

# A Prospective Evaluation of Adult Men with Iron-deficiency Anemia in Korea

Gak Won Yun<sup>1</sup>, Young Joon Yang<sup>2</sup>, Ik Chan Song<sup>1</sup>, Keon Uk Park<sup>3</sup>, Seung-Woo Baek<sup>1</sup>,  
Hwan Jung Yun<sup>1</sup>, Samyong Kim<sup>1</sup>, Deog Yeon Jo<sup>1</sup> and Hyo Jin Lee<sup>1</sup>

---

## Abstract

---

**Objective** Iron-deficiency anemia (IDA) is the most common nutritional deficiency worldwide. However, the information concerning various causes of IDA in adult men is still insufficient. The aim of our study was to evaluate adult men with IDA.

**Methods** We prospectively studied 206 adult men with IDA. All subjects had a direct history taken and underwent a physical examination. Esophagogastroduodenoscopy was performed in most patients, and colonoscopy was conducted if no lesion causing IDA was found or the fecal occult blood test was positive.

**Results** The history of prior gastrectomy and blood-letting cupping therapy that probably had caused IDA were reported in 24 (11.7%) and 11 (5.3%) patients, respectively. In terms of potential causes of IDA, 68 (33.0%) patients were found to have upper gastrointestinal disorders (34 peptic ulcers, 17 erosive gastritis, 16 gastric cancers, and one gastrointestinal stromal tumor). Colonoscopy showed 42 (20.4%) clinically relevant lesions that probably caused IDA: colon cancer (five patients), colon polyps (14 patients), ulcerative colitis (one patient), and hemorrhoids (22 patients). One small bowel tumor was detected at small bowel series. Concerning malignant lesions that were responsible for IDA, 22 malignant lesions were found in patients of 50 years or older, accounting for 16.8% (22 of 131 patients), while only one (1.3%) early gastric cancer was found in the younger patients.

**Conclusion** This study demonstrated that gastrointestinal blood loss is the main cause of IDA in adult men, and that there is a high rate of malignancy in men older than 50 years, emphasizing the need for a complete, rigorous gastrointestinal examination in this group of patients. Considering blood-letting cupping therapy, there is a need to consider culture-specific procedures as a possible cause of IDA.

**Key words:** iron deficiency anemia, adult men, gastrointestinal bleeding

(Intern Med 50: 1371-1375, 2011)

(DOI: 10.2169/internalmedicine.50.5289)

---

## Introduction

---

Iron deficiency is one of the most common disorders affecting humans, and it continues to be a major public health problem worldwide. There is an estimated 3.5 billion iron-deficient people in the world, with the majority in developing countries (1-3). The estimated prevalence of iron-deficiency anemia in adults ranges from 2 to 5%, although it varies widely depending on the population investi-

gated (4, 5). It is believed that iron-deficiency anemia generally results from chronic blood loss from the gastrointestinal tract or uterus and it is frequently a sign of serious underlying disease (6). Indeed, asymptomatic colonic and gastric cancer may present with iron-deficiency anemia and exclusion of these conditions is of great importance, whereas malabsorption, frequently due to celiac disease or gastrectomy, poor dietary intake, and non-steroidal anti-inflammatory drugs are other common possible causes (7-9). Consequently, appropriate management requires not only the

---

<sup>1</sup>Department of Internal Medicine, Chungnam National University School of Medicine, Korea, <sup>2</sup>Department of Internal Medicine, Daejeon St. Mary's Hospital, Korea and <sup>3</sup>Department of Internal Medicine, Dongsan Medical Center, Keimyung University School of Medicine, Korea  
Received for publication February 8, 2011; Accepted for publication March 23, 2011

Correspondence to Dr. Hyo Jin Lee, cymed@cnu.ac.kr

G.W.Y and Y.J.Y equally contributed to this work

**Table 1. Demographic Characteristics and Laboratory Data of the Patients with Iron Deficiency Anemia**

Total number of patients	206
Age (years)	
Median (range)	58 (18-86)
Prior gastrectomy* (%)	24 (11.7)
History of hemorrhoid (%)	31 (15.0)
Blood-letting cupping therapy* (%)	11 (5.3)
Hemoglobin (g/dL)	
Median (range)	7.8 (1.8-12.8)
Hematocrit (%)	
Median (range)	23.9 (6.5-41.3)
Serum ferritin (ng/mL)	
Median (range)	3.4 (0.1-35)
Serum iron (ug/dL)	
Median (range)	19 (4-141)
TIBC (mg/dL)	
Median (range)	459 (136-800)
FOBT (positive, %)	19 (9.2%)

FOBT, fecal occult blood test.

\*, that probably had caused iron deficiency anemia.

supplementation of adequate iron to replenish iron stores, but also meticulous investigations to identify the underlying cause in patients who are fit and willing to undergo further tests (6). Nevertheless, there is little information on the various causes of iron-deficiency anemia in adult men. This study prospectively evaluated adult men with iron-deficiency anemia.

## Patients and Methods

### Patients

Patients were referred from primary care and internal medicine clinics to the hematology section for the evaluation of anemia. The prospective study was conducted at Chungnam National University Hospital from January 2003 to December 2010.

Enrollment criteria included men  $\geq 18$  years old with iron-deficiency anemia giving informed written consent. The protocol was approved by the institutional review board. Anemia was defined as hemoglobin (Hb)  $< 13$  g/dL, using the World Health Organization criteria. Iron-deficiency anemia was considered to be present if the serum ferritin level was  $\leq 15$  ng/mL. In patients with iron-deficiency anemia plus inflammatory conditions, a serum ferritin  $< 50$  ng/mL associated with a red blood cell (RBC) mean cell volume (MCV) of 80 fL or less with a transferrin saturation  $< 10\%$  was considered diagnostic of iron-deficiency anemia.

### Evaluations

All subjects had an independent, direct history taken and underwent a physical examination. The history inquiry was regarding symptoms, such as fatigue, dyspnea on exertion,

and dizziness. A history of upper gastrointestinal tract symptoms, including dyspepsia, nausea, vomiting, early satiety, upper abdominal pain, dysphagia, heart burn, and lower gastrointestinal symptoms, including changes in bowel habits, constipation, diarrhea, bright red blood per rectum, and lower abdominal pain, was also obtained. All patients were also asked about blood-letting cupping therapy, aspirin use, and prior gastrointestinal disorders. All patients underwent a complete physical examination, including looking for traces of blood-letting cupping therapy and a fecal occult blood test (FOBT) of three spontaneously passed stools. All patients had laboratory analysis consisting of a complete blood count, serum iron and total iron-binding capacity, and a serum ferritin level. Most patients underwent esophagogastroduodenoscopy. Colonoscopy was performed if no lesion causing iron-deficiency anemia was found or the FOBT was positive. As an additional test, abdominal computed tomography (CT) or a small bowel series was performed at the clinician's discretion. Endoscopic procedures were performed by experienced gastroenterologists with standard hemodynamic monitoring. Clinically relevant lesions of chronic gastrointestinal blood loss as a cause of iron-deficiency anemia included cancer, adenomatous polyps  $\geq 1.5$  cm, vascular ectasia that numbered five or more or were at least 8 mm in diameter, severe erosive esophagitis or gastritis, single gastric or duodenal ulcer  $> 1$  cm in diameter, multiple gastric or duodenal ulcers  $> 0.5$  cm, hemorrhoids with bleeding or a history of recurrent bleeding, active colitis, or inflammatory bowel disease. Diverticula and esophageal varices were not considered to be sources of chronic gastrointestinal blood loss based on the study of Rockey and Cello (15).

### Statistical analysis

The categorical variables were analyzed using Fisher's exact test. *p* values  $< 0.05$  were considered to indicate statistical significance. All statistical analyses were conducted using the SPSS 13.0 software (SPSS, Chicago, IL).

## Results

We enrolled 206 patients who met the inclusion criteria. The median age was 58 (range 18-86) years. There were symptoms such as fatigue, dyspnea on exertion, dizziness, or digestive complaints in 178 of the 206 (86.4%) men with iron-deficiency anemia. Demographic and laboratory parameters of the patients are provided in Table 1. Twenty-one patients used aspirin or another non-steroidal anti-inflammatory drug regularly. A history of gastrectomy and hemorrhoids was reported in 24 and 31 patients, respectively. Eleven patients reported a history of repeated blood-letting cupping therapy, and typical signs were seen in some patients (Fig. 1). FOBT was positive in 9.2% of the subjects.

Table 2 summarizes the esophagogastroduodenoscopy (EGD) findings for the 184 (89.3%) patients who underwent



**Figure 1.** Characteristic traces of cupping performed on the neck and back.

EGD. The most common findings at EGD were gastritis (34 erosive gastritis and 18 chronic atrophic gastritis) and peptic ulcer (22 gastric ulcers and 13 duodenal ulcers). In terms of potential causes of iron-deficiency anemia, 68 patients were found to have upper gastrointestinal disorders (22 gastric ulcers, 17 erosive gastritis, 16 gastric cancers, 12 duodenal ulcers, and one gastrointestinal stromal tumor). In total, 104 (50.5%) patients underwent colonoscopy, which showed 42 clinically relevant lesions that probably caused iron-deficiency anemia: colon cancer (five patients), colon polyps (14 patients), ulcerative colitis (one patient), and hemorrhoids (22 patients; Table 3). A small bowel series and abdominal CT were conducted in 20 and 18 patients, respectively. Only one small bowel tumor was detected.

In terms of the cause of iron-deficiency anemia in this population, peptic ulcer was the most common cause of iron-deficiency anemia in adult men, followed by status of gastrectomy, gastrointestinal cancer, hemorrhoid, erosive gastritis, colon polyp, and blood-letting cupping therapy, in decreasing order (Table 4). Concerning malignant lesions that were responsible for iron-deficiency anemia, 23 (11.2%) malignant lesions were found in the population. When we separated the population into two groups using age 50 years as the cut-off, 22 malignant lesions were found in patients aged 50 years or older, accounting for 16.8% (22 of 131 patients), while only one (1.3%) early gastric cancer was found in the younger patients (Table 5).

## Discussion

In this prospective study, we found that chronic blood loss from the gastrointestinal tract was the main cause of iron-deficiency anemia in adult men (about 54%; 34 patients with peptic ulcer, 23 with gastrointestinal cancer, 22 with hemorrhoids, 17 with erosive gastritis, 14 with colon polyps, and one with ulcerative colitis; Table 4), and there was a higher rate of malignancy in men  $\geq 50$  years than in younger men (16.8% vs. 1.3%;  $p < 0.001$ ; Table 5), emphasizing the importance of a complete, rigorous gastrointestinal examination in this group of patients. It is necessary to

consider culture-specific procedures, such as blood-letting cupping therapy, and racial or geographical differences, such as the relatively high frequency of stomach cancer in Korea versus colon cancer in Western populations, when investigating possible causes of iron-deficiency anemia.

Although iron-deficiency anemia is a very common clinical problem, most studies have examined small, heterogeneous cohorts of patients with varying demographic and anemia parameters (10). The present study focused on men  $\geq 18$  years old to investigate the various causes of iron-deficiency anemia in a prospective fashion. More upper gastrointestinal tract lesions were detected than lower upper gastrointestinal tract lesions, similar to previous reports (11-18). The most common lesion causing iron-deficiency anemia was a peptic ulcer (34 of 206 patients; 22 gastric ulcers and 12 duodenal ulcers, comparable with other reports) (13-15). Prior gastrectomy, gastrointestinal cancer, hemorrhoids, erosive gastritis, colon polyps, and blood-letting cupping therapy were also causes of iron-deficiency anemia, in decreasing order. Regarding cancer, 23 cases of cancer (11.2%) were detected in our population, similar to previous reports of 7-28%; however, in our series, stomach cancer (16 cases) was more frequent than colon cancer (5 cases) compared with Western studies (12, 15, 16, 18). We suggest that the difference is due to the different incidence and prevalence of each cancer type in different regions: *i.e.*, stomach cancer is more common in East Asia, especially in Korea and Japan, suggesting special consideration of geographic or racial differences when we approach the patient with iron-deficiency anemia. Additionally, when we separated the patients according to age, 22 malignant lesions were found in those  $\geq 50$  years, accounting for 16.8% (22 of 131 patients), while only one younger patient was found to have early gastric cancer. These results suggest that a thorough, rigorous investigation of gastrointestinal cancer is needed in iron-deficiency anemia patients older than 50 years, consistent with other reports (10, 19).

Regarding hemorrhoids, Nikpour et al (20) reported that hemorrhoids are the most common (54.2% of the population) colonoscopic lesion in patients with minimal rectal bleeding. Park et al (21) also demonstrated that hemorrhoids with or without bleeding constitute the most prevalent (18.2% of the patients) lower gastrointestinal lesion in asymptomatic premenopausal women with iron-deficiency anemia. Additionally, hemorrhoids with bleeding as a cause of chronic blood loss were reported in about 6% of patients with iron-deficiency anemia (17, 22). Kluiber and Wolff (23) studied the incidence of hemorrhoidal bleeding that caused anemia in a stable population of patients seen at the Mayo Clinic and Olmsted Community Hospital in Rochester, Minnesota. Furthermore, Ibrahim et al (24) reported that hemorrhoids can cause substantial bleeding over long periods of time, suggesting that hemorrhoidal bleeding should be considered in the differential diagnosis of obscure gastrointestinal bleeding. In the present study, hemorrhoids were detected in 10.7% of the patients, reemphasizing it as

**Table 2. Esophagogastroduodenoscopic Finding (n=184)**

Finding	No. of patients	No. of potential cause of IDA
Reflux esophagitis	16 (8.7 %)	
Esophageal varix	7 (3.8 %)	
Chronic atrophic gastritis	18 (9.8 %)	
Erosive gastritis	34 (18.5 %)	17 (9.2 %)
Gastric ulcer	22 (12.0 %)	22 (12.0 %)
Angiodysplasia	3 (1.6 %)	
Gastric polyp	7 (3.8 %)	
Gastric cancer	16 (8.7 %)	16 (8.7 %)
GIST	1 (0.5%)	1 (0.5 %)
Duodenal ulcer	13 (7.1 %)	12 (6.5 %)

Severe erosive gastritis is considered a clinically relevant lesion of chronic gastrointestinal blood loss as a cause of iron-deficiency anemia. IDA, iron deficiency anemia; GIST, gastrointestinal stromal tumor

**Table 3. Colonoscopic Finding (n=104)**

Finding	No. of patients	No. of potential cause of IDA
Colon polyp	23 (22.1 %)	14 (13.5 %)
Angiodysplasia	1 (1.0 %)	
Non-specific colitis	3 (2.9 %)	
Diverticulosis	2 (1.9 %)	
Colon cancer	5 (4.8 %)	5 (4.8 %)
Hemorrhoid	24 (23.1 %)	22 (21.2 %)
IBD	1 (1.0 %)	1 (1.0 %)

IDA, iron deficiency anemia; IBD, inflammatory bowel disease

**Table 4. Potential Cause of Iron Deficiency Anemia in Adult Men (n=206)**

Order	Cause	No. of patients (%)
1	Peptic ulcer	34 (16.5)
	Gastric ulcer	
	Duodenal ulcer	
2	Gastrectomy	24 (11.7)
3	Gastrointestinal cancer	23 (11.2)
	Stomach cancer	
	Colon cancer	
	GIST	
	Small bowel tumor	
4	Hemorrhoid	22 (10.7)
5	Erosive gastritis	17 (8.3)
6	Colon polyp	14 (6.8)
7	Blood-letting cupping therapy	11 (5.3)
8	Inflammatory bowel disease	1 (0.5)

a potential cause of iron-deficiency anemia.

Blood-letting cupping therapy, which was detected in 5.3% of the patients, is often performed at acupuncture points, and always results in blood loss, in Eastern medicine. Thus, this therapy is capable of inducing iron-deficiency anemia if used over a prolonged period (25-27). For example, Lee et al (27) reported iron-deficiency anemia and Sohn et al (28) anemia-related cardiomyopathy induced by blood-letting cupping therapy, suggesting the need to consider culture-specific practices as possible causes of iron-

deficiency anemia.

In the present study, the cause of iron-deficiency anemia remained unidentified in 29% of the study population. This rate of negative work-ups is similar to previous studies, although each study had different definitions of clinically relevant lesion as a cause of iron-deficiency anemia and was conducted in a heterogenous cohort of the subjects with varying clinical parameters (11-18). For example, in our study, diverticula and esophageal varices were not considered to be sources of chronic gastrointestinal blood loss according to our predefined criteria which were based on the study of Rockey and Cello (15), although those lesions could cause chronic gastrointestinal blood loss. Additionally, those studies did not use small bowel capsule endoscopy or double-balloon enteroscopy, techniques that have revolutionized the management of patients with obscure gastrointestinal bleeding. The detection of lesions such as small intestinal angioectasia has become possible with the advent of capsule endoscopy, and such lesions can be treated with double-balloon enteroscopy. The use of these techniques will probably decrease the unresolved cases of iron-deficiency anemia in the future (29, 30). Considering the importance of history taking, in addition, we overlooked other possible causes of iron deficiency anemia such as a vegetarian diet and regular blood donation which could cause chronic blood loss (31).

In conclusion, this study demonstrated that gastrointestinal blood loss is the main cause of iron-deficiency anemia in



**Table 5. Malignant Cause of IDA in Adult Men According to Age**

Cause	Patients < 50 years (n=75)	Patients ≥ 50 years (n=131)	p value
Cancer (No)	74 (98.7 %)	109 (83.2%)	< 0.001
Cancer (Yes)	1 (1.3 %)	22 (16.8%)	
Stomach cancer	1	15	
Colon cancer	0	5	
GIST	0	1	
Small bowel tumor	0	1	

IDA, iron deficiency anemia; GIST, gastrointestinal stromal tumor

adult men, and that there is a high rate of malignancy in men older than 50 years, emphasizing the need for a complete, rigorous gastrointestinal examination in this group of patients. Considering blood-letting cupping therapy, there is a need to consider culture-specific procedures as a possible cause of iron-deficiency anemia of unknown cause.

**The authors state that they have no Conflict of Interest (COI).**

## References

- Alleyne M, Horne MK, Miller JL. Individualized treatment for iron-deficiency anemia in adults. *Am J Med* **121**: 943-948, 2008.
- Patel KV. Epidemiology of anemia in older adults. *Semin Hematol* **45**: 210-217, 2000.
- Killip S, Bennett JM, Chambers MD. Iron deficiency anemia. *Am Fam Physician* **75**: 671-678, 2007.
- Patterson RN, Johnston SD. Iron deficiency anaemia: are the British Society of Gastroenterology guidelines being adhered to? *Postgrad Med J* **79**: 226-228, 2003.
- Sayer JM, Long RG. A perspective on iron deficiency anaemia. *Gut* **34**: 1297-1299, 1993.
- Logan EC, Yates JM, Stewart RM, Fielding K, Kendrick D. Investigation and management of iron deficiency anaemia in general practice: a cluster randomised controlled trial of a simple management prompt. *Postgrad Med J* **78**: 533-537, 2002.
- Goddard AF, McIntyre AS, Scott BB. Guidelines for the management of iron deficiency anaemia. *British Society of Gastroenterology. Gut* **46** (suppl 3-4): IV1-IV5, 2000.
- Rasul I, Kandel GP. An approach to iron-deficiency anemia. *Can J Gastroenterol* **15**: 739-747, 2001.
- Pasricha SR, Flecknoe-Brown SC, Allen KJ, et al. Diagnosis and management of iron deficiency anaemia: a clinical update. *Med J Aust* **193**: 525-532, 2010.
- Niv E, Elis A, Zissin R, Naftali T, Novis B, Lishner M. Iron deficiency anemia in patients without gastrointestinal symptoms—a prospective study. *Fam Pract* **22**: 58-61, 2005.
- Cook IJ, Pavli P, Riley JW, Goulston KJ, Dent OF. Gastrointestinal investigation of iron deficiency anaemia. *Br Med J (Clin Res Ed)* **292**: 1380-1382, 1986.
- Zuckerman G, Benitez J. A prospective study of bidirectional endoscopy (colonoscopy and upper endoscopy) in the evaluation of patients with occult gastrointestinal bleeding. *Am J Gastroenterol* **87**: 62-66, 1992.
- Hsia PC, al-Kawas FH. Yield of upper endoscopy in the evaluation of asymptomatic patients with Hemoccult-positive stool after a negative colonoscopy. *Am J Gastroenterol* **87**: 1571-1574, 1992.
- McIntyre AS, Long RG. Prospective survey of investigations in outpatients referred with iron deficiency anaemia. *Gut* **34**: 1102-1107, 1993.
- Rockey DC, Cello JP. Evaluation of the gastrointestinal tract in patients with iron-deficiency anemia. *N Engl J Med* **329**: 1691-1695, 1993.
- Gordon SR, Smith RE, Power GC. The role of endoscopy in the evaluation of iron deficiency anemia in patients over the age of 50. *Am J Gastroenterol* **89**: 1963-1967, 1994.
- Kepeczyk T, Kadakia SC. Prospective evaluation of gastrointestinal tract in patients with iron-deficiency anemia. *Dig Dis Sci* **40**: 1283-1289, 1995.
- Reyes López A, Gómez Camacho F, Gálvez Calderón C, Miño Fugarolas G. Iron-deficiency anemia due to chronic gastrointestinal bleeding. *Rev Esp Enferm Dig* **91**: 345-358, 1999 (in Spanish).
- Ho CH, Chau WK, Hsu HC, Gau JP, You JY, Chen CC. Predictive risk factors and prevalence of malignancy in patients with iron deficiency anemia in Taiwan. *Am J Hematol* **78**: 108-112, 2005.
- Nikpour S, Ali Asgari A. Colonoscopic evaluation of minimal rectal bleeding in average-risk patients for colorectal cancer. *World J Gastroenterol* **14**: 6536-6540, 2008.
- Park DI, Ryu SH, Oh SJ, et al. Significance of endoscopy in asymptomatic premenopausal women with iron deficiency anemia. *Dig Dis Sci* **51**: 2372-2376, 2006.
- Park JS, Park DI, Park SK, et al. Endoscopic evaluation of significant gastrointestinal lesions in patients with iron deficiency with and without anaemia: a Korean Association for the Study of Intestinal Disease Study. *Intern Med J* **39**: 441-446, 2009.
- Kluiber RM, Wolff BG. Evaluation of anemia caused by hemorrhoidal bleeding. *Dis Colon Rectum* **37**: 1006-1007, 1994.
- Ibrahim AM, Hackford AW, Lee YM, Cave DR. Hemorrhoids can be a source of obscure gastrointestinal bleeding that requires transfusion: report of five patients. *Dis Colon Rectum* **51**: 1292-1294, 2008.
- Tham LM, Lee HP, Lu C. Cupping: from a biomechanical perspective. *J Biomech* **39**: 2183-2193, 2006.
- Iblher N, Stark B. Cupping treatment and associated burn risk: a plastic surgeon's perspective. *J Burn Care Res* **28**: 355-358, 2007.
- Lee HJ, Park NH, Yun HJ, Kim S, Jo DY. Cupping therapy-induced iron deficiency anemia in a healthy man. *Am J Med* **121**: e5-e6, 2008.
- Sohn IS, Jin ES, Cho JM, et al. Bloodletting-induced cardiomyopathy: reversible cardiac hypertrophy in severe chronic anaemia from long-term bloodletting with cupping. *Eur J Echocardiogr* **9**: 585-586, 2008.
- Rockey DC. Occult and obscure gastrointestinal bleeding: causes and clinical management. *Nat Rev Gastroenterol Hepatol* **7**: 265-279, 2010.
- Raju GS, Gerson L, Das A, Lewis B; American Gastroenterological Association. American Gastroenterological Association (AGA) Institute technical review on obscure gastrointestinal bleeding. *Gastroenterol* **133**: 1697-1717, 2007.
- Cook JD. Iron-deficiency anaemia. *Baillieres Clin Haematol* **7**: 787-804, 1994.