

# Men and postmenopausal women with iron deficiency had increased risk for gastrointestinal malignancy

Ioannou GN, Rockey DC, Bryson CL, Weiss NS. Iron deficiency and gastrointestinal malignancy: a population-based cohort study. *Am J Med.* 2002;113:276-80.

## QUESTION

Does iron deficiency, with or without anemia, increase the risk for gastrointestinal malignancy?

## DESIGN

Cohort study with 2 years of follow-up.

## SETTING

United States.

## PARTICIPANTS

9024 civilian, noninstitutionalized persons 25 to 74 years of age (60% women, 83% white) who participated in the National Health and Nutrition Examination Survey (NHANES I) and the NHANES I Epidemiologic Followup Study (NHEFS). Exclusion criteria were a history of cancer reported during NHANES I and missing iron saturation and hemoglobin measurements at baseline.

## ASSESSMENT OF

### RISK FACTORS

Baseline data were collected on iron deficiency (iron saturation < 15%) and anemia (hemoglobin level < 5th percentile for each age and sex group). Separate analyses were done for premenopausal women, men and postmenopausal women, age  $\geq 50$  years, and age  $\geq 65$  years. Within each group, participants were grouped into 4 diagnostic

categories based on their anemia and iron deficiency status.

## MAIN OUTCOME MEASURES

Diagnosis of gastrointestinal malignancy (i.e., any malignancy of the esophagus, stomach, small intestine, colon, or rectum) within 2 years of measurement of iron saturation and hemoglobin levels. Outcome assessors were blinded to iron saturation levels.

## MAIN RESULTS

716 participants (8%) were iron deficient; of these, 143 (1.6%) were also anemic. 18 participants (0.2%) had a diagnosis of gastrointestinal malignancy during the 2-year follow-up.

None of the 2708 premenopausal women had gastrointestinal malignancy at 2 years.

Men and postmenopausal women ( $n = 6227$ ) with iron deficiency alone ( $n = 223$ ) and iron deficiency anemia ( $n = 51$ ) had increased risk for gastrointestinal malignancy (Table). Similar results were found for persons  $\geq 50$  years of age ( $n = 4447$ ) and those  $\geq 65$  years of age ( $n = 2733$ ) (Table).

## CONCLUSION

Men and postmenopausal women with iron deficiency, with or without anemia, had increased risk for gastrointestinal malignancy at 2 years.

Source of funding: No external funding.

For correspondence: Dr. G.N. Ioannou, Veterans Affairs Medical Center, Seattle, WA, USA. E-mail georgei@medicine.washington.edu. ■

### Risk for gastrointestinal malignancy in persons with iron deficiency (ID) and ID anemia (IDA)

Group	Percentage	Relative risk (95% CI)*
Men and postmenopausal women		
ID vs control	1% vs 0.2%	5.0 (1.0 to 21)
IDA vs control	6% vs 0.2%	31 (9 to 107)
Age $\geq 50$ y		
ID vs control	1.3% vs 0.3%	5.0 (1.1 to 21)
IDA vs control	6% vs 0.3%	22 (6 to 78)
Age $\geq 65$ y		
ID vs control	2.3% vs 0.4%	6.0 (1.3 to 26)
IDA vs control	9% vs 0.4%	24 (7 to 81)

\*Control = patients without ID or IDA; CI defined in Glossary.

## COMMENTARY

In western countries, it is standard practice to recommend thorough gastrointestinal investigation for unexplained iron deficiency anemia in all patients, except some premenopausal women. The yield in terms of detection of serious conditions has been as high as 30% in some series. However, these studies were not population-based and primarily included selected cases referred to hospital, often with occult blood-positive stools (1). Recently, some clinicians have advocated investigation of iron deficiency in the absence of anemia, a condition that is far more prevalent than iron deficiency anemia (6.4% vs 1.6%) (2, 3).

Ioannou and colleagues took advantage of data collected in the NHANES on hemoglobin and iron status to examine the risk for gastrointestinal malignancy in patients with iron deficiency alone. As shown in the abstract table, risk for gastrointestinal cancer was greater than 5% only in patients with iron deficiency anemia. As expected, 13 of the 18 cases of cancer found were colorectal. All occurred in patients  $\geq 50$  years of age, and none occurred in premenopausal women. Although the relative risk for gastrointestinal cancer was increased in patients with iron deficiency without anemia, absolute risk was modest at 1% to 2.3% depending on the subgroup.

The study by Ioannou and colleagues provides firm evidence to support thorough gastrointestinal investigation in patients with iron defi-

ciency anemia. It also shows that investigation of patients incidentally found to be iron deficient (i.e., with no other indications of gastrointestinal disease) will have a low yield in terms of detection of gastrointestinal malignancy. Whether this low yield is sufficient to justify investigation will depend on the health care system and who is paying. As colorectal cancer screening is now recommended in some countries, such as the United States, perhaps the bottom line is that any person > 50 years of age found to be iron deficient should be encouraged to have a colonoscopy as part of routine colorectal cancer screening.

Richard F. Logan, MD  
University of Nottingham  
Nottingham, England, UK

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