five years after gastrectomy with no recurrence or metastasis. Anemia was defined by World Health Organization criteria (Hb < 12 g/dL in women and <13 g/dL in men).

Results: Hemoglobin levels decreased from 14.24 ± 1.23 mg/dL before surgery to 13.60 ± 1.57 mg/dL one year after surgery ($P < 0.001$). The cumulative incidence rate of anemia after surgery increased linearly from 18.7% in the first year to 39.5% in the fifth year. The risk of anemia was higher in females (RR, 2.00; 95% CI, 1.26–3.18), patients that received total gastrectomy (RR, 3.00; 95% CI, 2.09–4.30) and patient with diabetes (RR, 1.87; 95% CI, 1.05–3.22). A higher postoperative BMI decreased the risk of anemia (RR, 0.38; 95% CI, 0.22–0.67).

Conclusions: During five years of follow-up after gastrectomy, the incidence of anemia steadily increased, and the risk of anemia was higher in females, total gastrectomy patients, patients with diabetes, low BMI patients.

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1. Introduction

Gastric cancer is the second most common malignancy in Korea. Also, it is the most common malignancy in Korean men. However,

because of early detection and advances in treatment techniques, the number of long-term survivors of gastric cancer is increasing in Korea [1]. In 2012, 13.8% of Korean cancer patients had gastric cancer, and the rate of early gastric cancer is increasing as well. In 1995, 28.6% of Korean gastric cancer patients who underwent surgery had early gastric cancer. This increased to 32.8% in 1999 and 47.4% in 2004 [2]. According to data from the Korea National Cancer Center (2013), the five-year survival rate for gastric cancer in Korea was 42.8% from 1993 to 1995 and increased to 71.5% from 2008 to 2012. The five-year survival rate after gastrectomy for early gastric

* Corresponding author. Department of Family Medicine, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 138-736, South Korea. Tel.: +82 2 3010 3952; fax +82 2 3010 3815.

E-mail address: sws@amc.seoul.kr (S. Sunwoo).

cancer is >90% [3]. Therefore, the survival outlook is improving for long-term gastric cancer patients [4].

Anemia is caused by iron deficiency, vitamin B12 deficiency, or both, and frequently occurs after gastrectomy [5]. A previous study has reported that the risk of anemia increases with time after gastrectomy and affected 37.1% of early gastric cancer patients 48 months after surgery [6]. These deficiencies can result from malabsorption, reduction of food intake or chronic blood loss from the gastric mucosa. Vitamin B12 deficiency can occur because of decreased intrinsic factor, which is secreted by the parietal cells of the stomach [5].

Anemia is associated with the prognosis of gastric cancer patients. Patients with iron-related anemia might experience fatigue due to a lack of iron-containing enzymes in their tissues, resulting in a poor quality of life [7]. Anemia can also reduce work capacity in adults [8,9] and impact motor and mental development in adolescents [10]. Most previous studies have often reported the short term incidence of anemia, and few studies have followed long-term survivors after gastrectomy. One study examined anemia in early gastric cancer patients for 48 months of follow-up but mainly described the incidence of anemia, not its associated factors [6]. Therefore, we investigated the incidence of anemia and determined its risk factors in long-term gastric cancer survivors.

2. Methods

2.1. Study subjects

This study retrospectively reviewed medical records from gastric cancer patients referred to the Cancer Prevention Clinic at the Department of Family Medicine at Asan Medical Center (Seoul, Republic of Korea) from January 1, 2009 to December 31, 2014. This study was approved by the Asan Medical Center institutional review board. The inclusion criteria for this study were five year survival after gastrectomy (from January 1, 2004 to December 31, 2008) and no evidence of recurrence or metastasis. The exclusion criteria were anemia in pre-operative blood tests or incomplete blood tests for anemia. A total of 587 patients who survived for more than five years were referred. 138 were excluded due to follow up loss. Among them 30 people were missing in the first year of follow up period While 28 were missing in the 2nd year. In addition, 35 were missing in the 3rd year, 20 were missing in the 4th year, and 25 were missing in the 5th year of follow up period. Other than the follow up loss exclusion, 64 were excluded due to anemia in the initial blood test pre-operation. Among them, 24 patients were men and 40 patients were women. A final cohort of 385 patients was included in this study.

2.2. Data collection and follow-up

Medical records were reviewed, including age at gastrectomy, sex, height, weight, educational level, smoking status, alcohol consumption, chemotherapy, and previous medical history of chronic diseases such as diabetes, hypertension, and cardiovascular disease. Smoking status was used to classify patients into current smokers, ex-smokers, and never-smokers. Alcohol intake was assessed by asking patients if they usually drink alcoholic beverages. Body mass index (BMI) was calculated as $[\text{weight (kg)}] / (\text{height (m)}^2)$. Blood tests for anemia were performed at annual follow-up and included hemoglobin (Hb), iron, total iron binding capacity, ferritin, vitamin B12, and folate, regardless of fasting. We reviewed postoperative hemoglobin level (in 30 days after surgery), number of injection of Vitamin B12 in postoperative period, iron substitution in postoperative period, and the need for transfusion.

2.3. Definition of anemia

Anemia was defined by World Health Organization criteria (Hb < 12 g/dL in women and <13 g/dL in men) [8]. Iron deficiency anemia (IDA) was defined as serum ferritin <20 µg/d or prescription of oral iron supplements. Vitamin B12 deficiency anemia was defined as vitamin B12 < 200 pg/mL, oral vitamin B12 supplementation, or intramuscular vitamin B12 injections. Combined anemia was defined as anemia with both iron and vitamin B12 deficiency. Other unclassified anemia was defined as anemia of unknown origin. Anemia was measured as the cumulative incidence of anemia. If anemia occurred at least once in the post-operative follow-up period, it was included in the incidence of anemia continuously.

2.4. Statistical analysis

Continuous variables were presented as a mean \pm SD and categorical variables as numbers with percentages. The duration of follow-up was calculated as the interval between the operation date and the diagnosis of anemia or the date of the five-year follow-up after gastrectomy. Kaplan-Meier survival analysis was used to determine the cumulative incidence rate of anemia for five years. Cox regression analysis was used to examine the univariate and multivariate associations between different variables and the 5 year cumulative incidence of anemia. Results from the Cox regression analysis are presented with relative risk (RR), P values, and 95% confidence ratios (CI). A P value < 0.05 was considered statistically significant. All data were analyzed using SPSS version 21.0 (IBM SPSS Statistics Inc, Chicago, IL).

3. Results

3.1. Baseline characteristics

During the study period, 587 patients were referred to the Department of Family Medicine from the Department of Gastric Surgery. Of these patients, 138 were excluded due to follow-up loss or incomplete blood tests for anemia, and 64 patients were excluded since anemia was determined in the preoperative laboratory test. Therefore, a total of 385 patients were included in this study; 258 men (67.0%) and 127 women (33.0%). The percentage of early gastric cancer was 84.4%. The mean age was 53.21 ± 9.77 years, and the mean preoperative BMI was 24.29 ± 2.98 kg/m². The mean preoperative hemoglobin level was 14.80 ± 1.03 mg/dL in men and 13.11 ± 0.72 mg/dL in women. Billroth I was performed on 266 patients (69.1%), Billroth II was performed on 35 patients (9.1%), and total gastrectomy was performed on 84 patients (21.8%) (Table 1). Chi-square test results showed differences in age, pre-operative Hb, postoperative Hb, type of operation, inpatients medication, chemotherapy, preoperative BMI, education, occupation, and smoking between the anemia group and the non-anemia group (Table 1).

3.2. Incidence of anemia

Hemoglobin levels decreased from 14.24 ± 1.23 mg/dL before surgery to 13.60 ± 1.57 mg/dL one year after surgery ($P < 0.001$). Excluding patients with anemia before surgery, the cumulative incidence rates of anemia after surgery steadily increased; 18.7% after one year, 27.3% after two years, 31.7% after three years, 36.1% after four years, and 39.5% after five years. The five-year incidence rates of IDA alone, vitamin B12 deficiency anemia alone, and combined IDA and Vitamin B12 deficiency anemia were 19.5%, 5.3%, and 6.2%, respectively (Fig. 1).

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