Association Between Iron Therapies And Inflammatory Bowel Disease Progression In Patients With Iron Deficiency Anemia: A Retrospective Real-World Evidence Study In An Italian Setting

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Introduction

Inflammatory bowel diseases (IBDs) are characterized by several extra-intestinal symptoms, affecting 25–40% of patients [1]. **Anaemia** is a high incidence manifestation of IBD [2], and up to a half of anemic IBD patients (57%) were found to be iron deficient (**iron-deficiency anaemia**, IDA) [3]. Pharmacological treatment of IDA patients improves their quality of life, physical condition and alleviates fatigue and cognitive deficits [4]. Still, very few evidence on the beneficial effect of iron therapy in IBD progression and disease burden is available.

Objective

The present study aimed to evaluate the impact of iron-therapy supplementation in IBD patients with IDA in IBD disease progression and healthcare-resource consumption in real-world clinical practice.

Methods

A **retrospective study** was conducted using Italian entities' administrative databases, covering around 9.3 million health-assisted individuals. Across **01/01/2010-30/09/2017**, **adult IBD patients** [with a diagnosis for *ulcerative colitis and/or Crohn's Disease* (identified by at least one hospitalization with ICD-9-CM codes 556, 555 and/or active exemption codes 009.556, 009.555) and/or that have received at least one prescription for Vedolizumab (ATC code L04AA33)] were enrolled.

Among them, within 12 months from IBD diagnosis, **IDA was identified** by ≥1prescription for iron (ATC code B03A) and/or other anaemia treatments (ATC code B03XA) and/or IDA hospitalization (ICD-9-CM code 280) and/or blood transfusion (proxy of diagnosis, ICD-9-CM codes 99.0 and V58.2, specialistic code 99.07.1).

Based on the presence of an iron preparation prescription **during 12 month-period after the IDA inclusion date,** IBD-IDA patients were divided into two subgroups:

- **patients with iron preparation prescription**
- **patients without prescription of iron preparations.**

The Propensity Score Matching (PSM) methodology was applied to abate potential unbalances in baseline characteristics among the two cohorts. Before and after PSM, the IBD disease progression, healthcare-costs, healthcare-resource utilization were assessed during follow-up.

The present study has been approved by the Ethics Committee of each Region/Local Health Units involved in the analysis. The integration of administrative datasets makes it possible to represent the patient's entire clinical history and not just individual prescriptions. The analyses were conducted on exclusively anonymous data in full compliance with privacy regulations. Clicon s.r.l. has obtained the approval as per legislation by all the Ethics Committees to analyse these data. The results are exclusively in aggregated form and never attributable to a single institution, department, doctor, individual, or individual prescribing behaviours. The study was conducted in full compliance with current legislation for retrospective studies

Results

Overall, **1,753 IBD-IDA patients** were enrolled and sub-grouped in **untreated** (N=676, mean age 58.5 years, male 43%) and **iron-treated** (N=1,077, mean age 54.5 years, 45% male). Post-PSM, **676 patients were included in each cohort** (mean age 58 years), 43% and 42% were male (untreated and treated-cohort, respectively).

IBD PROGRESSION IN IBD-IDA PATIENTS TREATED OR NOT WITH IRON THERAPY

During the follow-up period, **the incidence of IBD-related hospitalization** was significantly **lower in patients receiving iron therapy** versus untreated ones (10.5% vs 14.3%, P<0.05) (**Table 1**); also, **in iron-treated patients**, **a slightly**, but not statistically significant **decrease of IBD-related surgical interventions** was found; the overall IBD progression, was significantly lower in patients under iron therapy versus the untreated cohort (11.0% vs. 15.7%, P<0.01) (Table 1). After applying PSM methodology, in IBD-IDA patients treated with iron therapy, the frequency of IBD-related hospitalization, IBD-related surgery and the overall IBD progression tended to be lower than that in the untreated group (Table 1).

Table 1. IBD progression during follow up period in IBD-IDA patients treated or not with iron therapy, before and after PSM

	Before PSM			After PSM		
	Without iron therapy	With iron therapy	P-value	Without iron therapy	With iron therapy	P-value
Patients, n	676	1,077		676	676	
IBD-related surgical interventions, n (%)	27 (4.0)	26 (2.4)	N.S.	27 (4.0)	19 (2.8)	N.S.
IBD-related hospitalizations, n (%)	97 (14.3)	113 (10.5)	<0.05	97 (14.3)	78 (11.5)	N.S.
IBD progression, n (%)	106 (15.7)	119 (11.0)	<0.01	106 (15.7)	83 (12.3)	N.S.

ESTIMATION OF HEALTHCARE RESOURCE CONSUMPTION AND COSTS

Figure 1. Mean annual health-care resource utilization during the follow up period in IBD-IDA patients treated or not with iron therapy. Before (A) and after (B) applying PSM methodology

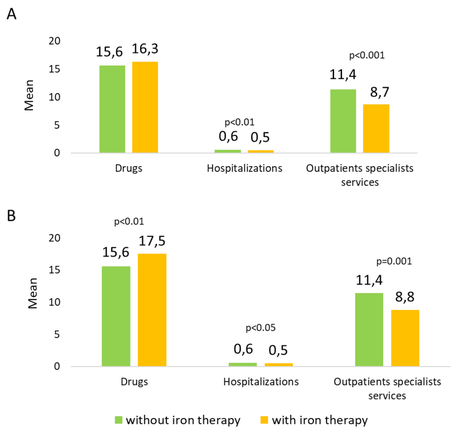
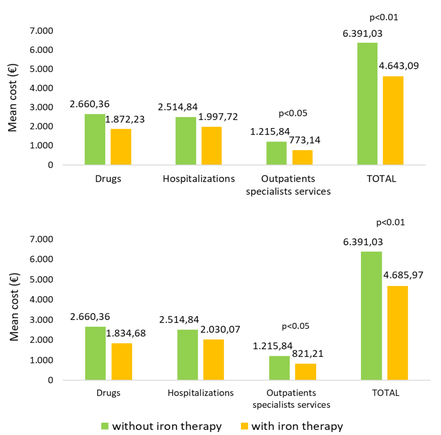


Figure 2. Mean annual costs during the follow up period in IBD-IDA patients treated or not with iron therapy. Before (A) and after (B) applying PSM methodology.



In **IBD-IDA patients receiving iron therapy**, a **significant reduction** of the mean annual **number of hospitalizations** (0.5 vs. 0.6, P<0.01) and **outpatient specialist service prescriptions** (8.7 vs. 11.4, P<0.001) was found, respect to untreated patients **(Figure 1A).** After applying the PSM methodology, the mean annual number of hospitalizations (0.5 vs. 0.6) and outpatient specialist services prescriptions (8.8 vs. 11.4) **were still significantly lower in patients** treated with iron therapy versus the counterpart cohort (**Figure 1B**).

In iron-treated versus untreated patients respectively, before applying the PSM methodology, the total healthcare costs were **4.643,09€ vs. 6.391,03€ (P<0.01),** during the follow-up period, were significantly lower (**Figure 2A**). The same trend was observed after PSM analysis (**Figure 2B**).

Conclusion

Several pieces of evidence support that treating anemia significantly improves the quality of life of anemic IBD patients, regardless of IBD symptoms [5]. The analysis of these real-world Italian data of IBD patients with a co-diagnosis of IDA has shown that supplementation with iron therapy could be associated with beneficial effects in terms of IBD disease progression and could restrain the healthcare-resource utilization and economic burden related to IBD disease.

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