

# Changes in admissions, and hospitalization outcomes of IBD patients in an Italian tertiary referral center over a 13-year period

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**Abstract. – OBJECTIVE:** The management of Inflammatory Bowel Disease (IBD) has changed significantly in recent years, mainly due to the introduction of biologic medications, however, other factors may also have a role. The aim of this study was to evaluate the evolution of IBD admissions, including trends, modality of admission and rates of surgical intervention, in a tertiary care center.

**PATIENTS AND METHODS:** Hospitalization of patients with a diagnosis of Crohn's disease (CD) or ulcerative colitis (UC) were identified between 2000 and 2013, using ICD-9-CM codes for IBD, from our hospital database. The following parameters were evaluated for each admission: type of admission (ordinary vs. day care service), mode of admission (elective vs. emergency care, for ordinary admissions only), admission code, surgical procedures and complication rates. Comparison between pre- and post-biologic therapy introduction years was also performed.

**RESULTS:** Between 2000 and 2013 a total of 8834 IBD-related admissions were recorded. Hospitalizations increased linearly reaching a peak in 2006, with a downward trend in the following years. The downward trend was especially marked for patients younger than 40 years. No significant differences in hospitalization trends between CD and UC were recorded. Disease

flare represented the cause of hospitalization in approximately 50% of cases. Overall, 10.8% of patients underwent surgery with no difference between the two conditions. Complications occurred in 28.7% of admissions.

**CONCLUSIONS:** Hospitalizations for IBD patients have decreased in recent years, especially in younger patients. However, a significant proportion of patients are still admitted to complete diagnostic workup, indicating the need to better implement outpatient services. A clear reduction in surgery occurrence over time could not be observed in our study.

*Key Words:*

Healthcare organization, Hospitalizations, Inflammatory bowel disease, Biologic therapy.

## Introduction

The management of inflammatory bowel disease (IBD), mainly ulcerative colitis (UC) and Crohn's disease (CD) has greatly evolved in recent years alongside increased incidence and prevalence rates of both conditions<sup>1</sup>. Most importantly, the introduction of biologic therapies has influenced the management of these diseases with a

possible impact on their natural history, especially in regard to hospitalization rates and the development of complications<sup>2</sup>. The recently published report by the Epidemiology Committee of ECCO evaluated in detail the impact of biologics on various outcomes of IBD, including a possible positive effect on hospitalization rates<sup>2</sup>. However, available studies on the matter are heterogeneous and it is difficult to provide definitive statements. Additionally, the indications for admissions are also likely to have changed over time. It is however recognized that other factors might have contributed to these changes, including the establishment of dedicated IBD units and the integrated management of patients by a multidisciplinary approach<sup>3</sup>. To our knowledge very few studies have addressed these issues, especially in Italy, and any available studies were conducted over short time frames<sup>4-6</sup>. In this study we sought to retrospectively assess the evolution of IBD admissions to our hospital between 2000 and 2013 in terms of number, indication and outcomes.

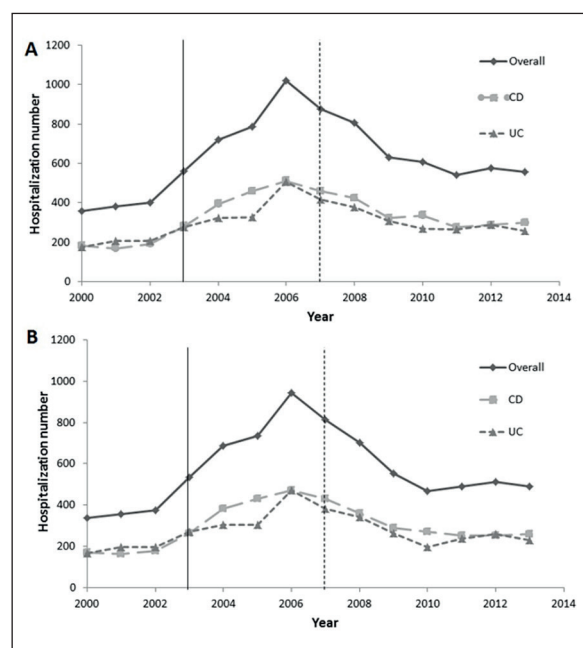
## Patients and Methods

All admission records between 2000 and 2013 were reviewed from the Policlinico “A. Gemelli” (Rome, Italy) databases ([Supplementary Table I](#)). Information was retrieved anonymously and analyzed. Hospital discharge records were reviewed and patients with an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code of IBD in at least one “diagnosis code” field were included. ICD9-CM codes 555.X and 556.X were used for CD and UC respectively.

Subsequently, for all identified IBD patients the following variables were assessed: type of admission (ordinary vs. day care service), mode of admission (elective vs. emergency care, for ordinary admissions only), admission code, surgical procedures carried out, and complication occurrence. Type and mode of admission, as well as surgery and complications were coded by the ICD-9-CM which were analyzed for every admission. For admission codes, based on the information provided by the chart code review, patients were stratified in 4 groups: “suspicion” of IBD, if the patient was admitted with symptoms suggestive of IBD but without a definite diagnosis, “flare”, if the admission was due to a relapse in known IBD patients, “complications”, in the case of IBD-related complications, and

“IBD-unrelated”, for IBD patients admitted for other diseases or conditions. Notably, all patients included in the analysis had a diagnosis of IBD at discharge. Complications, some directly related to IBD, were grouped as follow: (a) fistulae; (b) osteo-articular; (c) obstruction; (d) dermatological; (e) perforation; (f) hemorrhage; (g) toxic megacolon; (h) intestinal cancer; (i) extraintestinal cancer, (l) abscess; (m) stenosis; (n) infection; (o) sepsis; (p) other.

To evaluate whether the introduction of biologic therapies, mainly Infliximab and Adalimumab, has led to temporal changes in the variables, comparison between the pre- and -post biologic era was carried out. For CD the year 2003 was used as “cut-off” for pre- and post- biologic era, while for UC 2007 was used, as those were the years of introduction of biologics in Italy and at Fondazione Policlinico “A. Gemelli” (Rome, Italy). Infliximab administration, for approximately 3 years, was provided via elective hospitalization (mainly day care admission), requiring a 1-day hospital admission. A sub-analysis excluding 1-day admissions was performed (Figure 1B). This strategy has been used previously by other groups<sup>7</sup>.



**Figure 1.** A, Hospitalizations for Inflammatory bowel disease overall (solid) and stratified for disease, Crohn's disease (long dash) and Ulcerative colitis (short dash), between 2000 and 2013. Vertical lines show year of introduction of biologic therapy for Crohn's disease in 2003 (solid) and for Ulcerative Colitis in 2007 (dash); B, Same as Figure 1 excluding 1-day admissions.

**Table I.** Demographics and presentation of admitted patients.

Demographics	Overall	Crohn's disease	Ulcerative colitis	p-value
Admissions	8834	52.3%	47.7%	–
Sex (M/F)	51.9%/48.1%	51.8%/48.0%	52.0%/48.0%	NS†
Average age (years) (min; max)	44.9 (1; 105.6)	42 ± 15.6	47.6 ± 18	$p < 0.01^*$
Type of admission (%)				
Ordinary	85.1%	84.6%	85.8%	NS†
Day care	14.9%	15.4%	14.2%	
Mode of admission (%)				
Elective	83.4%	86.2%	80.4%	$p < 0.01^†$
Emergency care	16.6%	13.8%	19.6%	
Average number of admissions for single patients (n) (min; max)	9 (1; 53)	11 (1; 53)	6 (1; 51)	$p < 0.01^*$

†Chi Square Test; \*Unpaired *t*-test.

Statistical analysis was performed using the Chi2 test for qualitative variables and the unpaired *t*-test for quantitative variables. Statistical significance was defined as a *p*-value of less than 0.05.

## Results

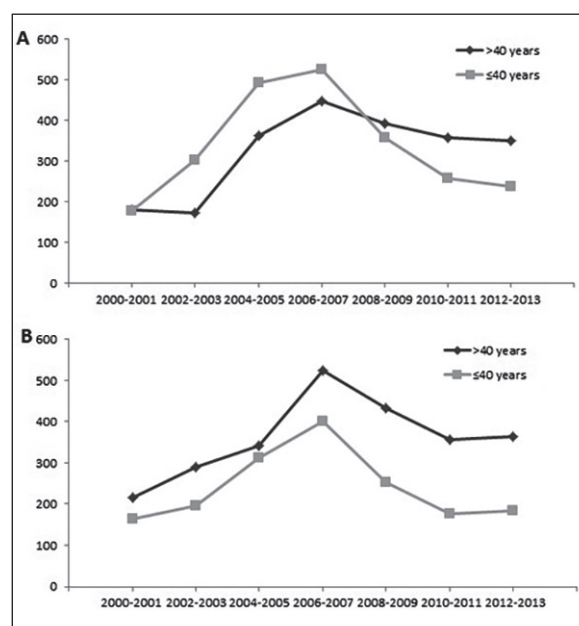
### Demographics

Between the years 2000 and 2013 a total of 8834 admissions were recorded at “Policlinico A. Gemelli IRCCS” (Rome, Italy) for patients with IBD, of which 52.3% and 47.7% were for CD and UC respectively. The total number of individual patients evaluated was 3861, as many patients were admitted more than once. Demographics are shown in Table I. Admission in patients with CD were slightly more frequent than in patients with UC, although this difference did not reach statistical significance. Of note, CD patients admitted to the hospital were approximately 5 years younger than UC patients ( $p < 0.05$ ). Hospitalizations due to IBD have increased since 2000, reaching a peak in 2006, with a downward trend in following years, and without great variability between CD and UC (Figure 1A). In particular, in 2006 a peak of 1020 hospitalizations for all IBD was recorded. In the years 2009-2013 hospitalizations ranged from 542 to 632, with the lowest number recorded in 2011. This trend does not seem to have been influenced by improvements in the organization of biologic therapy administration. Overall, 1-day admissions accounted for only 829 admissions (9.4% of total admissions), and a similar trend was observed in CD and UC patients when 1-day admissions were excluded from the analysis (Figure 1B). Age-specific hos-

pitalizations were also evaluated for both CD and UC (Figure 2), with a more evident decrease in admissions observed for patients younger than 40 years, especially in UC.

### Admission Modalities to the Hospital

Elective admission was the most common mode of admission, with day care accounting for approximately 15% of all admissions (Table I). Admission from the emergency department occurred in 16-20% of cases, being statistically more likely for UC than for CD ( $p < 0.05$ ) (Table I). As some patients were admitted more than



**Figure 2.** Hospitalizations stratified by age equal to or below 40 years and above 40 years for **A**, CD and **B**, UC patients.

once, we calculated that the average number of admissions per patient was 9 overall with an average of 11 admissions for CD, and 6 for UC (Table I). Interestingly, the admissions for individual patients were higher in the years 2003-2007 and then reduced in the subsequent years. CD patients had more admission days per single patient than UC ( $p<0.5$ ) (Table II). The overall admission days decreased over the years, being comparable in UC and CD, approximately 8-12 days per patient (Table II). Approximately 50% of patients, both UC and CD, were admitted for relapse of disease (Figure 3). Up to 30% of patients were admitted for suspicion of IBD, while only 10% were admitted for complications or unrelated reasons. No major differences in admission indication were found between day care, elective admission, and admission from the emergency department during any time period. Admissions for complications not related to IBD were more frequently observed in emergency department admission compared to elective admission ( $p<0.05$ ) (Figure 3). No major variations were observed in admission indication or modality when stratifying data from pre-biologic era and post-biologic era (Figure 3).

#### **Admission Outcomes**

Overall, 11% of the admitted patients underwent a surgical procedure (Table III). No major differences were found between UC and CD, however for UC patients, surgery was less likely during an admission from the emergency department ( $p<0.05$ ). No significant changes were found when patients were stratified between the pre and post biologic era. The majority of admitted patients had no complications (72.30% total, CD 68.39% vs. UC 74.51%). Stratification of complications has been reported in Figure 4. The most frequent complication for CD was the presence of fistulae (10.06%), followed by intestinal occlusion (5.13%), osteo-articular complication (5.13%) and extra-intestinal cancer (2.66%) (Figure 4A). The most frequent complication for UC was osteo-articular complications (6.60%), followed by extra-intestinal cancer (5.96%), hemorrhage (2.56%) and infection (1.87%) (Figure 4A). Toxic megacolon was reported in 0.04% of the cases (CD 0% vs. UC 0.07%) (Figure 4A). Intestinal cancer was relatively low, being 0.11% for CD and 0.78% for UC (Figure 4A). No major variations were observed in CD when data was stratified for the pre and post biologic era (Figure 4 B). No statistically significant differences

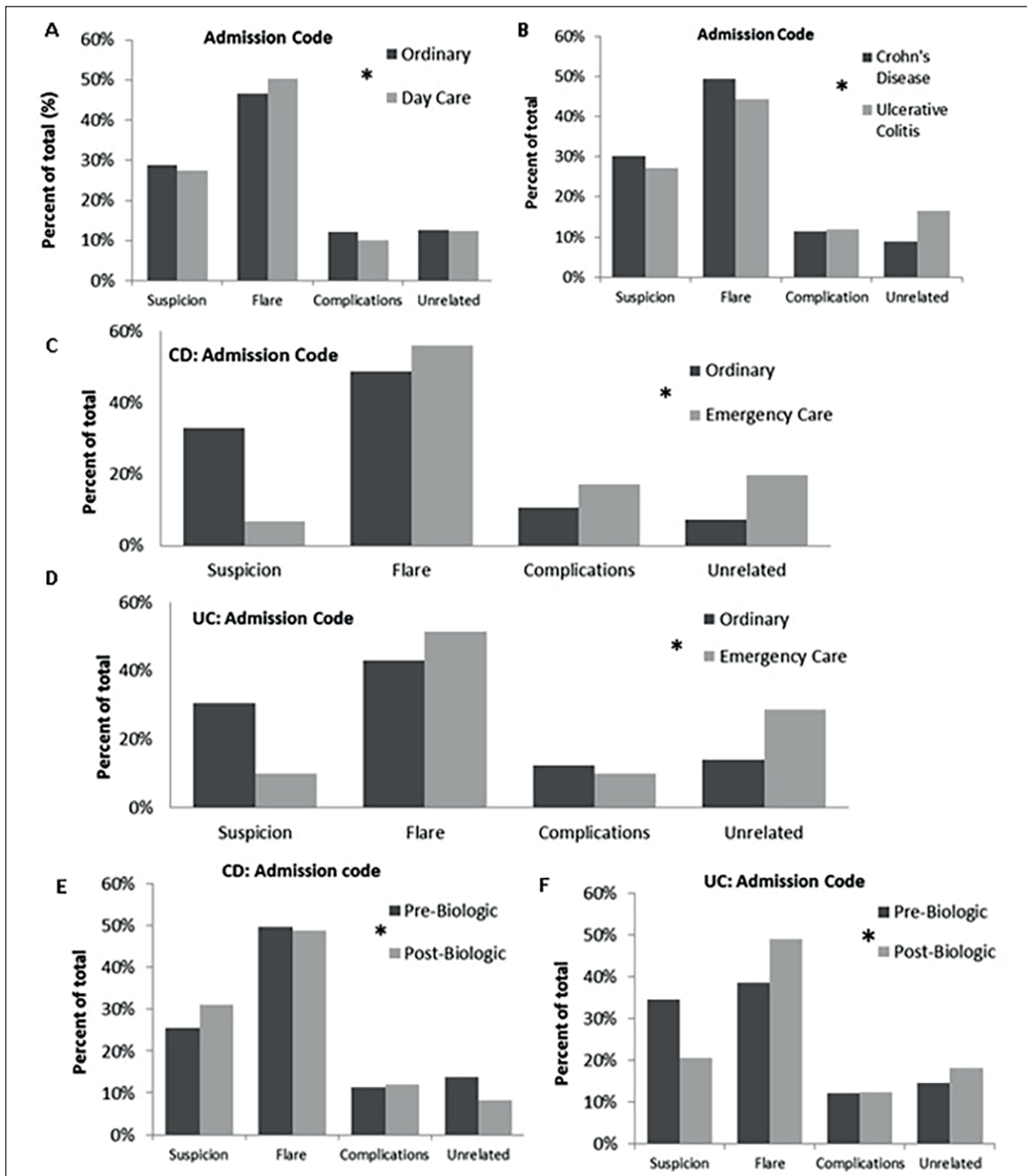
were found for UC, when data was stratified for the pre and post biologic era, however trends were observed showing a decrease in osteo-articular complications, and a slight rise in extra-intestinal cancer and hemorrhage (Figure 4C). Mortality was assessed for individual patients. Overall, 1.3% ( $n=50$ ) of patients received a discharge code of death, equally distributed between CD (25) and UC (25).

## **Discussion**

To the best of our knowledge, this study represents one of only few detailing this topic in Italy. A former study, published by Kohn et al<sup>5</sup>, analyzed mainly surgical outcomes and costs associated with admissions to the hospital in a selected cohort of patients. In contrast, our study is a descriptive study of the evolution of IBD admissions to a tertiary care hospital, and variations in the disease presentation over time. Furthermore, the study from Kohn et al<sup>5</sup> focused only on UC patients. Based on these important differences in the populations studied, these two studies are only partially comparable. Of note however, the rate of surgical interventions in the two studies is directly comparable, at approximately 10% of all admissions. Additionally, the overall length of admission is comparable, at approximately 10 days in both studies. In our study we found a 1.3% mortality rate for admitted IBD patients, with no difference between CD and UC. Sewell et al<sup>8</sup> analyzed more than 17,000 hospitalizations for IBD and found a mortality rate of 0.9%<sup>8</sup>. Rates of complications for IBD patients did not differ to what would be expected for the general IBD population; however, these results present more recent confirmatory data for clinical practice<sup>9</sup>. Finally, we found a significant decrease over time in hospitalization in patients below 40 years of age, especially in UC patients. In line with these findings, a recent study by Christian et al<sup>10</sup> analyzed predictors of early readmission for IBD patients, and found that readmitted patients were, on average, older in comparison to those not readmitted. In contrast, another study reported an increase in IBD hospitalizations which could not be attributed to age differences; however, this study was carried out during a different time period, between 1992 and 2003<sup>11</sup>. The present study highlights important considerations when comparing the Italian system to other healthcare systems. First, in Italy, for a long time, elective

**Table II.** Average hospital days and number of admissions for Crohn's disease and ulcerative colitis.

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
<b>Average Hospital Days</b>														
Overall (days)	11.7	11.1	11.3	9.2	9.0	8.9	7.0	8.2	8.7	9.4	9.0	11.4	11.3	9.5
Excluding 1d admissions	12.4	11.7	11.9	9.6	9.4	9.4	7.5	8.8	9.8	10.7	11.3	12.5	12.6	10.7
Crohn's Disease (days)	11.1	10.7	10.3	7.9	8.7	9.0	7.3	8.7	8.8	9.2	9.6	11.3	11.6	10.2
Excluding 1d admissions	11.9	11.5	11.1	8.4	9.0	9.6	7.9	9.2	10.2	10.3	11.7	12.3	13.0	11.7
Ulcerative Colitis (days)	12.4	11.4	12.2	10.5	9.4	8.6	6.8	7.6	8.6	9.6	8.3	11.5	11.0	8.6
Excluding 1d admissions	12.8	11.9	12.7	10.8	9.9	9.3	7.2	8.2	9.4	11.1	10.9	12.7	12.1	9.5
<b>Average number of admissions for single patients</b>														
Overall (n)	1.3	1.3	1.3	2.4	1.7	1.7	2.0	1.7	1.5	1.4	1.2	1.2	1.3	1.3
Crohn's Disease (n)	1.3	1.4	1.5	2.6	2.0	1.9	2.1	1.8	1.5	1.4	1.3	1.2	1.4	1.3
Ulcerative Colitis (n)	1.2	1.3	1.2	2.2	1.5	1.5	1.9	1.6	1.5	1.3	1.2	1.1	1.2	1.2



**Figure 3.** Admission to the hospital. **A**, Ordinary admissions (*dark grey*) and Day Care admissions (*light grey*) stratified for Admission Code. **B**, Admissions according to type of disease: CD (*dark grey*) and UC (*light grey*). **C**, CD: Ordinary admissions (*dark grey*) and Day Care admissions (*light grey*) stratified for Admission Code; **D**) UC: Ordinary admissions (*dark grey*) and Day Care admissions (*light grey*) stratified for Admission Code. **E**, and **F**, Pre-biologic era (*dark grey*) and Post-biologic era (*light grey*) admissions stratified for Admission Code for Crohn's disease (**E**) and Ulcerative Colitis (**F**). \* $p < 0.01$ .

admissions represented the primary modality of hospital admission. This may differ to other healthcare systems, where most admissions occur through the outpatient service as either urgent

admissions or via referral to the emergency department. Furthermore, admission to hospital to complete a diagnostic workup because of suspicion of IBD represents, in this cohort, up to 30%

**Table III.** Surgical outcome in IBD admissions.

	No Surgery	Surgery	<i>p</i> -value <sup>†</sup>
Overall	89.2%	10.8%	
Crohn's disease	89.0%	11.0%	
Ulcerative colitis	89.3%	10.7%	<i>p</i> = 0.675
Crohn's disease			
Elective	88.2%	11.8%	
Emergency care	85.7%	14.3%	<i>p</i> = 0.09
Ulcerative colitis			
Elective	87.1%	12.9%	
Emergency care	91.8%	8.2%	<i>p</i> < 0.01
Crohn's disease			
Pre-biologic era	88.5%	11.5%	
Post-biologic era	87.2%	12.2%	<i>p</i> = 0.672
Ulcerative colitis			
Pre-biologic era	89.0%	11.0%	
Post-biologic era	87.1%	12.9%	<i>p</i> = 0.07

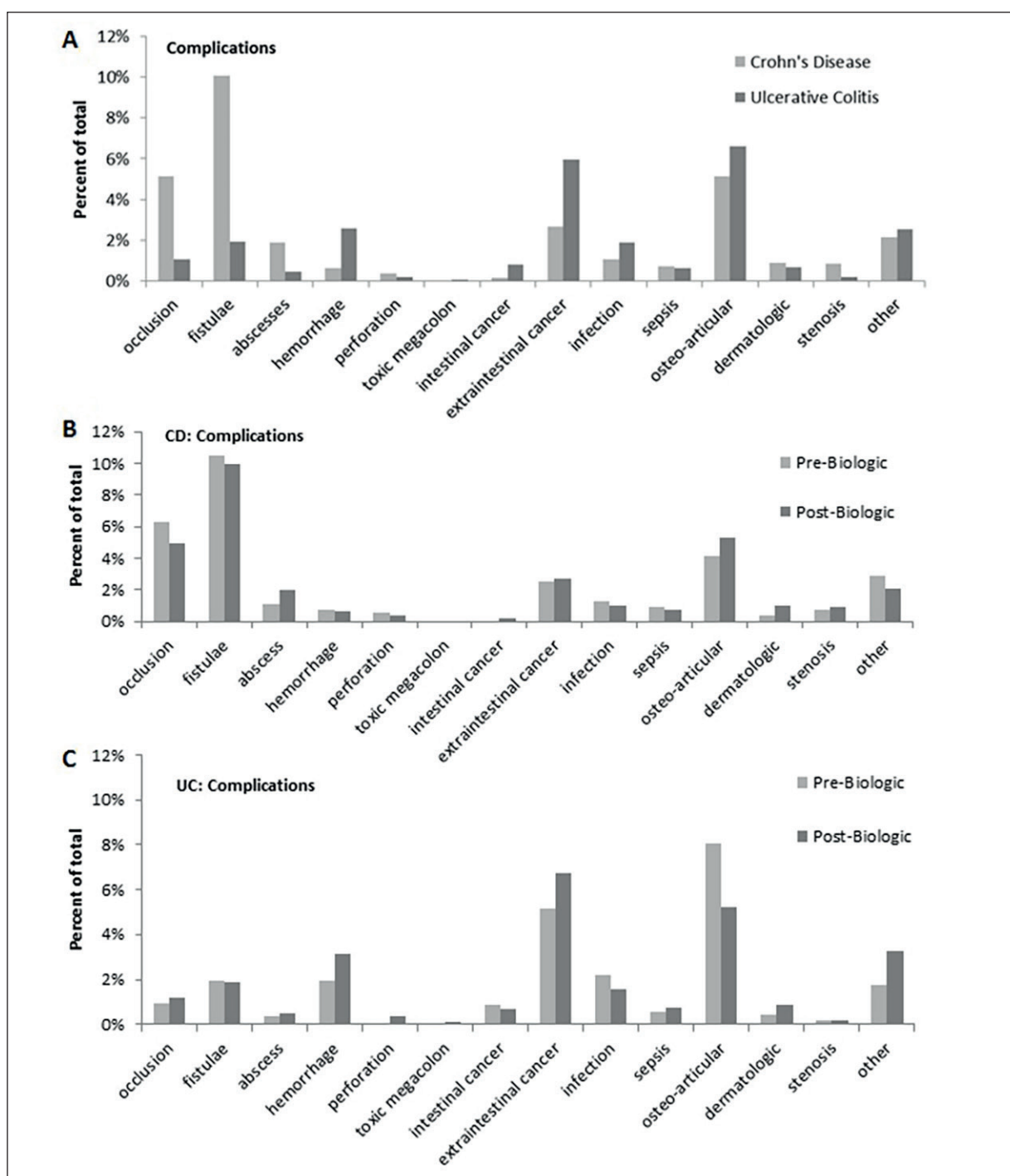
†Chi Square test.

of the cases, suggesting that outpatient resources were not implemented efficiently. In Italy, reimbursements for hospital admissions are calculated using the diagnosis-related group (DRG) system, whereas the outpatient clinic for IBD or other chronic diseases, has no real economic assessment system or a weighted reimbursement, other than the cost of each single outpatient attendance. Thus, the implementation of such units has been undertaken only recently, as a means of reducing hospital admission rates.

Our study showed that up to 50% of admissions for IBD occurred for disease flares, compared to 10% for IBD related complications, and 10% for reasons unrelated to IBD. No major variations were observed through the years in relation to admission indication. Of note, we found a rise in hospitalizations for IBD between 2003 and 2007. This is in line with reports from our regional healthcare system (unpublished data) and is mainly due to organizational strategies to manage patients undergoing biologic therapy. During this time as the outpatient service had not yet been implemented, elective hospitalization was required to administer biologic therapies, usually requiring a 1-day admission, which during this time period represented the principal modality of admission for these patients. However, we believe that the impact of this reorganization on the overall admission trend is not relevant, as shown by the sub analysis excluding 1-day admissions and as reported by other groups<sup>7</sup>.

No major decrease in admission were observed in the era of biologics in our cohort. Introduction of biologic therapy (infliximab) for CD in Italy

since 2003 did not seem to be correlated with an immediate decrease in hospitalizations. In fact, a clear decrease can only be observed from 2006. In contrast, most previous studies found a decrease in hospitalizations rates following introduction of biological therapy. Namely, Herrinton et al<sup>12</sup> found that the progressive increase in the use of infliximab was associated with a reciprocal decrease in IBD hospitalization rates, especially for CD. For UC, a downward trend was already present a year prior to the introduction of biologic therapy in 2007. Despite the contrast between this data and other previous reports, it could be argued that our study was not designed to assess the direct impact of biologic therapy on hospitalization rates of IBD patients, as they were not stratified for therapy received. Furthermore, the stable number of admissions of IBD patients observed, alongside significant organizational improvements in efficiency of the outpatient services, suggest that the overall population of IBD patients in our hospital is rising, in addition to the overall complexity of patients. The lack of outpatient data in our study represents a limitation, and future studies should address this issue to better clarify these results. In our study we did not find differences in rates of surgery between the pre and post biological era, in contrast to previous studies which mostly report a reduction in surgery rates in recent years<sup>13,14</sup>. However, another study has also reported no observed effect on rates of surgery attributable to biologic use<sup>4</sup>, meaning that at present, a direct role of biologics in the reduction of surgery is still a matter of debate<sup>15,16</sup>. A limitation of our



**Figure 4.** Complications diagnosed during the admission at hospital. **A**, Stratified for disease, Crohn's disease (*light grey*) and Ulcerative Colitis (*dark grey*). **B**, CD: stratified per time frame, pre-biologic era (*light grey*) and Post-biologic era (*dark grey*). **C**, UC: stratified per time frame, pre-biologic era (*light grey*) and Post-biologic era (*dark grey*) \* $p < 0.01$ .

study, due to its retrospective design, means that certain information, including the use of concurrent immunosuppressive therapy and other medications, was unavailable for comparison. As

a result, despite the temporal division in pre- and post-biological era, it is not possible to directly attribute observed changes to the introduction of biologic therapy. However, this study represents a



starting point towards a better understanding of the evolution of tertiary care admissions for IBD patients over time.

## Conclusions

The results of this study are of particular interest because they refer to the hospitalization of IBD patients over a decade in one of the largest Italian tertiary centers for the treatment of IBD. Data analysis suggests that a significant number of patients were hospitalized several times, especially in the first few years of data collection (from 2000 to 2006), likely due to the requirement for hospitalization for the reimbursement of the cost of biologic therapy (infliximab), by the Italian health system at that time. Fortunately, in following years biologic therapy was administered in an outpatient setting with a reduction in unnecessary hospitalizations. The average age of patients hospitalized with CD was significantly lower than patients with UC. The total number of admissions increased progressively until 2006 and then decreased reaching a plateau from 2009 to 2013, due to a significant number of hospitalizations required for diagnostic procedures not feasible on an outpatient basis. Interestingly, the hospitalization rate for IBD complications has not changed over the years and therefore does not seem to have been influenced by the introduction of anti-TNF- $\alpha$  therapy. No significant differences were observed in the frequency of surgical interventions during the study period, so an effect of biological therapy was not evident. Moreover, about 10% of hospitalizations resulted in surgery, with UC patients undergoing more elective interventions than those with CD. In conclusion, our study provides numerous insights for physicians coordinating the organization of health resources and for health policy makers. In particular, there is a need to improve performance in the outpatient setting, and to facilitate the monitoring of IBD patients with non-invasive methods, including telemedicine, especially in this period of the SARS-CoV-2 pandemic. Also, as regards the administration of biologic therapies, we should favor those with subcutaneous, or oral administration. Some changes have already been implemented to improve the efficiency of care, and reduce hospitalization, but much remains to be done. The limitations of our study have already been mentioned and they are mainly related to its retrospective design. However, in our opinion,

it represents a starting point for monitoring the health services available to IBD patients with the aim of progressively improving the care offered to our patients.

## Conflict of Interest

The Authors declare that they have no conflict of interests.

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