IRON DEFICIENCY ANEMIA IS ASSOCIATED WITH COLORECTAL AND STOMACH CANCER DIAGNOSES IN GERMANY

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Background

Iron deficiency anemia (IDA) is the most common form of anemia globally, resulting in a high global burden of disease. It is caused by a decreased availability of iron for erythropoiesis. The WHO defines IDA as a reduction of the hemoglobin (Hb) concentration in the blood below the age- and sex-specific normal values of 12 g/dL in women or 13 g/dL in men (1).

Evidence suggests that IDA may be involved in the development, progression, and treatment of cancer, particularly in the gastrointestinal tract (2-4). For instance, Kepczyk and Kadakia (5) reported a relatively high prevalence of gastrointestinal cancer of 14% among patients undergoing endoscopy for IDA . However, these studies were conducted more than 20 years ago, and the prevalence might be overestimated due to strong patient selection.

The aim of the present study was to investigate the association between IDA and the incidence of colorectal and stomach cancer in a large German cohort. Strong emphasis was put on excluding patients with IDA due to bleeding as a symptom of gastrointestinal cancer.

Methods

The present study used data from the Disease Analyzer database (IQVIA) that contains demographic, diagnosis, and prescription data collected in general and specialized practices in Germany (6).

Patients aged ≥18 years with an initial IDA diagnosis (ICD-10: D50) between January 2005 and December 2021 (index date) made at one of 1,284 general practices (GPs) in Germany were included. Propensity score matching (1:1) was used to match individuals without an IDA diagnosis to IDA patients based on age, sex, index year, average yearly consultation frequency during follow-up, and predefined co-diagnoses. Patients with a cancer diagnosis prior to, at, or within six months after the index date were excluded.

Patients were followed until the first diagnosis of colorectal or stomach cancer within ten years of their initial IDA diagnosis. The 10-year cumulative incidence of colorectal and stomach cancer was compared between patients with and without IDA using cumulative incidence plots.

Finally, univariable Cox regression analysis was used to assess the association between IDA and colorectal as well as stomach cancer.

Results

The present study included 122,502 patients with IDA and 122,502 matched patients without IDA. Basic characteristics of included patients are displayed in **Table 1**.

Colorectal cancer: Within 10 years of follow-up, 1.4% of patients with IDA versus 0.8% of patients without IDA were diagnosed with colorectal cancer (**Figure 1**). In the regression analysis, there was a considerable association between IDA and subsequent colorectal cancer (HR: 2.05; 95% CI: 1.83 - 2.30). This association was strongest in the age group >80 and slightly stronger in men (**Table 2**).

Stomach cancer: Within 10 years of follow-up, 0.3% of patients with IDA versus 0.2% of patients without IDA were diagnosed with stomach cancer (**Figure 2**). The association between IDA and subsequent stomach cancer was weaker compared to the association for colorectal cancer (HR: 1.41; 95% CI: 1.13 - 1.75). This association was driven by the age group >80 and men (**Table 2**).

Conclusion

The results of the present study support the findings of other studies that report an association between IDA and gastrointestinal cancers. A major strength of this study is the exclusion of IDA due to gastrointestinal bleeding.

Since IDA affects a large proportion of the world's population, IDA treatment might play an important role in gastrointestinal cancer prevention.

Further research is needed to establish an immunologic cause model and to study the benefit of IDA treatment in the prevention of gastrointestinal cancer.

Table 1. Baseline characteristics of the study sample (after propensity score matching)

	Individuals with iron deficiency anemia (%) n = 122,502	Individuals without iron deficiency anemia (%) n = 122,502
Age		
mean, SD	54.2 (20.3)	54.2 (20.3)
≤ 50 years	47.9	47.3
51-60 years	12.3	12.9
61-70 years	11.8	11.9
71-80 years	15.7	15.6
>80 years	12.4	12.3
Sex		
Women	74.1	74.1
Men	25.9	25.9
Number of physician visits per year during follow-up (mean, SD)	8.0 (4.0)	8.0 (4.0)
Diagnoses documented within 12 months prior to or at index date		
Gastrointestinal ulcers	3.8	3.8
Gastritis	27.9	27.9
Diabetes	22.1	22.1
Obesity	13.1	13.1

Figure 1. Cumulative incidence of **colorectal cancer** in individuals with and without iron deficiency anemia

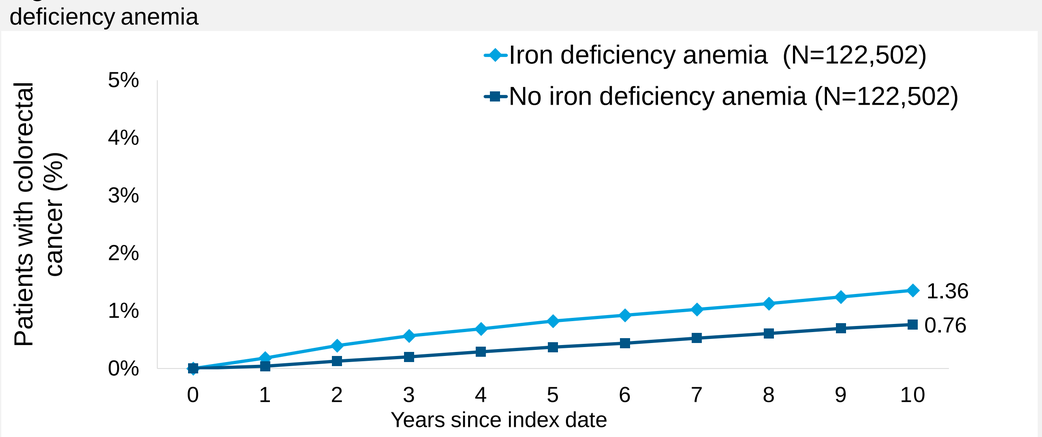

Figure 2. Cumulative incidence of **stomach cancer** in individuals with and without iron deficiency anemia

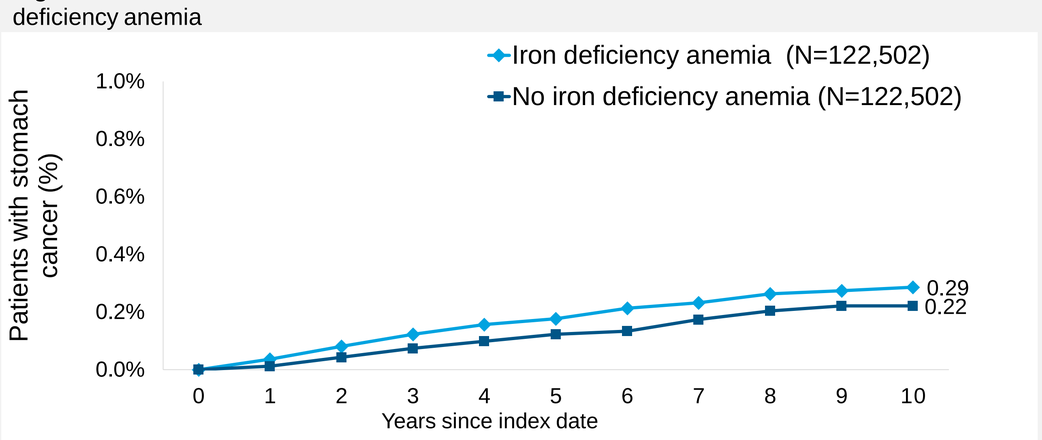

Table 2. Association between iron deficiency anemia and subsequent colorectal and stomach cancer in patients followed in general practices in Germany (univariable Cox regression models)

Subcohorts	Incidence per 1000 person years in individuals with iron deficiency anemia (%)	Incidence per 1000 person years in individuals without iron deficiency anemia (%)	HR (95% CI)
Colorectal cancer			
Total	1.5	0.7	2.05 (1.83-2.30)
≤ 50 years	0.3	0.2	1.69 (1.20-2.39)
51-60 years	1.1	0.7	1.48 (1.07-2.06)
61-70 years	2.4	1.1	2.12 (1.63-2.74)
71-80 years	3.8	1.9	2.00 (1.65-2.41)
>80 years	5.4	1.7	3.07 (2.39-3.95)
Women	1.2	0.6	2.01 (1.73-2.33)
Men	2.7	1.2	2.17 (1.82-2.59)
Stomach cancer			
Total	0.3	0.2	1.41 (1.13-1.75)
≤ 50 years	0.1	0.1	1.16 (0.65-2.08)
51-60 years	0.3	0.3	0.98 (0.57-1.70)
61-70 years	0.6	0.4	1.42 (0.88-2.28)
71-80 years	0.7	0.5	1.34 (0.91-1.97)
>80 years	1.1	0.4	2.73 (1.60-4.67)
Women	0.2	0.2	1.08 (0.80-1.46)
Men	0.8	0.4	1.90 (1.38-2.61)

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