BASELINE PREDICTORS OF ONE-YEAR DISEASE-RELATED MORBIDITY IN PATIENTS WITH NEWLY DIAGNOSED ULCERATIVE COLITIS

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BASELINE PREDICTORS OF ONE-YEAR DISEASE-RELATED MORBIDITY IN PATIENTS WITH NEWLY DIAGNOSED ULCERATIVE COLITIS (Abstract): Early identification of factors predicting disease course in ulcerative colitis (UC) is essential for guiding therapeutic decisions and improving patient outcomes. Recognizing patients at higher risk of unfavorable evolution allows closer monitoring and timely treatment escalation. Clinical severity, disease extent, biochemical abnormalities, and concomitant infections may all influence prognosis. Among these, *Clostridioides difficile* infection (CDI) is increasingly recognized in UC, although its independent impact on disease course remains uncertain. **Aim:** To assess baseline clinical and biochemical severity markers, as well as concomitant CDI at diagnosis, as predictors of disease-related morbidity during the first year following UC diagnosis. **Materials and methods:** We conducted a retrospective study including 125 patients newly diagnosed with UC and followed for at least 12 months. Collected data included demographic characteristics, clinical presentation, biochemical markers, endoscopic findings, and the presence of CDI at diagnosis. Disease-related morbidity was defined as any UC-related hospitalization occurring within the first year after diagnosis, excluding the initial diagnostic admission. Statistical analysis comprised bivariate testing and multivariate logistic regression to identify independent predictors of hospitalization. **Results:** Independent predictors of UC-related hospitalization were Mayo clinical score (OR=1.28; 95% CI 1.00-1.64; p=0.043), pancolitis (OR=3.45; 95% CI 1.35-8.79; p=0.009), and hypoalbuminemia (OR=3.73; 95% CI 1.09-12.71; p=0.035). CDI was present in 20% of patients but did not independently predict hospitalization (OR=1.84; p=0.265). **Conclusions:** Baseline clinical activity, disease extent, and hypoalbuminemia are independent predictors of early UC-related morbidity. These findings underscore the importance of comprehensive initial assessment to support early risk stratification and individualized management strategies. **Keywords:** ULCERATIVE COLITIS, DISEASE-RELATED MORBIDITY, HOSPITALIZATION, BASELINE PREDICTORS.

INTRODUCTION

Ulcerative colitis (UC) is a chronic condition characterized by mucosal inflammation, characterized by a relapsing - remitting course. It typically begins in the rectum and extends proximally throughout the colon in a continuous manner.

During the past decades, the incidence

of inflammatory bowel disease (IBD) has increased, especially in developing countries. Immune system dysfunction and intestinal microbiome imbalance, along with the influence of environmental factors on genetically predisposed individuals, are the main mechanisms involved in the development of ulcerative colitis. Currently, the treatment of ulcerative colitis relies on corticosteroids for acute flares, amino salicylates, conventional immunosuppressants, and targeted biologic or small-molecule agents (1).

Therapeutic goals in IBD have recently evolved into a structured framework of short-term, intermediate and long-term targets, as outlined in the STRIDE-II consensus (2).

Short-term targets include symptomatic relief and normalization of C-reactive protein (CRP) as a general inflammatory marker, intermediate targets focus on decrease of fecal calprotectin, while long-term goals aim for achieving endoscopic healing, improved quality of life, and prevention of disease-related complications, disability and surgery. While not formally defined as treatment target, transmural healing in Crohn's disease and histological healing in UC are recognized as valuable therapeutic milestones (2). The lack of histological inflammation is linked to decreased relapse rates, as well as fewer hospital admissions, surgical interventions, and lower risk of neoplastic complications (3).

Accordingly, current strategies emphasize individualized care and close monitoring to guide therapy optimization. Furthermore, the early identification of factors that predict disease course in ulcerative colitis is essential to guide therapeutic decisions and improve patient outcomes. Timely recognition, ideally at diagnosis, of patients at higher risk of unfavorable evolution allows for more intensive monitoring and appropriate escalation of therapy within the "window of opportunity".

Certain baseline parameters, including clinical and laboratory characteristics, disease phenotype, laboratory findings, and histological grading have been associated with poor prognosis (4). Additionally, superimposed infections such as *Clostridioides difficile* may further complicate the clinical course.

The aim of our study was to identify baseline predictors of unfavorable disease progression, with a specific focus on early relapse during the first year after diagnosis.

MATERIALS AND METHODS

Study design and patients. We conducted a retrospective observational study including 125 consecutive patients newly diagnosed with UC who were followed for at least 12 months after diagnosis.

Patients were eligible for inclusion if they were newly diagnosed with UC based on clinical, endoscopic, and histologic criteria, and had at least 12 months of documented follow-up. Exclusion criteria were: previous total or subtotal colectomy, unconfirmed diagnosis, missing key data regarding *Clostridioides difficile* testing, endoscopic or histologic assessment, or loss to follow-up before completing the 12-months monitoring period.

The primary endpoint of our study was one-year disease-related morbidity, defined as any UC-related hospitalization occurring in the first year after diagnosis, including admissions due to disease flares or UC-related complications. Hospitalizations unrelated to UC were excluded from the analysis.

Data collection. Clinical, demographic, biochemical, endoscopic, and histologic data were collected from electronic medical records at the time of diagnosis. Disease severity and extent were assessed using the Mayo clinical score, Mayo endoscopic sub score, and the Montreal classification. All hospitalizations occurring within the first 12 months following baseline presentation were reviewed for each patient using the institutional electronic medical database.

Statistical analysis. Descriptive statistics were used to summarize baseline characteristics. Between-group comparisons were performed using the Mann-Whitney U test for continuous variables and the Chi-square test for categorical variables. Variables with a p-value <0.1 in univariate analysis were entered into a multivariate logistic regression model to identify independent predictors of UC-related hospitalization. Results were expressed as odds ratios (OR) with corresponding 95% confidence intervals (CI). A two-tailed p-value <0.05 was considered statistically significant. Analyses were performed using IBM *SPSS Statistics*, version 26 (IBM Corp., Armonk, NY, USA).

RESULTS

Patients' characteristics and one-year UC-related morbidity rate

A total of 125 patients with newly diagnosed UC were included in the study. The median age at diagnosis was 39 years (interquartile range [IQR] 26-49), and 54,4% were male. Extensive colitis (E3) was present in 36,5% of patients. The baseline demographic, clinical, and laboratory characteristics of patients are summarized in first table.

During the first year after diagnosis, 40 patients required UC-related hospitalization, predominantly for disease flares, corresponding to a 1-year morbidity rate of 32%.

Predictive factors for one-year UC-related morbidity

The correlations between baseline clinical, biological and endoscopic parameters and the risk of hospitalization were assessed by univariate and multivariate models. Results of the univariate analysis are presented in second table.

TABLE I.

Demographic, clinical and biological characteristics of patients

Parameter	Patients, n Total number=125
Age(years), median (IQR) Range, years	39 (26-49) 18-74
Gender ratio, n (%)	
Female Male	57 (45,6%) 68 (54,4%)
Hemoglobin value, g/dL, median (IQR)	12.9 (11.3-14.2)
White blood cells x10^3/μL, median (IQR)	8.08 (6.6-10.38)
C-reactive protein, mg/dL, median (IQR)	1.13 (0.38-3.86)
Serum albumin, g/dL, median (IQR)	4.12 (3.5-4.54)
Fecal calprotectin μg/g, median (IQR)	742 (323.5-1750)

Parameter	Patients, n Total number=125
Mayo score	
3-5 (mild), n (%) **6-10 moderate), n (%)** **11-12 (severe), n (%)**	37 (29.4%) 84 (66.7%) 4 (3.2%)
Mayo endoscopic sub score	
1 (mild UC), n (%) **2 (moderate UC), n (%)** **3 (severe UC), n (%)**	6 (4.8%) 70 (56%) 49 (39,2%)
Extension	
E1 (proctitis), n (%) **E2 (left-sided UC), n (%)** **E3 (extensive UC), n (%)**	13 (10.3%) 66 (52.4%) 46 (36.5%)
CDI, n (%)	25 (20%)

TABLE II.

Correlation between clinical, biological and endoscopic parameters and hospitalization risk; parameters marked with * were included in multivariate analysis (p<0.1)

Variable	Not hospitalized within 1 year (n=85)	Hospitalized within 1 year (n=40)	p-value
Age, years **Median (IQR)**	37 (26-48)	42 (27-52)	0.268
Gender, n (%)			
Female **Male**	45 (78.9%) 40 (58.8%)	12 (21.2%) 28 (41.2%)	0.016*
Mayo score **Median (IQR)**	6 (4-7)	8 (6-9)	0.002*
EIM at diagnosis, n (%)	6 (85.7%)	1 (14.3%)	0.301
Extension E3, n (%)	22 (47.8%)	24 (52.2%)	<0.001*
CDI at diagnosis, n (%)	12 (48%)	13 (52%)	0.017*
Hemoglobin g/dL **Median (IQR)**	13.3 (11.9-14.2)	12.2 (9.7-13.7)	0.010*
C-reactive protein mg/dL **Median (IQR)**	0.99 (0.25-3.5)	1.62 (0.7-4)	0.026*
White blood cells (x10^3/µL) **Median (IQR)**	7.84 (6.6-10.5)	9.04 (7-11.4)	0.148
Albumin g/dL **Median (IQR)**	4.30 (3.75-4.61)	3.72 (3.20-4.27)	0.001*
Fecal calprotectin µg/g	687 (299-1489)	857 (347-2232)	0.255
MES 3, n (%)	26 (53%)	23 (47%)	0.004*

Patients who were hospitalized within the first year had significantly higher baseline Mayo scores (p=0.002), lower hemoglobin (p=0.010), lower serum albumin (p=0.001), and higher CRP levels (p=0.026). Hospitalization was also more frequent among male patients (p=0.016), those with extensive colitis (E3) (p < 0.001), and patients with *Clostridioides difficile* infection (CDI) at diagnosis (p=0.017).

The Mayo endoscopic sub score was strongly associated with hospitalization risk (*p*=0.004), with more severe endoscopic activity corresponding to increased morbidity rates.

Multivariate logistic regression identified the following independent baseline predictors of one-year hospitalization (tab. III): higher Mayo clinical score (OR=1.28; 95% CI 1.00-1.64; p=0.043), extensive colitis (OR=3.45; 95% CI 1.35-8.79; p=0.009) and hypoalbuminemia (OR=3.73; 95% CI 1.09-12.71; p=0.035).

Although gender, hemoglobin levels and CDI status were associated with hospitalization in univariate analysis, they did not retain independent significance in the multivariate model (p > 0.05). Interestingly, C-reactive protein showed an inverse association with hospitalization risk (OR=0.86; 95% CI 0.77-0.97; p=0.015), likely reflecting the influence of extreme CRP elevations observed in patients with concomitant *C. difficile* infection.

A sub analysis comparing CRP levels between CDI-positive and CDI-negative patients at diagnosis revealed higher inflammatory activity among CDI-positive patients (median 1.74 mg/dL vs 0.98 mg/dL; p=0.055) (tab. IV).

TABLE III.

Independent predictive factors for hospitalization - multivariate analysis

Variable	B	P	Exp (B)	95% C.I for Exp (B)	
				Lower	Upper
Mayo score	0.25	0.043	1.28	1.00	1.64
CRP	-0.14	0.015	0.86	0.77	0.97
Hypoalbuminemia (< 3,5 g/dL)	1.31	0.035	3.73	1.09	12.71
Extension (E3)	1.23	0.009	3.45	1.35	8.79
CDI at diagnosis	-0.27	0.608	0.75	0.26	2.19
Gender	0.91	0.063	2.50	0.95	6.57
Hemoglobin	-0.14	0.287	0.86	0.67	1.12

TABLE IV.

Correlation between CRP levels in CDI positive and negative patients at diagnosis

Variable	CDI positive	CDI negative	p-value
C-reactive protein mg/dL, Median (IQR)	1.74 (0.87-6.11)	0.98 (0.33-3.42)	0.055

DISCUSSION

Demographic and clinical characteristics such as age, gender and disease phenotype at onset have been explored as potential prognostic indicators in UC. The impact of age remains debated. Unlike Crohn's disease, the Montreal classification for UC does not include age at diagnosis as a defining parameter, owing to inconsistent findings across studies. Some reports associate younger age, female sex, and extraintestinal manifestations with higher relapse rates, whereas others link male sex and extensive colonic involvement with an increased risk of colectomy (5-7). In our study no correlation between group age and gender was noted.

Clinical and laboratory markers reflecting high disease activity at diagnosis are key prognostic determinants in UC. Stratifying disease severity is crucial for guiding treatment decisions and anticipating disease progression. A combination of clinical, biological and endoscopic indicators provides valuable prognostic information. Features as persistent fever, frequent bloody stools, elevated inflammatory markers, and low serum albumin levels have been consistently associated with poor response to therapy and higher colectomy rates (4). Among biological markers, CRP remains a widely used and accessible inflammatory biomarker. Elevated CRP at diagnosis is associated with more extended disease and an increased risk of colectomy. Persistently high CRP levels during follow-up are also correlated with worse outcomes, regardless of treatment, highlighting its value as a surrogate for disease burden and prognosis (8).

In our analysis, a higher Mayo score - incorporating both clinical and endoscopic activity, was an independent predictor of UC-related hospitalization during the first year. These findings confirm the Mayo score's prognostic utility beyond activity assessment, suggesting that greater baseline disease severity translates into a higher morbidity burden over time.

Although CRP and fecal calprotectin are established inflammatory markers, they were not independently associated with one-year morbidity in our cohort. This may reflect their limited prognostic value once acute inflammation diminishes after treatment initiation. They primarily indicate inflammatory burden at diagnosis but do not necessarily predict mid-term outcomes in newly diagnosed patients.

Disease extent is another well-recognized prognostic factor. Patients with extensive colitis typically experience a more aggressive disease course, are more likely to require immunosuppressive or biologic therapy, and have lower response rates to amino salicylates (4). In our cohort, extensive colitis emerged as an independent predictor of UC-related hospitalization (OR=3.45; p=0.009), emphasizing the importance of accurately determining disease extent at baseline, ideally by colonoscopy and, when needed, supported by cross-sectional imaging.

Serum albumin is classified as a negative acute phase reactant, and its levels tend to decrease in the presence of inflammation. In UC, hypoalbuminemia results from increased catabolism and protein loss through the inflamed mucosa, while additional factors such as malnutrition and malabsorption further contribute to decreased levels (9). Previous studies have identified hypoalbuminemia as a strong predictor of poor outcomes, including treatment failure, colectomy,

and non-response to thiopurines or anti-TNF therapy (9,10). In line with these findings, our study demonstrated that hypoalbuminemia is associated with an increased risk of hospitalization in the first year after diagnosis (OR=3.73; p=0.035). These results underscore the prognostic value of albumin as a simple, cost-effective marker for early risk stratification in UC.

The impact of CDI in UC remains controversial. CDI occurs more frequently during UC flares and has been linked to worse short- and medium-term outcomes, including increased healthcare costs, longer hospital stays, higher colectomy rates, and more frequent hospital visits (8). However, data are conflicting. Some studies reported increased colectomy and mortality in CDI-positive UC patients (11, 12), while others found no significant long-term impact (13, 14). In our cohort, CDI at diagnosis was associated with higher CRP levels, indicating greater inflammatory activity, but did not independently predict one-year hospitalization. These findings support the hypothesis that CDI may exacerbate inflammation or unmask preexisting mucosal disease without directly worsening long-term prognosis.

Interestingly, 20% of our patients were diagnosed with UC in the context of CDI, suggesting that infection may act as a trigger in genetically or immunologically susceptible individuals.

Several limitations should be acknowledged. The retrospective, single-center design limits causal inference. The relatively small number of CDI-positive patients may reduce statistical power to detect differences in some outcomes. Additionally, although hospitalization was used as an objective marker of morbidity, we did not perform subgroup analyses based on the cause of admissions (e.g., flare vs. complication), which may have limited specificity. Moreover, using hospitalization as a marker of morbidity may overlook important aspects such as health-related quality of life or outpatient care requirements.

CONCLUSIONS

This study identified a higher Mayo clinical score, extensive colitis, and hypoalbuminemia as independent baseline predictors of UC-related hospitalizations within the first year after diagnosis. These findings highlight the importance of a comprehensive initial assessment, integrating clinical, biochemical, and endoscopic parameters to improve early risk stratification and guide timely, individualized treatment decisions.

Clostridioides difficile infection was associated with more pronounced biochemical inflammation, but it did not independently predict one-year morbidity. This suggests that CDI may exacerbate mucosal inflammation or unmask underlying disease rather than directly worsening mid-term outcomes.

From a clinical perspective, patients presenting at diagnosis with extensive colonic involvement, elevated Mayo score, and low albumin levels may benefit from closer surveillance and timely therapeutic escalation.

CONFLICT OF INTERESTS AND FUNDING

The authors declare that there is no conflict of interests, and they received no specific funding regarding this scientific research.

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