

## Original Paper

# Upper Digestive Tract Lesions in Inflammatory Bowel Diseases

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## REZUMAT

### *Leziuni de tub digestiv superior in bolile inflamatorii intestinale*

**Obiective:** Studiul de față își propune: aprecierea frecvenței leziunilor de tub digestiv superior în bolile inflamatorii intestinale, caracterizarea lor din punct de vedere endoscopic și histopatologic și determinarea semnificației acestora în evoluția pacienților cu boala inflamatorie intestinală.

**Material și metodă:** am efectuat un studiu retrospectiv ce a inclus 52 de pacienți, internați în Clinica de Gastroenterologie și Hepatologie Fundeni în perioada 2009-2012, cu diagnosticul de boală Crohn (BC), respectiv rectocolită ulcero-hemoragică (RCUH), la care s-a efectuat endoscopie digestivă superioară. Pentru analiza statistică am efectuat testul exact al lui Fisher și Mann-Whitney.

**Rezultate:** 19,23% dintre pacienții cu rectocolită au avut afectare duodenală și 15,26 % leziuni gastrice. În BC am decelat afectare gastrică în 23,08% din cazuri și duodenală în 15,38%, singurele tipuri de leziuni histopatologice descrise fiind gastrita focală și duodenita focală. În RCUH au fost prezente 3 tipuri de leziuni: gastrita focală 11,53%, gastrita difuză 3,84% și duodenita difuză 19,23%.

**Concluzii:** Afectarea tubului digestiv superior este prezentă atât în BC cât și în RCUH, corelându-se cu forme de boală mai extinse: localizare ileocolonică în BC ( $p=0,001$ ) și pancolită în RCUH ( $p=0,003$ ) și cu pusee de activitate mai severe în fiecare dintre cele două BII ( $p=0,03$ ).

**Cuvinte cheie:** boala inflamatorie intestinală, gastrită, duodenită, boala Crohn, rectocolită ulcerohemoragică

## ABSTRACT

**Objectives:** The aims of the present study are: assessing the frequency of lesions in the upper digestive tract in inflammatory bowel diseases, endoscopic and histological characterization of these lesions and revealing their significance in the evolution of patients with inflammatory bowel disease.

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**Methodology:** We realized a retrospective study that included 52 patients hospitalized in the Fundeni Gastroenterology and Hepatology Department between 2009-2012, diagnosed with Crohn's disease and respectively ulcerative colitis, in which upper gastrointestinal endoscopy was performed. For statistical analysis we used Fisher's exact test and Mann-Whitney.

**Results:** 19.23 % of ulcerative colitis patients had duodenal lesions and 15.26 % gastric lesions. In Crohn's disease we found gastric lesions in 23.08% of the cases and duodenal lesions in 15.38 %, the only types of histological lesions described being focal gastritis and focal duodenitis. In ulcerative colitis there were present three types of lesions: focal gastritis 11,53%, diffuse gastritis 3,84% and diffuse duodenitis 19,23%.

**Conclusions:** Upper digestive tract impairment is present both in Crohn's disease and ulcerative colitis, and correlates with extended forms: ileocolonic localization in Crohn's Disease ( $p=0,001$ ) and pancolitis in ulcerative colitis ( $p=0,003$ ) and with severe flairs of activity in both inflammatory bowel diseases ( $p=0,03$ ).

**Key words:** inflammatory bowel disease, gastritis, duodenitis, Crohn's disease, ulcerative colitis

## INTRODUCTION

Inflammatory bowel diseases, Crohn's disease (CD) and ulcerative colitis (UC), are chronic, idiopathic diseases characterized by the inflammation of the wall tube (1). Ulcerative colitis was first described in the mid-1800s (2), whereas Crohn's disease was first reported later, in 1932, as "regional ileitis" (3). Because Crohn's disease can involve the colon and shares clinical manifestations with ulcerative colitis, these entities have often been conflated and diagnosed as inflammatory bowel disease, although they are clearly distinct physiopathological entities. Ulcerative colitis is the most common form of inflammatory bowel disease worldwide. In contrast to Crohn's disease that can extend in the entire intestinal wall, ulcerative colitis is a disease of the mucosa that is less prone to complications and can be cured by means of colectomy, and in many patients, its course is mild (4).

Until recently, it was considered that, unlike Crohn's disease (whose location can be at any level of the digestive tract), ulcerative colitis is strictly localized in the colon. However, in the recent years, increasingly more studies reveal the existence of a moderate, chronic, diffuse gastroduodenitis in patient with ulcerative colitis, which normally causes no macroscopical lesions being highlighted only based on histopathologic examination (5). Most of these studies invoke the presence in the duodenum of a diffuse inflammation with neutrophilic infiltration in the glandular crypts, with redness and swelling during an acute exacerbation. In the stomach the predominant lesions are chronic focal gastritis (5,6,7).

Histopathological examination of biopsies from

the stomach and duodenum in patients with Crohn's disease show two inflammatory patterns: a focal inflammation with basal limfoplasmocytic infiltrates and diffuse, discontinuous inflammation affecting the mucosal architecture (8). In the duodenum focal inflammation occurs in the base of the glandular crypts causing focal appearance (9).

## Objectives

In this context the aims of the present study are: assessing the frequency of lesions in the upper digestive tract in inflammatory bowel diseases, endoscopic and histological characterization of these lesions and revealing the significance of their presence in the evolution of patients with inflammatory bowel disease.

## Methodology

We performed a retrospective study that included a group of 52 patients hospitalized in the Gastro-enterology and Hepatology Department of Fundeni Clinical Institute between 2009-2012, diagnosed with Crohn's disease and respectively ulcerative colitis. The study included patients who had upper gastrointestinal endoscopy during the evolution of their inflammatory disease. Biopsies were taken from the lesions that were discovered during the endoscopic procedure. Depending on the type of disease the patient group was divided into two equal subgroups: 26 patients with Crohn's disease and 26 with ulcerative colitis.

Data were collected from patient observation sheets. Thus was achieved a patient tracking sheet that included: demographic data (age, gender), severity of flare activity present in the hospitalization period in which the upper endoscopy was performed

(quantified by CDAI score for BC, Truelove and Witts respectively for ulcerative colitis), location of disease and type of damage to the upper digestive tract.

All this information was centralized and structured using Microsoft Excel 2007. Statistical analysis was performed using SPSS statistical program using the following tests: Fisher's exact test and Mann-Whitney.

## RESULTS

After centralizing data were established demographic and clinical characteristics of the patients presented in **Table 1**.

Regarding the involvement of the upper digestive tract observe in **Table 2** that there are 10 patients with Crohn's disease who have upper digestive tract lesions and 9 patients with ulcerative colitis. We also

found that in the subgroup of patients with Crohn's disease there is a predominance of gastric damage; unlike this, ulcerative colitis patients had a higher frequency of duodenal damage.

Referring to the description of endoscopic lesions in the stomach we observed the predominance of corporeal erythematous gastritis: 3 cases in Crohn's disease and 2 cases in ulcerative colitis. In the duodenum we found that the only endoscopic lesions that were present were erythematous and erosive duodenitis, both in the same proportion in Crohn's disease, unlike in ulcerative colitis where prevails erythematous duodenitis (4 cases).

With regard to Crohn's disease histopathological characterization of lesions in the stomach and duodenum is shown in **Table 3**. We noted that the most common pattern of gastric lesion was the focal gastritis (6 cases) consisting of a focal active chronic inflammation of the gastric mucosa. Regarding

**Table 1. Clinical and demographical characteristics**

	Crohn's disease	Ulcerative colitis
<b>Age</b>	35 ± 14.36 years	56 + 17.24 years
<b>Male: Female</b>	1:1	1:1,16
<b>Disease localization</b>	Ileocolonic disease n=11 (42.31 %) Jejunoleal disease n= 8 (30.77 %) Colonic disease n=7 (26.92 %)	Proctitis n=6 (19.23 %) Left- side colitis n=11 (42.31%) Pancolitis n=9 (34.61 %)
<b>Flare of activity</b>	Mild flare n= 8 (30.77 %) Moderate flare n=11 (42.31 %) Severe flare n= 7 (26.92 %)	Mild flare n=8 (30.76 %) Moderate flare n=12 (46.15%) Severe flare n=6 (23.06 %)
<b>Evolving forms</b>	Inflammatory forms n=19 (73.08%) Stenosing forms n=4 (15.38 %) Penetrating forms n=3 (11.54 %)	Acute Fulminating n=2 (7.6%) Chronic continuos n=7 (26.92%) Chronic intemitent n=17 (65.38%)

**Table 2. Endoscopic lesions of the upper digestive tract**

	Crohn's disease	Ulcerative colitis
Eritematouse antrum gastritis	n=2 (7.69%)	n=0 (0.00%)
Erozive antrum gastritis	n=1 (3.85%)	n=1 (3.85%)
Eritematouse corporeal gastritis	n=0 (0.00%)	n=2 (7.65%)
Erozive corporeal gastritis	n=3 (11.54%)	n=1 (3.85%)
Eritematouse pangastritis	n=0 (0.00%)	n=0 (0.00%)
Erosive pangastritis	n=0 (0.00%)	n=0 (0.00%)
<b>Total</b>	<b>6</b>	<b>4</b>
Eritematouse duodenitis	n=2 (7.69%)	n= 4 (15.38%)
Erosive duodenitis	n=2 (7.69%)	n=1 (3.85%)
<b>Total</b>	<b>4</b>	<b>5</b>

Table 3. Histological lesions of the upper digestive tract

	Crohn's disease	Ulcerative colitis
Diffuse gastritis	n=0 (0.00%)	n=1 (3.85%)
Focal gastritis	n=6 (23.07%)	n=3 (11.54%)
Diffuse duodenitis	n=0 (0.00%)	n=5 (19.23%)
Focal duodenitis	n=4 (15.38%)	n=0 (0.00%)
Total	10	9

duodenal lesions, the main pattern is the focal duodenitis described as a limfoplasmocytic infiltrate in the glandular crypt base, named focal cryptitis.

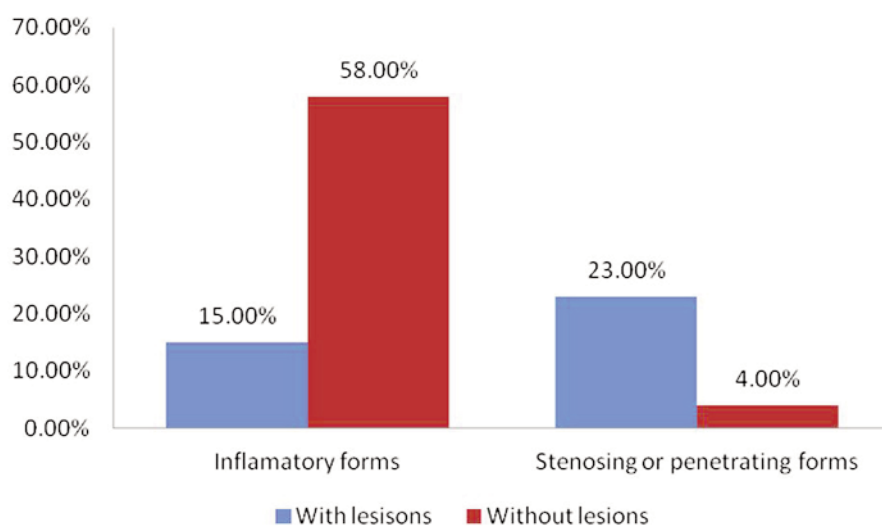
Referring to ulcerative colitis (**Table 3**) we noticed that the type of lesion that occurs most frequently in the stomach is focal gastritis (3 cases), which is a focal active, chronic inflammation of the gastric mucosa and that the main lesion pattern in the duodenum is a diffuse duodenitis, which consists of a diffuse, chronic inflammatory condition associated with damage to the architecture of the mucosal glands.

To see the correlation of these lesions of the upper digestive tube with the status of the patients with IBD, we investigated the association between the presence of the upper digestive tract lesions and three criteria: (1) the form of development, (2) severity of flare activity and (3) the extension of the inflammatory bowel disease.

In the subgroup of patients with Crohn's disease we noticed that there is a significant association

between the form of development and gastroduodenal lesions ( $p = 0.003$ ), existing a higher frequency of stenosis and penetrating forms in the group with severe gastroduodenal disease compared to those without (**Chart 1**). There is also a correlation between the presence of lesions and more severe flare ups ( $p = 0.003$ ), noting that severe flare activity predominates in the group with gastroduodenal disease (**Chart 2**). Patients with damage to the upper gastrointestinal tract had a more extensive form of Crohn's disease (ileocolonic) ( $p=0.001$ ) (**Chart 3**).

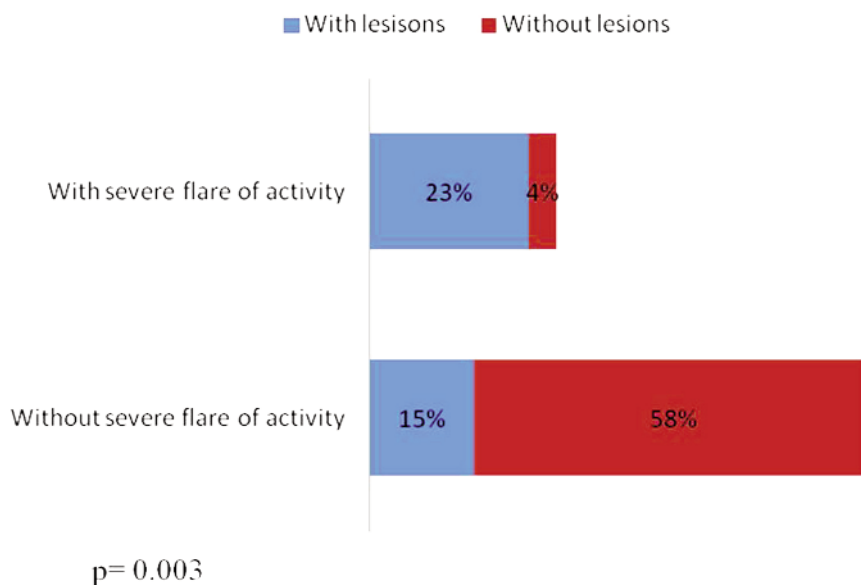
In ulcerative colitis we noticed that gastroduodenal damage does not correlate with a less favorable form of evolution ( $p = 0.08$ ). There is a significant correlation with the severity of flare activity ( $p=0.0352$ ) (**Chart 4**) and with the extension of the disease in the colon ( $p = 0.003$ ), observing that a higher proportion of patients with upper gastrointestinal tract involvement have had pancolitis compared with those without lesions in the stomach or duodenum (**Chart 5**).



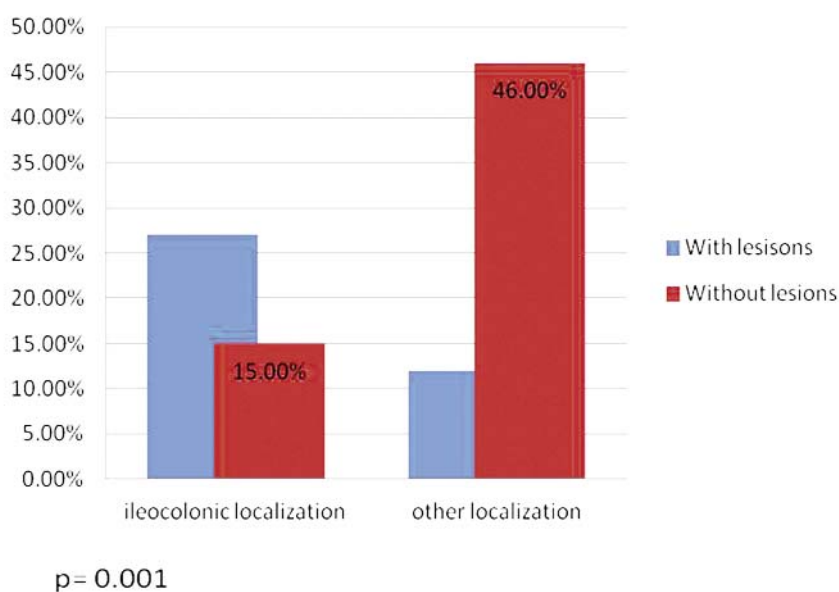
**Chart 1.** Correlation between gastroduodenal lesions and form of evolution in CD

$p = 0.003$

**Chart 2.** Correlation between gastroduodenal lesions and flare of activity in CD



**Chart 3.** Correlation between gastroduodenal lesions and localization in CD



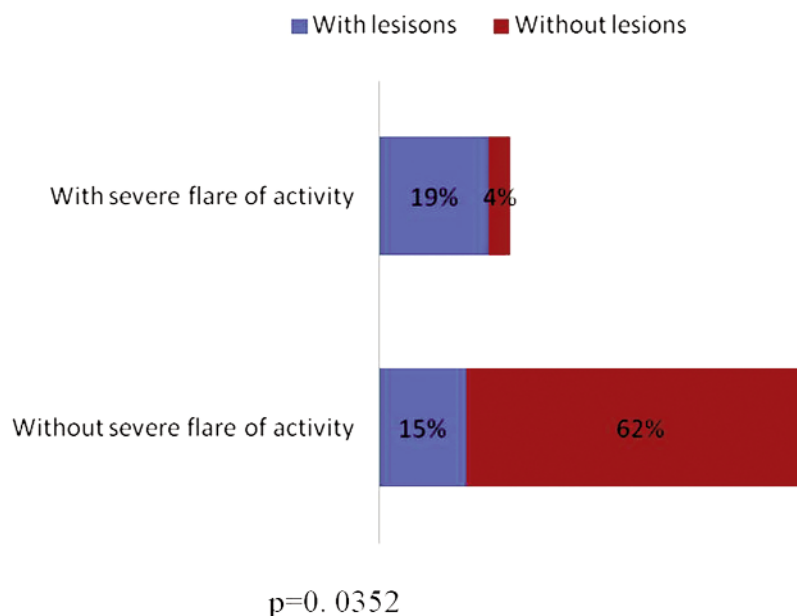
## DISCUSSION

Inflammatory bowel disease's evolution is curled, with periods of activity and periods of remission, and the first situation can be accompanied with serious complications with possible threat to vital prognosis of the patient. Thus any approach to knowledge of these conditions is considered to be a very important step in the long-term control of these diseases, all steps leading to obtain a patient's quality of life as good as possible.

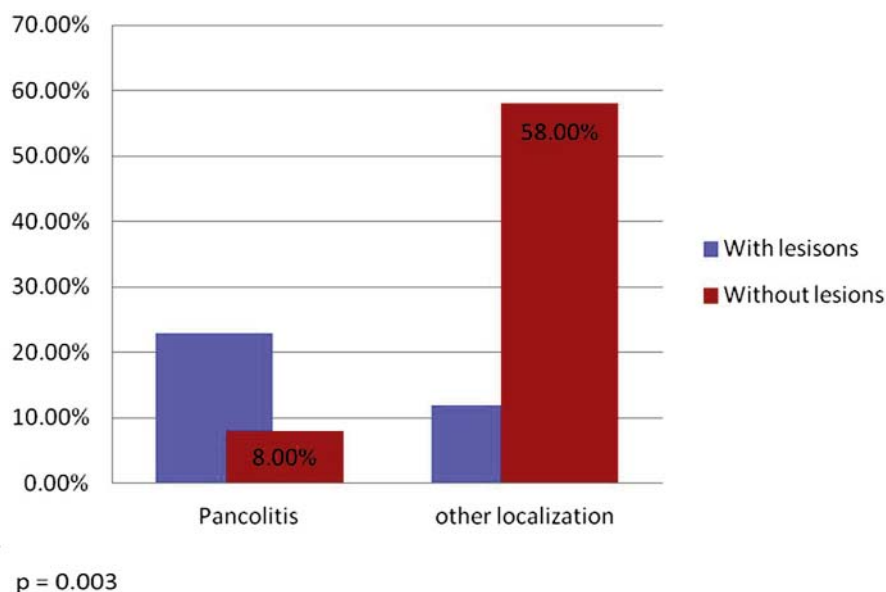
Regarding the onset age of Crohn's disease and ulcerative colitis the epidemiological data shows that there are two peaks of maximum incidence: the first between the ages of 15-30 years and the second at 60-80 years (10). Our data, obtained in the study showed a mean age of  $35 \pm 14$  years for CD and  $56 \pm 17$  years for UC.

In terms of gender distribution, literature data shows that both men and women are equally affected by the disease in regard to UC and there is a slight predominance of females in CD: male /female ratio 1:1 for UC, respectively 1:1.1-1.8 for

**Chart 4.** Correlation between gastroduodenal lesions and flare of activity in UC



**Chart 5.** Correlation between gastroduodenal lesions and localization in UC



CD (11). In our study the ratio male/female was 1:1.16 in UC and 1:1 for CD, respectively.

It is well known that CD affects many segments of the gastrointestinal tract, being necessary to make a classification based on the location of the disease. Currently there are described three major topographic forms: (1) ileocolonic CD (about 40% of cases, most commonly the terminal ileum, the cecum and ascending colon), (2) jejunoleal CD (about 30% of the cases), (3) Colonic CD (about 25% of cases) (12). The data obtained in our study are consistent

with the literature. Thus the distribution of patients in the group with CD shows that 42.31% (n = 11) of patients had ileocolonic disease, 26.92% (n = 7) had strict localization in the colon and 30.77% (n = 8) had jejunoleitis.

Data from the literature show a frequency of gastroduodenal damage between 29.6% and 43% for CD, respectively between 12% and 22% for UC (12,13,14), indicating that lesions of the upper digestive tract disease are more common in Crohn's disease compared with ulcerative colitis (12). Our



results support this information providing 38% (n= 10) for Crohn's disease respectively 34 % (n=9) for colitis.

About the endoscopic appearance of these lesions in UC, we can speak of a predominance of the erythematous duodenitis (present in 4 of the 9 patients with gastroduodenal involvement), while in CD there is a mild predominance of erosive corporeal gastritis (3 of the 10 patients with gastroduodenal lesions). However, clinical trials data points out that in CD the erosive pattern is more commonly encountered than the erythematous one (15).

Regarding histological examination of biopsies from the stomach and duodenum in patients with CD, studies consider that there are two inflammatory patterns: (1) a focal inflammation with basal lymphoplasmocytic infiltrates and (2) discontinuous diffuse inflammation affecting mucosal architecture (16). Focal gastritis is indicated as a histopathological feature in CD, noting that although it is quite common, it is not exclusive and can also occur in UC (16).

Like wise, in UC more studies bring up the existence of a chronic, moderate, diffuse gastroduodenitis, characterized by the presence of a diffuse inflammation with neutrophilic infiltration in the glandular crypts, edema and hyperemia associating a flare of activity. However, in ulcerative colitis, histological examination of biopsies from stomach reveal predominance of focal gastritis, despite diffuse gastritis (17). The results obtained in our study were similar to those described above: we found that in CD the most common type of lesion was focal gastritis (n=6, 23.07%), this type of lesion being noticed also in UC (n=3, 11.54%), but less frequently. In regard to duodenal impairment, there are clear differences between the two groups, noting the presence of focal duodenitis as the only type of lesion (n= 4) in Crohn's disease, respectively the exclusive presence of diffuse duodenitis (n=5) in ulcerative colitis .

We observed that the presence of lesions in the upper digestive tract described above correlates with ileocolonic localization in Crohn's disease (p=0.001), and pancolitis in ulcerative colitis (p=0.003). Both patients with ulcerative colitis and those with Crohn's disease who had gastroduodenal lesions have more severe flares of activity (p=0.0352, p=0.003). In Crohn's disease damage to the stomach or duodenum correlates with stenosis and penetrating forms of evolution (p=0.003), while in UC no such correlation

regarding severity of the colonic mucosal impairment or complications exists (p=0.08).

## CONCLUSIONS

Upper digestive tract involvement is more common in Crohn's disease (38%) than in ulcerative colitis (34%).

In ulcerative colitis, duodenal damage predominates (n=5), while in Crohn's disease the stomach is more affected (n=6).

The most frequent histopathological lesion in Crohn's disease is focal gastritis (present in all the six cases of gastric damage), while in ulcerative colitis diffuse duodenitis predominates (present in all 5 cases with duodenal impairment).

In Crohn's disease damage to stomach or duodenum correlates with stenosis and penetrating forms of evolution (p=0.003), while in UC no statistically significant correlation regarding severity of the colonic mucosal impairment or complications exists (p=0.08).

Lesions of the upper digestive tract correlates with ileocolonic Crohn's disease (p=0.001), and with pancolitis in ulcerative colitis (p=0.003).

Both patients with ulcerative colitis and those with Crohn's disease, which have gastroduodenal lesions have more severe flares of activity (p=0.0352, p=0.003)

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