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Clinical relevance of tissue cytomegalovirus detection in inflammatory bowel disease: differences between polymerase chain reaction and immunohistochemistry in real-world practice

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Abstract

Background Cytomegalovirus (CMV) infection in patients with inflammatory bowel disease (IBD) is frequent, but its clinical relevance remains controversial. Current diagnostic approaches, including tissue polymerase chain reaction (PCR) and immunohistochemistry (IHC), show variable correlation with disease severity and outcomes. The aim of this study was to evaluate the clinical significance of CMV detection in intestinal biopsies according to the diagnostic method used, with a particular focus on isolated PCR positivity vs. histological detection.

Methods We conducted a retrospective observational study including 60 adult patients with IBD, most with ulcerative colitis, who had CMV-positive intestinal biopsies detected by PCR and/or IHC/hematoxylin–eosin staining between 2018 and 2025. Clinical, biochemical, and endoscopic data were analyzed. Patients were stratified according to the CMV detection method, and associations with disease severity, corticosteroid refractoriness, treatment, and outcomes were assessed.

Results Isolated PCR positivity was the most frequent finding. However, combined PCR+/IHC+ status was associated with more severe flares and higher corticosteroid refractoriness (48% vs. 22%, P=0.03). Concordance between diagnostic methods was poor for PCR vs. IHC. Patients with severe flare-ups or corticosteroid-refractory disease were predominantly PCR+/IHC+. Likewise, antiviral therapy was more frequently used in PCR+/IHC+ patients and in corticosteroid-refractory cases. No significant differences were observed in clinical remission or colectomy rates.

Conclusions Among CMV-positive patients, combined PCR+/IHC+ positivity was more frequently observed in severe flares and corticosteroid-refractory disease, whereas isolated PCR positivity showed limited clinical relevance.

Keywords Cytomegalovirus, polymerase chain reaction, immunohistochemistry, corticosteroid refractoriness, disease severity

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Introduction

Cytomegalovirus (CMV) is a member of the herpesvirus family that typically follows an asymptomatic course in healthy individuals, but it can cause severe symptomatic infections in immunocompromised patients. Patients with inflammatory bowel disease (IBD) represent a population at risk of CMV colitis, due to their underlying disease, immunosuppressive treatment, and/or their nutritional status [1,2].

The importance of CMV in the course of the disease has been highlighted in multiple studies as a potential modifier of the clinical course [3]. Its presence has been associated with

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a poorer prognosis, including increased flare severity, longer hospital stays, corticosteroid refractoriness, a greater need for rescue therapy, and a higher risk of colectomy [3,4].

The main challenge lies in distinguishing true reactivation from latent infection. The virus may act as a risk factor for lack of therapeutic response (reactivation), or simply as a marker of severe inflammation via its tropism for inflamed tissue (latent infection) [5,6]. Therefore, the clinical relevance of a positive result and the benefit of antiviral treatment remain uncertain. Consequently, controversy persists regarding the true role of CMV as either a causal agent or an innocent bystander in the course of IBD [6,7].

According to the guidelines of the European Crohn's and Colitis Organisation (ECCO), screening for CMV is recommended in hospitalized patients with a severe flare or corticosteroid-refractory disease. Similarly, antiviral therapy is reserved for corticosteroid-refractory patients in whom CMV is detected in intestinal biopsy specimens. Nevertheless, evidence regarding the benefit of antiviral treatment, even in these cases, remains limited, with heterogeneous results across studies [6,8,9].

Diagnostic methods for CMV include noninvasive tests, such as serology, pp65 antigenemia and polymerase chain reaction (PCR) in blood. However, these methods do not distinguish between latent and active infection. Invasive techniques based on intestinal biopsy include immunohistochemistry (IHC), which detects the viral pp65 protein in tissue, identification of inclusion bodies by hematoxylin–eosin (H&E) staining, and tissue PCR [5,10]. The gold standard is the combination of IHC and tissue PCR [9,10]. Some authors have proposed distinguishing between "high-grade" and "low-grade" infection, according to the viral load detected in tissue. High-grade infection is characterized by high viral loads and is often associated with positive IHC, as well as with clinical severity and corticosteroid refractoriness. In contrast, low-grade infection is characterized by a low viral load and is usually IHC-negative, probably reflecting limited viral replication without clear clinical relevance [11,12]. Therefore, the clinical relevance of an isolated positive tissue PCR is limited. A knowledge gap remains, as its diagnostic value and the viral load thresholds that indicate reactivation have not yet been clearly established [13].

The primary aim of this study was to evaluate the clinical significance of CMV detection in intestinal biopsies from patients with IBD, according to the diagnostic technique used (PCR, IHC or H&E). In particular, we sought to determine whether isolated PCR positivity differs from histological detection in terms of disease severity, steroid refractoriness, therapeutic decisions, and clinical outcomes.

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Materials and methods

An observational, retrospective study was conducted at a tertiary hospital to collect cases of patients with IBD in whom CMV was detected by intestinal PCR, or by IHC or H&E staining on intestinal biopsy, between 2018 and 2025. The inclusion criteria were all CMV-positive biopsies, either by PCR or by IHC, from patients older than 18 years referred by the Gastroenterology Department during the aforementioned period. The only exclusion criterion was the absence of a diagnosis of IBD.

The presence of CMV in intestinal tissue was evaluated by PCR, IHC and H&E staining. Biopsies were usually obtained from patients with IBD and endoscopic activity; however, the indication for CMV testing was not protocolized and was based on clinical judgement, particularly in patients with moderate-to-severe disease, suspected corticosteroid refractoriness or poor clinical evolution.

For PCR analysis, tissue samples were first digested with proteinase K and heated for 24 hours. Nucleic acid extraction was performed automatically using the MagCore® system (RCBioscience) and the Viral Nucleic Acid Extraction Kit cartridges (RCBioscience). CMV detection by PCR was carried out using RealCycler HERPLX-UX reagents (Progenie Molecular). Results were interpreted using the BioVisor Pro-Q software (Progenie Molecular). A positive PCR (PCR+) was defined as detection of CMV at a cycle threshold value <40. All PCR analyses included appropriate positive and negative controls, according to the manufacturer's protocol.

For histological analysis, 3-4 μm sections of formalin-fixed, paraffin-embedded tissue were stained with H&E. Cases were considered positive when basophilic/amphophilic nuclear inclusions with a clear perinuclear halo and characteristic "owl's eye" morphology were identified in epithelial, endothelial or stromal cells. Evaluation was performed by light microscopy at high magnification (400×). At least 1 unequivocal nucleus was required for a positive result.

For IHC, a monoclonal anti-CMV antibody (clones CCH2+DDG9, Agilent/Dako) was used on the automated Dako Omnis® platform, following the manufacturer's standardized protocol, with antigen retrieval by heat-induced epitope retrieval and a polymer-based detection system with DAB chromogen. Appropriate positive and negative controls were included. The presence of at least 1 cell with intense nuclear staining compatible with CMV infection was considered positive.

Sociodemographic variables collected included age, sex, and disease duration. Baseline disease variables included IBD type and disease extent, maintenance therapy and treatment for the flare. Disease activity at the time of sample collection was assessed clinically using validated indices (the Harvey–Bradshaw Index for Crohn's disease and the partial Mayo score for ulcerative colitis). Patients were classified as being in clinical remission or as having mild, moderate or severe flare according to established cutoff values [14,15]. The same disease-specific indices were used to assess clinical remission during follow up. C-reactive protein levels and fecal calprotectin were also

recorded as biochemical parameters. Endoscopic activity was classified using the Mayo endoscopic score in patients with ulcerative colitis and the Simple Endoscopic Score for Crohn's Disease in patients with Crohn's disease. In addition, the presence or absence of deep ulcers was recorded, defined as ulcers ≥5 mm [16].

Systemic corticosteroid treatment was also recorded, and patients were classified as corticosteroid-refractory or corticosteroid-responsive. Initiation of antiviral therapy (yes/no; ganciclovir or valganciclovir) and the need for rescue therapy, defined as initiation of ciclosporin or biological therapy, were also recorded. Corticosteroid refractoriness was defined as persistent clinically active disease despite an adequate course of systemic corticosteroids, as specified by ECCO recommendations, including patients requiring rescue therapy. Given the retrospective design, response assessment was based on physician-recorded clinical evolution, requirement for rescue therapy, and validated activity indices when available.

The subsequent response was evaluated in all patients, regardless of the treatment received. The rate of clinical remission in the short (<4 weeks) and medium term (<12 weeks) was analyzed, as well as the proportion of patients who ultimately required colectomy.

The primary objective of this study was to analyze the clinical significance of CMV detection in intestinal biopsies from patients with IBD, according to the diagnostic technique used (PCR, IHC or H&E). Secondary objectives included analyzing the association between CMV status (PCR+/IHC+, PCR+/IHC−, IHC+/PCR−) and flare severity, corticosteroid refractoriness and therapeutic decisions, including initiation of antiviral therapy or escalation of baseline treatment. In addition, the patients' clinical course was evaluated, including rates of clinical remission and need for colectomy, and the agreement between the different diagnostic techniques used for CMV detection in intestinal tissue was assessed.

This retrospective observational study was designed and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.

Statistical analysis

Quantitative variables were represented as mean ± standard deviation or median and interquartile range, depending on the distribution of the data. Normality was assessed using the Shapiro-Wilk test. Comparisons between 2 groups were performed using Student's t-test or the Mann-Whitney *U* test, as appropriate. A P-value <0.05 was considered statistically significant. Categorical variables were represented as absolute frequencies and percentages, and were compared using the chi-square test or Fisher's exact test. Agreement between the different diagnostic techniques for CMV detection (PCR, IHC and H&E) was evaluated using Cohen's kappa coefficient. Multivariate analysis was not performed, as the limited sample size and the low number of events precluded the construction of reliable multivariate models. Statistical analyses were performed using R version 4.4.0 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Study population and baseline characteristics

A total of 789 intestinal biopsies were evaluated for CMV during the study period. After exclusion of patients without IBD, 60 patients with CMV-positive intestinal biopsies were included in the final analysis. The patient selection process and distribution according to the diagnostic method are shown in Fig. 1.

Baseline demographic and clinical characteristics are summarized in Table 1. The cohort had a mean age of 56.9±17.2 years and consisted predominantly of patients with ulcerative colitis (88%). Most patients presented with moderate-to-severe clinical and endoscopic disease activity and received systemic corticosteroids for the index flare.

Corticosteroid treatment was initiated in 48 patients (84%). In most cases, biopsies were obtained during colonoscopies performed after a disease flare. In 2 patients, however, biopsies were taken during screening colonoscopies, and both were in remission at the time of the study.

CMV detection patterns and diagnostic agreement

Isolated tissue PCR positivity was the predominant pattern of CMV detection (Supplementary Fig. 1). Concordance between PCR and IHC was poor (Cohen's kappa (κ)=0.17), as was concordance between PCR and H&E (κ=0.04), whereas agreement between IHC and H&E was good (κ=0.63).

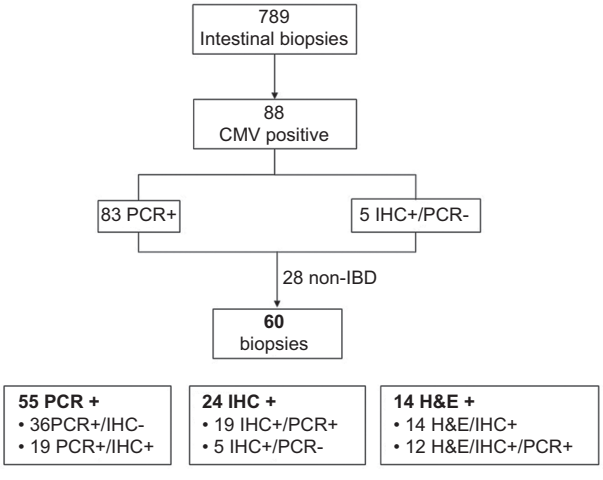


Figure 1 PCR/IHC/H&E results of the intestinal biopsies analyzed
PCR, polymerase chain reaction; IHC, immunohistochemistry; H&E, hematoxylin–eosin stain

Association between CMV detection pattern and disease severity

Patients classified as having a moderate or severe flare were predominantly double positive, with a significant difference: 18/19 (95%) in the PCR+/IHC+ group vs. 16/36 (44%) in the PCR+/IHC− group (odds ratio [OR] 22.5, 95% confidence interval [CI] 2.71-187.13; P<0.001). In contrast, among patients with a mild flare, no significant differences were observed between groups: 11/36 (31%) PCR+/IHC− vs. 4/19 (21%) PCR+/IHC+ (P=0.5).

Table 1 Baseline characteristics of the patients

Characteristics	Total (60)
Mean age (years)	56.9±17.2
Disease duration	12.6±7.3
Sex	
Male	28 (47%)
Female	32 (53%)
Type of IBD	
UC	53 (88%)
CD	6 (10%)
IBD-U	1 (2%)
Extent of UC	
Left-sided	23 (43%)
Pancolitis	28 (53%)
Proctitis	2 (4%)
Maintenance therapy	
Mesalazine	17 (28%)
Thiopurines	11 (18%)
Biologic therapy	20 (34%)
None	12 (20%)
Use of corticosteroids for the flare	
Yes	48 (84%)
No	10 (17%)
Rescue therapy	
Yes	29 (48%)
No	31 (51%)
Type of flare	
Mild	15(25%)
Moderate	21 (35%)
Severe	22 (37%)
In remission	2 (3%)
Endoscopic activity	
UC (53)	
Mayo 0	3 (6%)
Mayo 1	2 (4%)
Mayo 2	12 (23%)
Mayo 3	36 (68%)
CD (6)	
SES-CD > 8	6 (100%)
CRP	35.4±62.7 (mg/L)
FC	1444.6±1662.5 (μg/g)

IBD, inflammatory bowel disease; UC, ulcerative colitis; CD, Crohn's disease; IBD-U, unclassified IBD; anti-TNF, tumor necrosis factor inhibitors; SES-CD, Simple Endoscopic Score for Crohn's Disease; CRP, C-reactive protein; FC, fecal calprotectin

Combined PCR/IHC positivity was significantly associated with corticosteroid refractoriness (OR 3.58, 95%CI 1.11-11.48; P=0.03), whereas isolated PCR positivity was more frequently observed among corticosteroid-responsive patients (Table 2).

Regarding endoscopic activity, deep ulcers were observed in 24 patients (40%). Double positivity (PCR+/IHC+) was not more frequent in patients with deep ulcers compared with those without (9/24 vs. 10/36; P=0.3).

Antiviral treatment and clinical outcomes

Antiviral therapy was administered predominantly to patients with features suggestive of clinically relevant CMV infection, particularly those with combined PCR+/IHC+ positivity, in whom it was prescribed in 16/19 patients (84%) compared with 18/36 patients (50%) with isolated PCR positivity (OR 5.33, 95%CI 1.32-21.53; P=0.02). Similarly, antiviral treatment was used more frequently in corticosteroid-refractory patients, being administered to 22/23 patients (96%) vs. 15/37 (41%) corticosteroid-responsive patients (OR 32.27, 95%CI 3.92-265.82; P<0.001). In contrast, treatment decisions in patients with isolated PCR positivity appeared to be guided mainly by the overall clinical severity, rather than by CMV detection alone (Tables 3 and 4).

Despite this treatment pattern, no clear differences in short-term clinical remission or colectomy rates were observed according to CMV detection profile. Among corticosteroid-refractory patients, only 2 of 23 patients (9%) achieved remission with antiviral therapy alone, whereas most required rescue therapy to achieve remission. In corticosteroid-responsive patients, outcomes were generally favorable, regardless of CMV status (Tables 3 and 4).

At 12 weeks, clinical remission had been achieved in 20/23 corticosteroid-refractory patients (87%) and 32/37 corticosteroid-responsive patients (86%), while colectomy was required in 3/23 (13%) and 1/37 (3%), respectively.

Discussion

The role of CMV in IBD remains controversial, as its presence may represent either a mere innocent bystander

Table 2 Comparison between corticosteroid-refractory and corticosteroid-responsive patients according to PCR/IHC/H&E status*

Group	Corticosteroid-refractory (n=23)	Corticosteroid-responsive (n=37)	P-value
PCR+/IHC+ (n=19)	11 (48%)	8 (22%)	0.03
PCR+/IHC- (n=36)	10 (44%)	26 (70%)	0.05
IHC+/PCR- (n=5)	2 (9%)	3 (8%)	>0.99
H&E+ (n=14)	7 (30%)	7 (19%)	0.5

*Statistical comparisons were performed using Fisher's exact test
PCR, polymerase chain reaction; IHC, immunohistochemistry; H&E, hematoxylin–eosin stain

Table 3 Clinical outcomes of corticosteroid-refractory patients according to CMV status and antiviral treatment received

Group	CMV status	N	Antiviral treatment	Clinical remission (<4 weeks)	Colectomy
Corticosteroid-refractory	PCR+/IHC+	11	11 (100%)	6 (55%)	1 (9%)
	PCR+/IHC-	10	9 (90%)	6 (60%)	2 (20%)
	IHC+/PCR-	2	2 (100%)	1 (50%)	0 (0%)
	Total	23	22 (96%)	13 (57%)	3 (13%)
				P-value	P-value
				P=0.95	P=0.64

CMV, cytomegalovirus; PCR, polymerase chain reaction; IHC, immunohistochemistry

Table 4 Clinical outcomes of non–corticosteroid-refractory patients according to CMV status and antiviral treatment received

Group	CMV status	N	Antiviral treatment	Clinical remission (<4 weeks)	Colectomy
Non–corticosteroid-refractory	PCR+/IHC+	8	5 (62%)	6 (75%)	0 (0%)
	PCR+/IHC-	26	9 (35%)	18 (69%)	1 (4%)
	IHC+/PCR-	3	1 (33%)	3 (100%)	0 (0%)
	Total	37	15 (41%)	27 (73%)	1 (3%)
				P-value	P-value
				P=0.52	P=0.80

CMV, cytomegalovirus; PCR, polymerase chain reaction; IHC, immunohistochemistry

in inflamed tissue, or a potential marker of corticosteroid refractoriness. Consequently, the interpretation of a positive result remains uncertain and has been widely debated in the literature [10,17].

One of the main methodological challenges lies in the heterogeneity of the diagnostic procedures used, which makes comparisons between studies difficult. In addition, in many cases detection is performed using noninvasive techniques, which do not reliably distinguish between active and latent infection. In our study, we analyzed 60 intestinal biopsies from patients with IBD, mostly ulcerative colitis, that were positive for CMV by PCR and/or IHC/H&E. Isolated PCR positivity was the most frequent finding. However, double positivity (PCR+/IHC+) was associated with more severe flares, corticosteroid refractoriness, and a greater tendency to initiate antiviral therapy. Nevertheless, the presence of CMV, regardless of the diagnostic technique used, did not translate into significant differences in clinical remission or colectomy rates, which limits the immediate clinical applicability of these findings.

These results are consistent with previous studies suggesting that isolated PCR positivity has limited clinical value, whereas combined PCR+/IHC+ appears to be more closely associated with severe disease features [5,13,18].

A key observation in our study was the association between double positivity (PCR+/IHC+) and greater flare severity and corticosteroid refractoriness. This subgroup of patients accounted for most of the cases in which antiviral therapy was initiated, in line with current clinical practice guideline recommendations [4,10]. However, no significant differences were observed in clinical remission or colectomy rates after treatment, which is consistent with other studies that question the clinical impact of antiviral therapy, even in patients with CMV detected in intestinal biopsy specimens [3,8,19]. Taken together, these findings suggest that CMV detection patterns may be more useful for the phenotypic characterization of severe disease than as reliable predictors of prognosis or treatment response.

In this context, immunosuppression is a key factor, as exposure to high-dose corticosteroids, thiopurines or calcineurin inhibitors increases the risk of active viral replication [20,21]. Studies have shown a higher prevalence of PCR+/IHC+ in patients who have received these treatments, as observed in our cohort [3,7]. However, patients with isolated PCR positivity were predominantly corticosteroid responsive and presented with milder flares. In this group, antiviral therapy was not initiated systematically but was more often guided by flare severity.

A systematic review and meta-analysis of 15 observational studies (N=333) showed no benefit of antiviral therapy in this subgroup, identifying corticosteroid refractoriness and double positivity as the most relevant factors for initiating treatment. In that study, lower colectomy rates were observed after antiviral treatment (OR 0.2, 95%CI 0.08-0.49) in the corticosteroid-refractory group, but only in patients with PCR+/IHC+ and not in those with PCR+/IHC−. However, in the same study, no differences were found with either IHC or PCR in the group of corticosteroid responsive patients, supporting the hypothesis that CMV detection in these cases may reflect underlying inflammation, rather than clinically relevant viral disease [8].

Isolated PCR positivity was the most frequent finding in our cohort, reflecting its high sensitivity but limited specificity for identifying active CMV infection [10,22]. In contrast, IHC and/or H&E, although less sensitive, are more specific and correlate more closely with viral load [12,23]. Recent ECCO guidelines similarly emphasize the importance of tissue-based CMV detection and the concept of tissue viral burden when assessing clinically relevant CMV infection [9]. Studies using quantitative PCR have shown that IHC positivity tends to increase with tissue viral load, and may therefore serve as a proxy for "high-grade" infection, which has been associated with corticosteroid refractoriness and poorer clinical outcomes [12,24]. This association was observed in PCR+/IHC+ cases in our study, but not in PCR+/IHC– cases, which probably represent a heterogeneous group that includes low-grade viral reactivation as well as latent infection. Future studies incorporating quantitative viral load thresholds may help better distinguish clinically relevant CMV reactivation from incidental viral detection in inflamed mucosa.

Finally, CMV has been mainly associated with ulcerative pancolitis, severe flares and moderate-to-severe endoscopic activity, features present in most patients in our cohort [17,21]. However, we found no association between deep ulcers and CMV double positivity (PCR+/IHC+), a finding that remains controversial in the literature. While some studies link CMV with "punched-out" ulcers, others suggest that ulceration is more closely related to flare severity [25,26]. Our findings support the hypothesis that CMV detection may reflect severe underlying inflammation, rather than a specific endoscopic phenotype [27,28].

Our study had several limitations, including its retrospective design and the relatively small sample size, which limits the ability to fully compare subgroups. In addition, CMV testing was not protocolized, and was mainly performed according to clinical judgment, particularly in patients with severe flares or suspected corticosteroid refractoriness. This may have introduced selection bias toward more severe cases, and could have overestimated the observed associations between CMV detection patterns and disease severity. In addition, the absence of multivariate analysis limits the ability to account for potential confounding factors, such as immunosuppressive therapy, corticosteroid exposure and disease duration. Furthermore, the cohort mainly consisted of patients with ulcerative colitis, limiting the extrapolation of the findings to Crohn's disease. An important limitation is the absence of a CMV-negative comparator group, which precludes determining whether CMV detection is independently associated with disease severity, or simply reflects severe underlying inflammation. In addition, the PCR used was qualitative rather than quantitative; therefore, we were unable to distinguish between high-grade and low-grade infection—in contrast to more recent studies that appear to show better correlation with IHC, and may represent the future direction of this field. The lack of quantitative tissue PCR limits the interpretation of isolated PCR-positive cases, as viral load could not be assessed. Therefore, some PCR+/IHC– cases may represent low-grade or incidental CMV detection, rather than clinically relevant infection. At our center, qualitative tissue PCR represented the standard diagnostic approach during the study period and reflects real-world clinical practice.

Conversely, our study also had several strengths. It addressed a clinically relevant and still unresolved issue: the role of CMV in IBD in a real-world setting at a tertiary hospital, with a long inclusion period and a large initial screening cohort. Multiple diagnostic methods (PCR and IHC/H&E) were used to determine the presence of CMV in biopsy specimens, allowing assessment of concordance between techniques. In addition, clinical, biochemical and endoscopic variables were comprehensively described to contextualize CMV detection in relation to IBD activity and the treatments received. Therapeutic variables and predefined clinical outcomes (remission and colectomy) were also collected to facilitate interpretation of the findings in clinical practice.

Taken together, in our predominantly ulcerative colitis cohort, combined PCR+/IHC+ positivity was more frequently observed in patients with severe flares and corticosteroid refractoriness among CMV-positive cases. However, given the absence of a CMV-negative comparator group, it remains unclear whether CMV detection represents a causative factor or simply reflects severe underlying inflammation. These findings support the need for cautious interpretation of isolated tissue PCR positivity and suggest that combined diagnostic approaches (PCR and IHC) may provide better clinical contextualization of CMV detection in IBD.

Summary Box

What is already known:

- Cytomegalovirus (CMV) is frequently detected in inflammatory bowel disease (IBD), especially during severe ulcerative colitis flares
- Tissue polymerase chain reaction (PCR) is highly sensitive but cannot reliably distinguish clinically relevant reactivation from latent infection
- Antiviral therapy is mainly recommended for corticosteroid-refractory IBD patients with CMV detected in intestinal biopsies

What the new findings are:

- Isolated tissue PCR positivity was the most common pattern but showed limited clinical relevance
- Combined PCR/immunohistochemistry positivity was associated with severe flares, corticosteroid refractoriness, and more frequent antiviral treatment
- These findings support a cautious interpretation of isolated PCR positivity, and suggest that combining PCR with histology better identifies clinically relevant CMV infection

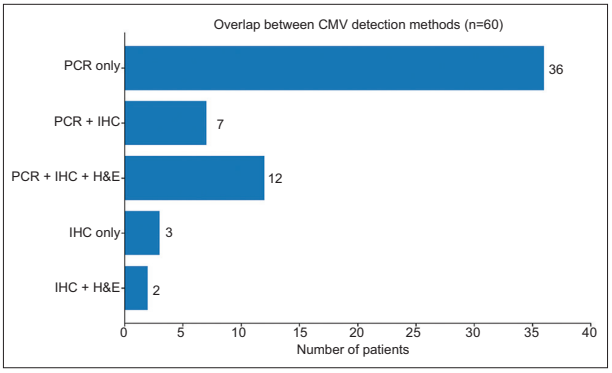
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During the preparation of this manuscript, the authors used ChatGPT (OpenAI, version GPT-5.3) for assistance with parts of the statistical analysis and the preparation of tables. The authors have reviewed and edited the output and take full responsibility for the content of this publication.

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Supplementary material



Supplementary Figure 1 Overlap between CMV detection methods. Distribution of patients according to the combinations of tissue PCR, IHC and H&E positivity. Among the 60 patients, 36 were PCR-positive only, 7 were PCR+/IHC+, 12 were positive by all 3 methods, 3 were IHC-positive only, and 2 were IHC+/H&E+ but PCR-negative
CMV, cytomegalovirus; PCR, polymerase chain reaction; IHC, immunohistochemistry; H&E, hematoxylin–eosin stain