

Anemia after gastrectomy for early gastric cancer: Long-term follow-up observational study

Chul-Hyun Lim, Sang Woo Kim, Won Chul Kim, Jin Soo Kim, Yu Kyung Cho, Jae Myung Park, In Seok Lee, Myung-Gyu Choi, Kyo-Young Song, Hae Myung Jeon, Cho-Hyun Park

Chul-Hyun Lim, Sang Woo Kim, Won Chul Kim, Jin Soo Kim, Yu Kyung Cho, Jae Myung Park, In Seok Lee, Myung-Gyu Choi, Department of Internal Medicine, The Catholic University of Korea College of Medicine, Seoul 137-701, South Korea

Kyo-Young Song, Hae Myung Jeon, Cho-Hyun Park, Department of Surgery, The Catholic University of Korea College of Medicine, Seoul 137-701, South Korea

Author contributions: Lim CH, Kim SW and Kim WC designed the research; Lim CH, Kim SW, Kim JS, Cho YK, Park JM, Lee IS, Choi MG, Song KY, Jeon HM and Park CH performed the research; Lim CH and Kim SW analyzed the data; and Lim CH wrote the paper.

Correspondence to: Sang Woo Kim, MD, PhD, Department of Internal Medicine, The Catholic University of Korea College of Medicine, No. 505 Banpo-Dong, Seocho-Gu, Seoul 137-701, South Korea. viper@catholic.ac.kr

Telephone: +82-2-22586021 Fax: +82-2-22582055

Received: July 27, 2012 Revised: September 20, 2012

Accepted: September 29, 2012

Published online: November 14, 2012

Abstract

AIM: To identify the incidence and etiology of anemia after gastrectomy in patients with long-term follow-up after gastrectomy for early gastric cancer.

METHODS: The medical records of those patients with early gastric adenocarcinoma who underwent curative gastrectomy between January 2006 and October 2007 were reviewed. Patients with anemia in the preoperative workup, cancer recurrence, undergoing systemic chemotherapy, with other medical conditions that can cause anemia, or treated during follow up with red cell transfusions or supplements for anemia were excluded. Anemia was defined by World Health Organization criteria (Hb < 12 g/dL in women and < 13 g/dL in men). Iron deficiency was defined as serum ferritin < 20 µg/dL. Vitamin B₁₂ deficiency was defined

as serum vitamin B₁₂ < 200 pg/mL. Iron deficiency anemia was defined as anemia with concomitant iron deficiency. Anemia from vitamin B₁₂ deficiency was defined as megaloblastic anemia (mean cell volume > 100 fL) with vitamin B₁₂ deficiency. The profile of anemia over 48 mo of follow-up was analyzed.

RESULTS: One hundred sixty-one patients with gastrectomy for early gastric cancer were analyzed. The incidence of anemia was 24.5% at 3 mo after surgery and increased up to 37.1% at 48 mo after surgery. The incidence of iron deficiency anemia increased during the follow up and became the major cause of anemia at 48 mo after surgery. Anemia of chronic disease and megaloblastic anemia were uncommon. The incidence of anemia in female patients was significantly higher than in male patients at 12 (40.0% vs 22.0%, $P = 0.033$), 24 (45.0% vs 25.0%, $P = 0.023$), 36 (55.0% vs 28.0%, $P = 0.004$), and 48 mo (52.0% vs 31.0%, $P = 0.022$) after surgery. Patients with total gastrectomy showed significantly higher incidence of anemia than patients with subtotal gastrectomy at 48 mo after surgery (60.7% vs 31.3%, $P = 0.008$). The incidence of iron deficiency was significantly higher in female patients than in male patients at 6 (35.4% vs 13.3%, $P = 0.002$), 12 (45.8% vs 16.8%, $P < 0.001$), 18 (52.1% vs 22.3%, $P < 0.001$), 24 (60.4% vs 20.9%, $P < 0.001$), 36 (62.5% vs 29.2%, $P < 0.001$), and 48 mo (66.7% vs 34.7%, $P = 0.001$) after surgery.

CONCLUSION: Anemia was frequent after gastrectomy for early gastric cancer, with iron deficiency being the major cause. Evaluation for anemia including iron status should be performed after gastrectomy and appropriate iron replacement should be considered.

© 2012 Baishideng. All rights reserved.

Key words: Gastrectomy; Stomach neoplasms; Anemia; Iron deficiency; Vitamin B₁₂ deficiency

Peer reviewer: Luigi Bonavina, Professor, Department of Surgery, IRCCS Policlinico San Donato, Piazza Malan, 20097 Milano, Italy

Lim CH, Kim SW, Kim WC, Kim JS, Cho YK, Park JM, Lee IS, Choi MG, Song KY, Jeon HM, Park CH. Anemia after gastrectomy for early gastric cancer: Long-term follow-up observational study. *World J Gastroenterol* 2012; 18(42): 6114-6119 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v18/i42/6114.htm> DOI: <http://dx.doi.org/10.3748/wjg.v18.i42.6114>

INTRODUCTION

Gastric cancer is the most common malignancy in Korea and the second most frequent cause of cancer-related death worldwide^[1,2]. Curative resection has proven to be the only successful treatment modality for locally confined gastric cancer^[3]. Anemia is a frequent complication after gastrectomy and deficiencies of iron, vitamin B₁₂, or folate, either alone or in combination, have been reported after gastric surgery^[4-6]. However, these studies included relatively small numbers of patients, follow-up visits were not systematically scheduled, and the definition and biochemical markers of anemia were ambiguous or insufficient. There are limited reports concerning anemia in patients who undergo gastrectomy for early gastric cancer who have systematically scheduled serial follow-up visits, but do not receive supplements for anemia.

The incidence of gastric bypass surgery for morbid obesity is increasing, and anemia after bypass surgery has been reported^[7-11]. Dietary life after gastric surgery in patients with gastric cancer may differ from that in patients with morbid obesity: in contrast to patients with obesity, patients having gastrectomy for gastric cancer do not restrict their dietary intake for weight reduction. The aim of this study was to identify the natural history of anemia after gastrectomy in a cohort of patients undergoing gastrectomy for early gastric cancer who were systematically followed up in the long term.

MATERIALS AND METHODS

Study population

This study was a retrospective chart review of the registry of all patients who had undergone gastrectomy for early gastric cancer at Seoul St Mary's Hospital, Seoul, Korea between January 2006 and October 2007. Patients with anemia in the preoperative workup, cancer recurrence, undergoing systemic chemotherapy, with other medical conditions that can cause anemia, or treated during follow up with red cell transfusions or supplements for anemia were excluded from the study.

Follow-up program

Patients with early gastric cancer were followed up at 3, 6, 9, 12, 18, 24, 48 and 60 mo after surgery. The follow-up

program consisted of interim history taking, physical examination, imaging studies, endoscopic examination, hematology, and blood chemistry panels. Mean cell volume (MCV), serum iron, serum ferritin, total iron-binding capacity, serum vitamin B₁₂, and serum folate level were included in the follow-up program.

Definition of anemia and related conditions

Anemia was defined by World Health Organization criteria (Hb <12 g/dL in women and <13 g/dL in men)^[9]. Iron deficiency was defined as serum ferritin < 20 µg/dL. Vitamin B₁₂ deficiency was defined as serum vitamin B₁₂ < 200 pg/mL. Iron deficiency anemia was defined as anemia with concomitant iron deficiency. Anemia of chronic illness was defined as anemia with serum ferritin > 20 µg/dL. Anemia from vitamin B₁₂ deficiency was defined as megaloblastic anemia (MCV >100 fL) with vitamin B₁₂ deficiency.

Statistical analysis

Continuous data are presented as the mean ± SD and categorical data are presented as proportions. The data were analyzed using the paired *t* test to assess the differences in continuous data during follow up and a χ^2 test or Fisher's exact test to assess the differences according to sex and the type of gastrectomy. Differences were considered significant if the *P* value was less than 0.05. All statistical analysis were performed using SAS software (SAS Institute, Cary, NC, United States).

RESULTS

Four hundred fifty-eight patients with early gastric adenocarcinoma underwent curative gastrectomy in our institution during the study period. Of these, 297 were excluded from the analysis (anemia in preoperative workup in 45 patients, systemic chemotherapy in 79, other medical conditions that can cause anemia in 13, follow-up loss in 86, insufficient biochemical profile for anemia in 73, red cell transfusion during the follow-up in one). Finally, 161 patients undergoing gastrectomy for early gastric cancer were analyzed. No patient in the study population received iron or vitamin B₁₂ replacement therapy. Follow-up after surgery was possible at 3 mo in 159, 6 mo in 161, 12 mo in 161, 18 mo in 160, 24 mo in 158, 36 mo in 154, and 48 mo in 142.

The characteristics of the study population are shown in Table 1. The mean age was 56.2 ± 10.9 years (range, 23-78 years) and 113 patients were men (70.2%). Thirty-nine (24.2%) patients underwent Billroth I subtotal gastrectomy, 90 (55.9%) Billroth II subtotal gastrectomy, and 32 (19.9%) total gastrectomy.

The incidence of anemia was 24.5% at 3 mo after surgery and increased to 37.1% at 48 mo after surgery. The incidence of iron deficiency anemia increased during the follow-up and became the major cause of anemia at 48 mo after surgery (Figure 1). Anemia of chronic disease and megaloblastic anemia were uncommon. Only one

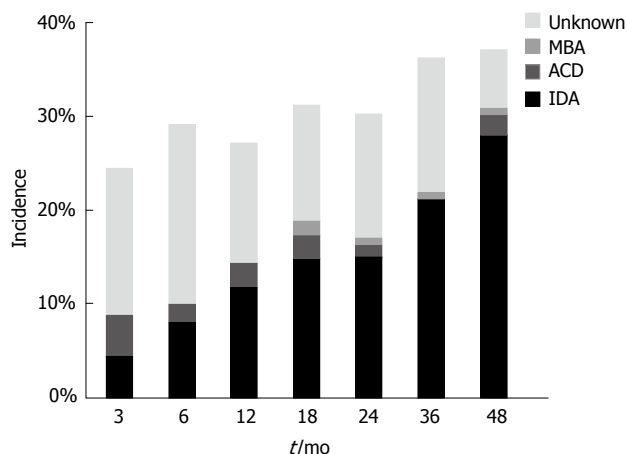


Figure 1 Incidence and distribution of anemia after gastrectomy. IDA: Iron deficiency anemia; ACD: Anemia of chronic disease; MBA: Megaloblastic anemia.

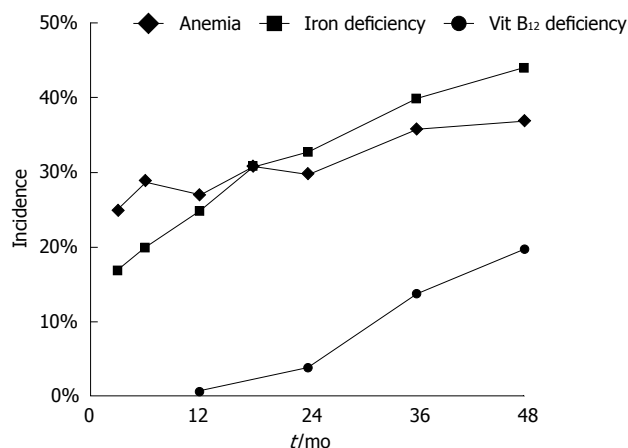


Figure 2 Incidence of anemia, iron deficiency state, and vitamin B₁₂ deficiency state after gastrectomy.

Variable	Value n (%)
Age (yr) ¹	56.2 ± 10.9
Gender	
Male	113 (70.2)
Female	48 (29.8)
Preoperative hemoglobin (g/dL) ¹	14.2 ± 1.1
Male	14.6 ± 0.9
Female	13.2 ± 0.8
Combined disease	
Hypertension	20 (12.4)
Diabetes mellitus	19 (11.8)
Pulmonary disease	2 (1.2)
Coronary artery disease	2 (1.2)
Chronic liver disease	2 (1.2)
Type of operation	
Billroth I subtotal gastrectomy	39 (24.2)
Billroth II subtotal gastrectomy	90 (55.9)
Total gastrectomy	32 (19.9)
Nodal Stage	
N0	143 (88.8)
N1	15 (9.4)
N2	2 (1.2)
N3	1 (0.6)

¹Data are presented as mean ± SD.

patient had a picture consistent with megaloblastic anemia with vitamin B₁₂ deficiency at 48 mo after surgery. The incidence of anemia, iron deficiency, and vitamin B₁₂ deficiency increased during follow-up after surgery (Figure 2). The incidence during follow-up of iron deficiency without anemia was considerable. Most vitamin B₁₂ deficiency occurred in patients who had total gastrectomy. At 48 mo after gastrectomy, the incidence of vitamin B₁₂ deficiency was 3.2% in patients with Billroth I subtotal gastrectomy, 7.5% in Billroth II subtotal gastrectomy, and 76.9% in total gastrectomy. The incidence of vitamin B₁₂ deficiency in patients with total gastrectomy was 0%, 16.1%, 50.0% and 76.9% at 12, 24, 36 and 48 mo after gastrectomy, respectively.

Serial follow-up hematology and blood chemistry data are shown in Table 2. Hemoglobin level, serum

ferritin level, and vitamin B₁₂ level decreased during the follow-up. The average serum albumin level was 3.3 ± 0.4 g/dL before surgery and recovered to 4.2 ± 0.3 g/dL at 3 mo after surgery.

The incidence of anemia in female patients was significantly higher than in male patients at 12 mo, 24 mo, 36 mo, and 48 mo after surgery (Figure 3A). Patients with total gastrectomy showed significantly higher incidence of anemia at 48 mo after surgery than patients with subtotal gastrectomy (60.7% *vs* 31.3%, *P* = 0.008) (Figure 3B). There was no significant difference in the incidence of anemia 48 mo after surgery between patients having Billroth I and Billroth II subtotal gastrectomy (18.8% *vs* 36.1%, *P* = 0.078). The incidence of iron deficiency was also significantly higher in female patients than in male patients at all times in the follow-up period except at 3 mo after surgery (Figure 3C). The incidence of iron deficiency was significantly higher in patients with total gastrectomy than those with subtotal gastrectomy only at 36 mo after surgery (58.1% *vs* 35.0%, *P* = 0.024) (Figure 3D). There was no significant difference in the incidence of anemia and iron deficiency between patients with Billroth I and II subtotal gastrectomy at 48 mo after surgery (28.1% *vs* 45.8%, *P* = 0.095).

DISCUSSION

In this study, we identified the incidence and etiology of anemia after gastrectomy in a cohort of patients having gastrectomy for gastric cancer who were systematically followed up over the long term. We found that the incidence of anemia in the patients with gastrectomy increased during follow-up. Iron deficiency anemia became the major cause of anemia after gastrectomy, and megaloblastic anemia with vitamin B₁₂ deficiency was rare.

In this study, anemia was relatively frequent after gastrectomy for early gastric cancer. Anemia was detected shortly after surgery and increased during the follow-up period. The incidence of anemia was 24.5% at 3 mo after surgery and increased to 37.1% at 48 mo after surgery. Anemia has been reported to occur in up to 60% of

Table 2 Biochemical marker after gastrectomy

	Before surgery	3 mo	6 mo	12 mo	18 mo	24 mo	36 mo	48 mo
Hemoglobin (g/dL)	14.2 ± 1.1	13.4 ± 1.2	13.3 ± 1.2 ^a	13.4 ± 1.3	13.2 ± 1.3 ^a	13.2 ± 1.4 ^a	13.1 ± 1.5 ^a	13.1 ± 1.6 ^a
Serum ferritin (μg/L)		70.8 ± 59.1	63.9 ± 52.4 ^a	55.2 ± 43.4 ^a	49.3 ± 51.3 ^a	43.3 ± 46.0 ^a	34.7 ± 32.2 ^a	33.7 ± 30.7 ^a
Serum vitamin B ₁₂ (pg/mL)				1167.7 ± 597.6		1113.9 ± 629.4	773.7 ± 999.9 ^c	560.3 ± 472.9 ^c
Serum albumin (g/dL)	3.3 ± 0.4	4.2 ± 0.3	4.2 ± 0.4	4.3 ± 0.3	4.3 ± 0.3	4.3 ± 0.3	4.3 ± 0.3	4.3 ± 0.3

^a*P* < 0.05 vs 3 mo; ^c*P* < 0.05 vs 12 mo.

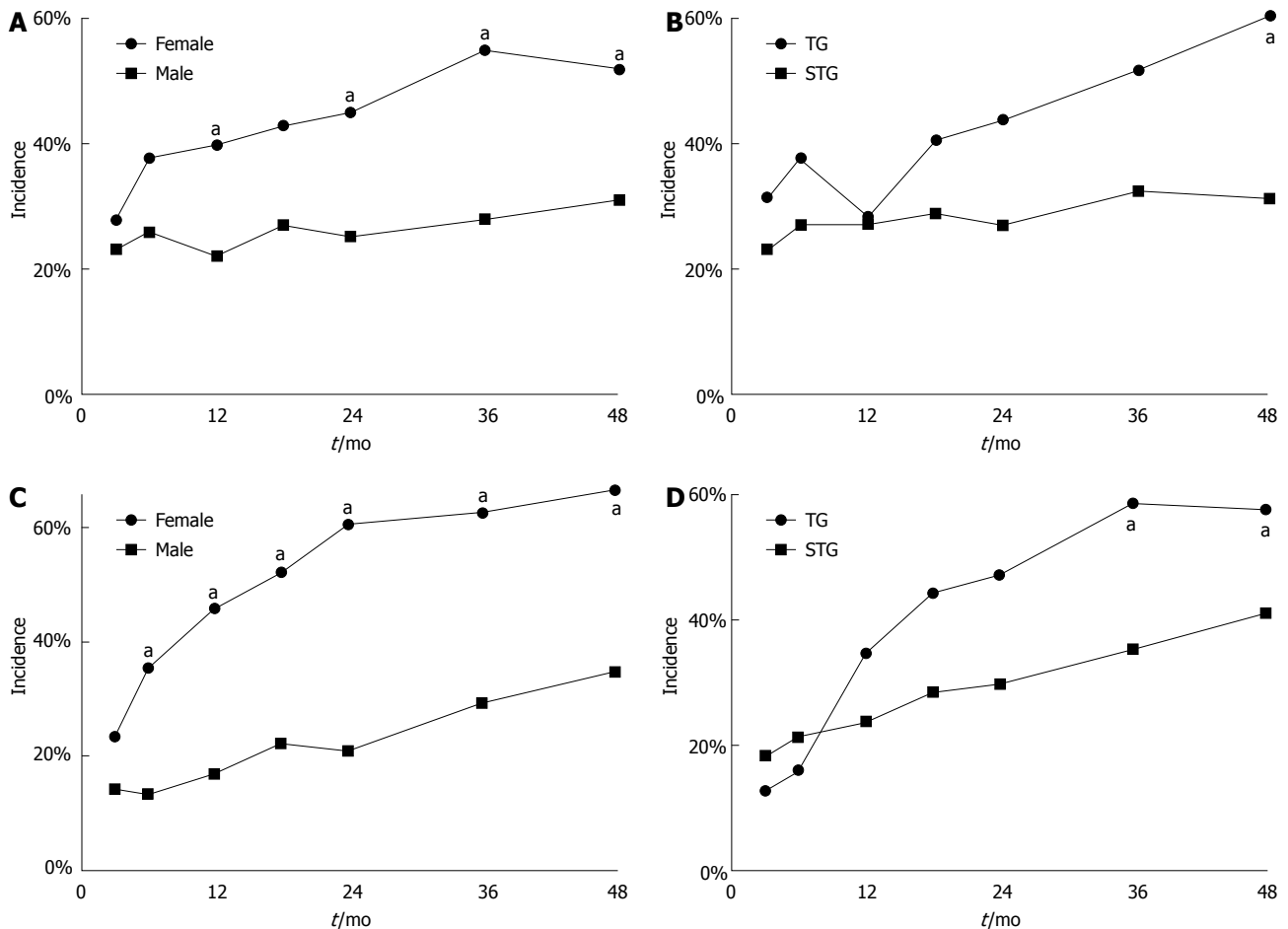


Figure 3 Incidence of anemia and deficiency state after gastrectomy. A: Significantly higher incidence of anemia in female patients than in male patients at 12, 24, 36 and 48 mo after surgery, ^a*P* < 0.05 vs female group; B: Significantly higher incidence of anemia in patients with total gastrectomy (TG) than in patients with subtotal gastrectomy (STG) at 48 mo after surgery, ^a*P* < 0.05 vs STG group; C: Significantly higher incidence of iron deficiency state in female patients than in male patients at all times in the follow-up period except at 3 mo after surgery, ^a*P* < 0.05 vs male group; D: Significantly higher incidence of iron deficiency in patients with TG than in patients with STG at 36 mo after surgery, ^a*P* < 0.05 vs STG group.

patients after partial gastrectomy^[12,13]. The incidence of anemia after bypass surgery has been reported as from 5% to 64%^[7-9,14-17]. A recent study of postsurgical anemia after gastrectomy reported that the incidence of anemia was 37.9%, 33.5% and 34.7% at 3, 6 and 12 mo after surgery, respectively^[18].

Our study showed that iron deficiency anemia increased during follow-up and was the major cause of anemia at 48 mo after surgery. Serial follow-up showed that serum ferritin gradually decreased from 70.8 μg/L to 30.1 μg/L during follow up and the incidence of iron deficiency gradually increased to 44% at 48 mo after gastrectomy. Our results are similar to those of a previous

study of patients after Roux-en-Y gastric bypass^[19]. Iron deficiency anemia was reported to be very common in post-gastrectomy patients at twenty five to thirty years after surgery^[20]. Iron deficiency after gastrectomy or bypass results from malabsorption of iron because of a surgically altered gastrointestinal tract. Inadequate oral intake or occult blood loss may also contribute to this condition. Iron is absorbed in the duodenum and proximal jejunum and its absorption is enhanced by gastric acid secretion. A lack of acidity results in impaired conversion of ingested ferric iron to absorbable ferrous iron^[21]. Duodenal bypass also contributes to iron deficiency in patients with gastrectomy or bypass surgery. Atrophic gastritis

and *Helicobacter pylori* infection were reported to play an important role in iron deficiency after gastrectomy for cancer of the stomach^[22]. In our study, the patients with Billroth I subtotal gastrectomy showed the lowest incidence of iron deficiency compared with all groups of patients with duodenal bypass (total gastrectomy and Billroth II subtotal gastrectomy) at 48 mo after surgery (28.1% vs 48.6%, $P = 0.045$). Our study showed a higher incidence of anemia and iron deficiency in patients with total gastrectomy than in those with subtotal gastrectomy. This difference may originate from the more depleted nutritional status of patients with total gastrectomy^[15,23,24]. In contrast to the subjects of other studies of severe obesity, our study population was patients with early gastric cancer and did not need weight reduction. They were recommended an adequate oral intake and serum albumin level was maintained at an adequate level. Therefore, our results show an etiology and natural course of postgastrectomy anemia that is close to reality.

The incidence of vitamin B₁₂ deficiency gradually increased to 20% of patients in our study at 48 mo after gastrectomy. The majority of the patients with vitamin B₁₂ deficiency at 48 mo were those with total gastrectomy. Vitamin B₁₂ deficiency causes megaloblastic anemia and neurological symptoms, and is known to develop within 5 or 6 years after total gastrectomy, a delay that reflects the time needed to exhaust cobalamin stores after cobalamin absorption ceases^[25]. Our study showed that 16.1%, 50.0% and 76.9% of the patients with total gastrectomy presented with vitamin B₁₂ deficiency at 24, 36 and 48 mo after gastrectomy, respectively. Although the incidence of vitamin B₁₂ deficiency at 48 mo after gastrectomy was high in our study, only one patient with vitamin B₁₂ deficiency presented with megaloblastic anemia. Because 70% of patients with vitamin B₁₂ deficiency at 48 mo after gastrectomy showed anemia and the majority of these were iron-deficient, the generation of macrocytosis by concomitant iron deficiency should be considered^[26]. Vitamin B₁₂ deficiency can develop within 2 years after total gastrectomy and vitamin B₁₂ replacement may be considered for post-gastrectomy patients with persistent anemia despite iron replacement or with neurological symptoms combined with vitamin B₁₂ deficiency.

Our study has some limitations. This study was a single-center retrospective study. The symptoms of anemia and other nutritional parameters such as body weight or body mass were not investigated. However, a strength of our study is the tightly controlled long-term follow-up of the patient cohort after gastrectomy for early gastric cancer, with systematically and prospectively scheduled serial follow-up visits and without any supplement for anemia. Our results enabled us to understand the development of post-gastrectomy anemia.

In conclusion, anemia was frequent after gastrectomy for early gastric cancer and iron deficiency was the major cause. Evaluation for anemia including iron status should be performed after gastrectomy and appropriate iron replacement should be considered.

COMMENTS

Background

Curative resection has proven to be the only successful treatment modality for locally confined gastric cancer. Anemia is a frequent complication after gastrectomy. The present study identified the natural history of anemia after gastrectomy in a cohort of patients undergoing gastrectomy for early gastric cancer who were systematically followed up in the long term.

Research frontiers

Anemia was frequent after gastrectomy for early gastric cancer, with iron deficiency being the major cause.

Innovations and breakthroughs

Anemia is a common complication of gastrectomy, particularly in female patients and it worsens as follow-up lengthens in a cohort with long-term follow-up for 48 mo. The incidence of iron deficiency gradually increased during follow up and became the major cause of anemia. Megaloblastic anemia is uncommon although the incidence of vitamin B₁₂ deficiency gradually increased after gastrectomy, particularly particularly after total gastrectomy.

Applications

The results of this study suggest that evaluation for anemia including iron status should be performed after gastrectomy and appropriate iron replacement should be considered.

Peer review

This study examined anemia in a large cohort of patients undergoing gastrectomy for early gastric cancer. The results of this study can serve as a benchmark in the follow up of patients undergoing partial or total gastrectomy for gastric carcinoma.

REFERENCES

- 1 **Shin HR**, Jung KW, Won YJ, Park JG. 2002 annual report of the Korea Central Cancer Registry: based on registered data from 139 hospitals. *Cancer Res Treat* 2004; **36**: 103-114
- 2 **Parkin DM**, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin* 2005; **55**: 74-108
- 3 **Song KY**, Park SM, Kim SN, Park CH. The role of surgery in the treatment of recurrent gastric cancer. *Am J Surg* 2008; **196**: 19-22
- 4 **Wastell C**. Malabsorptive states after gastrointestinal surgery. *Br Med J* 1968; **3**: 661-664
- 5 **Harju E**. Metabolic problems after gastric surgery. *Int Surg* 1990; **75**: 27-35
- 6 **Beyan C**, Beyan E, Kaptan K, Ifran A, Uzar AI. Post-gastrectomy anemia: evaluation of 72 cases with post-gastrectomy anemia. *Hematology* 2007; **12**: 81-84
- 7 **Skroubis G**, Sakellaropoulos G, Pougouras K, Mead N, Nikiforidis G, Kalfarentzos F. Comparison of nutritional deficiencies after Roux-en-Y gastric bypass and after biliopancreatic diversion with Roux-en-Y gastric bypass. *Obes Surg* 2002; **12**: 551-558
- 8 **Toh SY**, Zarshenas N, Jorgensen J. Prevalence of nutrient deficiencies in bariatric patients. *Nutrition* 2009; **25**: 1150-1156
- 9 **Cable CT**, Colbert CY, Showalter T, Ahluwalia R, Song J, Whitfield P, Rodriguez J. Prevalence of anemia after Roux-en-Y gastric bypass surgery: what is the right number? *Surg Obes Relat Dis* 2011; **7**: 134-139
- 10 **Amaral JF**, Thompson WR, Caldwell MD, Martin HF, Randall HT. Prospective hematologic evaluation of gastric exclusion surgery for morbid obesity. *Ann Surg* 1985; **201**: 186-193
- 11 **Beutler E**, Waalen J. The definition of anemia: what is the lower limit of normal of the blood hemoglobin concentration? *Blood* 2006; **107**: 1747-1750
- 12 **Hines JD**, Hoffbrand AV, Mollin DL. The hematologic complications following partial gastrectomy. A study of 292 patients. *Am J Med* 1967; **43**: 555-569
- 13 **Tovey FI**, Clark CG. Anaemia after partial gastrectomy: a neglected curable condition. *Lancet* 1980; **1**: 956-958

- 14 **Brolin RE**, Gorman JH, Gorman RC, Petschenik AJ, Bradley LJ, Kenler HA, Cody RP. Are vitamin B12 and folate deficiency clinically important after roux-en-Y gastric bypass? *J Gastrointest Surg* 1998; **2**: 436-442
- 15 **Braga M**, Molinari M, Zuliani W, Foppa L, Gianotti L, Radaelli G, Cristallo M, Di Carlo V. Surgical treatment of gastric adenocarcinoma: impact on survival and quality of life. A prospective ten year study. *Hepatogastroenterology* 1996; **43**: 187-193
- 16 **Vargas-Ruiz AG**, Hernández-Rivera G, Herrera MF. Prevalence of iron, folate, and vitamin B12 deficiency anemia after laparoscopic Roux-en-Y gastric bypass. *Obes Surg* 2008; **18**: 288-293
- 17 **Coupaye M**, Puchaux K, Bogard C, Msika S, Jouet P, Clerici C, Larger E, Ledoux S. Nutritional consequences of adjustable gastric banding and gastric bypass: a 1-year prospective study. *Obes Surg* 2009; **19**: 56-65
- 18 **Jeong O**, Park YK, Ryu SY. Prevalence, severity, and evolution of postsurgical anemia after gastrectomy, and clinicopathological factors affecting its recovery. *J Korean Surg Soc* 2012; **82**: 79-86
- 19 **Ruz M**, Carrasco F, Rojas P, Codoceo J, Inostroza J, Rebollo A, Basfi-fer K, Csendes A, Papapietro K, Pizarro F, Olivares M, Sian L, Westcott JL, Hambidge KM, Krebs NF. Iron absorption and iron status are reduced after Roux-en-Y gastric bypass. *Am J Clin Nutr* 2009; **90**: 527-532
- 20 **Tovey FI**, Godfrey JE, Lewin MR. A gastrectomy population: 25-30 years on. *Postgrad Med J* 1990; **66**: 450-456
- 21 **Jacobs A**, Miles PM. Role of gastric secretion in iron absorption. *Gut* 1969; **10**: 226-229
- 22 **Roviello F**, Fotia G, Marrelli D, De Stefano A, Macchiarelli R, Pinto E. Iron deficiency anemia after subtotal gastrectomy for gastric cancer. *Hepatogastroenterology* 2004; **51**: 1510-1514
- 23 **Bae JM**, Park JW, Yang HK, Kim JP. Nutritional status of gastric cancer patients after total gastrectomy. *World J Surg* 1998; **22**: 254-260; discussion 260-261
- 24 **Bozzetti F**, Ravera E, Cozzaglio L, Dossena G, Agradi E, Bonfanti G, Koukouras D, Gennari L. Comparison of nutritional status after total or subtotal gastrectomy. *Nutrition* 1990; **6**: 371-375
- 25 **Maclean LD**, Sundberg RD. Incidence of megaloblastic anemia after total gastrectomy. *N Engl J Med* 1956; **254**: 885-893
- 26 **Mahmud K**, Ripley D, Swaim WR, Doscherholmen A. Hematologic complications of partial gastrectomy. *Ann Surg* 1973; **177**: 432-435

S- Editor Gou SX L- Editor A E- Editor Lu YJ