Can Video Capsule Endoscopy Replace Biopsy in the Diagnosis of Celiac Disease?

Yaron Niv MD FACG AGAF

Adelson Faculty of Medicine, Ariel University, Ariel, Israel

ABSTRACT Celiac disease (CD) is diagnosed by demonstrating gluten-induced villous atrophy on duodenal biopsy in patients with positive serology. Duodenal histology remains the gold standard, although pediatric guidelines allow a no-biopsy approach in highly seropositive children. Video capsule endoscopy (VCE) can visualize mucosal changes typical of active CD, such as flattening of mucosal folds, fissuring, scalloping, ulcerations, throughout the small bowel, overcoming the regular endoscopy capability of reaching the proximal duodenum and missing distal and patchy lesions. In this review, I discussed whether VCE can replace duodenal biopsy for diagnosing celiac disease. I summarized diagnostic yield, sensitivity/specificity, and clinical contexts favoring VCE as well as its limitations and potential future role (including artificial intelligence enhancement). I found that video capsule endoscopy is a valuable adjunctive tool to diagnose CD, but currently it complements, rather than outright replaces, duodenal biopsy.

IMAJ 2026; 28: 196–198

KEY WORDS: celiac disease (CD), flat intestinal mucosa, refractory celiac disease, scalloping, video capsule endoscopy (VCE)

Celiac disease (CD) is diagnosed by demonstrating gluten-induced villous atrophy on a duodenal biopsy in patients with positive serology. Duodenal histology remains the gold standard; however, pediatric guidelines permit a non-biopsy approach in highly seropositive children [1]. Video capsule endoscopy (VCE) provides non-invasive, high-resolution imaging of the entire small intestine. Early studies suggested capsule findings (e.g., scalloping of folds, mucosal mosaicism, micro nodularity, loss of folds) correlate with CD [2,3]. VCE can visualize mucosal changes throughout the small bowel, whereas standard endoscopy samples only the proximal duodenum. I integrated data from recent meta-analyses and case series [2-6]. A meta-analysis of six studies (166 patients) found VCE sensitivity 89% (95% confidence interval [95%CI] 82–94%) and specificity 95% (95%CI 89–98%) [3]. Another review that cited guidelines reported identical specificity (100%) and higher sensitivity than standard endoscopy (70% vs. 60%) in a study of Marsh III CD [4]. Nonetheless, in real-world cohorts of known celiac patients, many on a gluten-free diet or with mild disease, the diagnostic yield of VCE is lower [2] [Table 1].

In this review, I discussed whether VCE can replace duodenal biopsy for diagnosing CD. I summarized diagnostic yield, sensitivity/specificity, and clinical contexts favoring VCE as well as its limitations and potential future role (including enhancement with artificial intelligence [AI]).

Table 1. Diagnostic performance of capsule endoscopy in celiac disease

Parameter	Video capsule endoscopy
Sensitivity (untreated CD) [3]	89% (95%CI 82–94%)
Specificity [3]	95% (95%CI 89–98%)
Overall diagnostic yield (CD patients) [2]	60%
Visualization of the small bowel [2-6]	Complete small bowel view achieved 97%
Tissue sampling	Not possible (no biopsy)
Detection of complications [2]	Yes (ulcers, strictures, lymphoma)
Recommended indications	If biopsy infeasible

95%CI = 95% confidence interval

A RECENT META-ANALYSIS

A recent meta-analysis (22 studies, 1585 patients) found any diagnostic finding (villous atrophy, fissures, mosaic pattern, scalloping, ulcer, or ulcerations) on VCE in only 60% of cases [2]. Common VCE findings in CD include villous atrophy (60% of cases), scalloping (57%), mosaic pattern (44%), mucosal fissures (44%), and ulcers (25%).

A complete small-bowel examination was usually achieved (97% completion). Many patients in these studies had been treated with a gluten-free diet and were in clinical remission. This result may explain the 60% positive in the VCE (100% were diagnosed with CD according to biopsy).

CLINICAL SCENARIOS WHERE VCE MAY SERVE AS A BIOPSY ALTERNATIVE

Biopsy contraindications or refusal

VCE can confirm characteristic changes in patients unwilling or unable to undergo endoscopy. For example, Chang et al. [5] reported eight patients with high clinical suspicion and positive serology who either refused or could not have an endoscopy. All had diagnostic changes on VCE, and follow-up confirmed CD by diet response. The United European Gastroenterology guideline explicitly advises VCE only for patients with positive serology who are unwilling or unable to undergo biopsy [4]. Seehusen [6] reviewed the diagnostic tests for CD recommended by the American Academy of Family Physicians and recommended VCE as an alternative when biopsy is declined.

CELIAC DISEASE IS DIAGNOSED BY DEMONSTRATING GLUTEN-INDUCED VILLOUS ATROPHY ON DUODENAL BIOPSY IN PATIENTS WITH POSITIVE SEROLOGY.

High seropositivity, equivocal biopsy

In patients with very high tissue transglutaminase antibody titers, a normal duodenal biopsy may reflect patchy disease or sampling error. VCE can visualize distal villous atrophy beyond biopsied sites. For example, Chang et al. [5] described a patient with positive serology and normal duodenal biopsy. VCE revealed distal duodenal/jejunal atrophy not seen on standard endoscopy [7]. Capsule imaging can uncover patchy or more distal lesions that biopsies may miss.

DUODENAL HISTOLOGY REMAINS THE GOLD STANDARD, ALTHOUGH PEDIATRIC GUIDELINES ALLOW A NO-BIOPSY APPROACH IN HIGHLY SEROPOSITIVE CHILDREN.

Refractory or non-responsive CD

VCE is particularly valuable in patients with persistent symptoms or those who are not healing despite a gluten-free diet. In refractory CD (RCD), ongoing inflammation, and complications are concerns. RCD is classified into type 1 (normal-appearing intraepithelial lymphocytes) and type 2 (aberrant intraepithelial lymphocytes) [4]. In RCD, VCE can document extensive small-bowel involvement, persistent atrophy, ulcers, or strictures. VCE even detects neoplasia. The guideline notes that VCE frequently finds stenoses, ulcerations, or lymphoma in slow-responsive or refractory cases [4]. In practice, VCE may reveal ulcerative jejunitis or enteropathy-associated T-cell lymphoma that routine endoscopy may have missed. Thus, VCE is recommended for the assessment of suspected complications in RCD. VCE findings of ulcers or masses in RCD should prompt further evaluation.

Refractory CD is the setting where VCE has its greatest clinical impact, detecting ulcerative jejunitis, strictures, and lymphoma, and guiding device-assisted enteroscopy. It is also the context where capsule retention risk is highest, making patency capsule testing particularly relevant.

In a recent meta-analysis [2], 22 data sets included 956 patients with non-refractory celiac disease, and 16 included 393 patients with refractory celiac disease. Villous atrophy was demonstrated in 38.91% of non-refractory celiac cases versus 55.23% in refractory celiac cases ($P < 0.0001$). Other findings were scalloping, mosaic pattern, fissures, and ulcers/erosions in 37.65% vs. 44.78% ($P = 0.015$), 28.66% vs. 30.78% (not statistically significant), 20.39% vs. 20.86% (not statistically significant), and 9.10% vs. 19.33% ($P < 0.0001$), in non-refractory vs. refractory celiac disease, respectively. Thus, mucosal atrophy, scalloping, and ulcers/erosions were significant in refractory celiac disease, while mucosal mosaic patterns and fissures were not.

LIMITATIONS

VCE cannot obtain histologic samples, the cornerstone of CD confirmation. Without tissue, diagnoses of conditions mimicking CD (e.g., common variable immunodeficiency with enteropathy, tropical sprue, Whipple's disease, Crohn's disease) cannot be excluded, and associated disorders (e.g., *Helicobacter pylori* gastritis, eosinophilic enteritis) are undetected. Capsule features also lack absolute sensitivity. Studies have shown reduced sensitivity for partial or mild disease. For example, European guidelines noted that Marsh I–II lesions may escape VCE detection [4]. Some meta-analyses report wide variability, such as pooled sensitivity ranges (70–95%) and specificity (64–100%) [3]. These findings reflect heterogeneity in patient selection (treated vs. untreated), scoring criteria, and observer expertise. VCE interpretation is operator dependent. Interobserver agreement is moderate (κ 0.4–0.7), even among experienced readers [7]. In practical terms, a normal VCE does not entirely rule out

CD. In addition, capsule retention is a small but real risk (especially in stricturing disease). Last, VCE generally has a higher cost and may not be covered by all insurers. Nonetheless, although there is a differential diagnosis for villous atrophy, in the setting of an elevated transglutaminase, VCE stigmata would be highly suggestive of CD.

FUTURE DIRECTIONS (ARTIFICIAL INTELLIGENCE/ COMPUTER VISION)

Emerging studies are applying machine learning to analyze capsule images. Early reports suggest AI algorithms can identify villous atrophy patterns with sensitivity and specificity comparable to expert readers [8,9]. For example, convolutional neural networks trained on capsule images have achieved 90–95% accuracy in detecting celiac lesions. As this technology matures, it may improve the consistency and diagnostic yield of VCE. Integration with clinical data, serology, and HLA typing could also support non-biopsy diagnostic algorithms, though prospective validation is needed.

CONCLUSIONS

Duodenal biopsy remains the definitive standard for the diagnosis of CD. VCE cannot fully replace biopsy due to the inability to obtain histology, and variable sensitivity in treated/mild disease. However, VCE has a high sensitivity (80–90%) and specificity (> 90%) in active CD. It is especially useful as an alternative in selected situations, such as patients with contraindications or refusal of endoscopy and those with high serologic likelihood but non-diagnostic biopsy. VCE may also help to evaluate refractory or complicated disease presentation. In such cases, characteristic capsule findings (e.g., scalloping, mosaic pattern, ulcers) can effectively confirm CD when combined with serology. Future advances, including AI-supported image analysis, may enhance VCE's accuracy and utility. Overall, VCE is a valuable adjunctive tool in the CD diagnostic arsenal, but at present it complements, rather than outright replaces, duodenal biopsy. Given the established no-biopsy guidelines for children, using VCEs in this population is even more limited to highly selected cases, such as those with refractory disease.

Correspondence

Dr. Y. Niv
Adelson Faculty of Medicine, Ariel University, Ariel 4077625, Israel
Email: nivy@ariel.ac.il; nivyaron80@gmail.com

References

1. Kelly CP, Bai JC, Liu E, Leffler DA. Advances in diagnosis and management of celiac disease. *Gastroenterology* 2015; 148 (6): 1175-86.
2. Shapiro M, Niv Y. Diagnostic yield of video capsule endoscopy in celiac disease: systematic review and meta-analysis. *J Clin Gastroenterol* 2025; 59 (7): 598-606.
3. Rokkas T, Niv Y. The role of video capsule endoscopy in the diagnosis of celiac disease: a meta-analysis. *Eur J Gastroenterol Hepatol* 2012; 24 (3): 303-8.
4. Al-Toma A, Volta U, Auricchio R et al. European Society for the Study of Coeliac Disease (ESsCD) guideline for coeliac disease and other gluten-related disorders. *Uni Eur Gastroenterol J* 2019; 7 (5): 583-613.
5. Chang MS, Rubin M, Lewis SK, Green PH. Diagnosing celiac disease by video capsule endoscopy when EGD/biopsy is non-diagnostic or infeasible: a case series. *BMC Gastroenterol* 2012; 12: 90.
6. Seehusen DA. Comparative accuracy of diagnostic tests for celiac disease. *Am Fam Physic* 2017; 95: 727-9.
7. Spada C, Riccioni ME, Uregesi R, Costamagna G. Capsule endoscopy in celiac disease. *World J Gastroenterol* 2008; 14 (26): 4146-51.
8. Zammit SC, McAlindon ME, Greenblattt E et al. Quantification of celiac disease severity using video capsule endoscopy: a comparison of human experts and machine learning algorithms. *Curr Med Imaging* 2023; 19 (12): 1455-62.
9. Pennazio M, Rondonotti E, Despott EJ, et al. Small-bowel capsule endoscopy and device-assisted enteroscopy for diagnosis and treatment of small-bowel disorders: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2022. *Endoscopy* 2023; 55 (1): 58-95.

Capsule

Averting aberrant T cell activity

Dendritic cells (DCs) are a diverse group of innate immune cells that present antigens to T cells. Maturation of DCs, independent of infection, is essential to guide the development of regulatory T (T_{reg}) cells that help to prevent autoimmune responses. **Adams** et al. found that the transcription factor Etv3 was essential for controlling tolerogenic transcriptional programs in DCs in mice. In its absence, DCs expressed higher levels of costimulatory molecules, the differentiation of T_{reg} cells was dysregulated, and mice developed multiorgan inflammation as they aged. DCs from patients with systemic lupus erythematosus that have variants in the *ETV3* gene previously linked to the disease had lower expression of *ETV3* compared with DCs from individuals that did not carry the allele.

Science 2026; 391: 682
Eitan Israeli