Preendoscopic serologic test with duodenal biopsy in high-risk patients had high sensitivity and low specificity for celiac disease

Hopper AD, Cross SS, Hurlstone DP, et al. **Pre-endoscopy serological testing for coeliac disease: evaluation of a clinical decision tool.** BMJ. 2007;334:729.

Clinical impact ratings: Gastroenterology ★★★★★☆☆

QUESTION

Does a clinical decision tool (CDT) based on preendoscopic serologic testing with duodenal biopsy for high-risk patients accurately diagnose celiac disease?

METHODS

Design: 2 cohort studies, 1 for derivation and 1 for validation.

Setting: Endoscopy department at the Royal Hallamshire Hospital, Sheffield, England, United Kingdom.

Patients: 1464 patients in the retrospective derivation cohort and 2000 patients 16 to 94 years of age (mean age 56 y, 58% women) in the prospective validation cohort who were referred for gastroscopy. Exclusion criteria were previously known celiac disease, coagulopathy (international normalized ratio > 1.3 or platelets < 80 x 10^9/L), active gastrointestinal bleeding, or suspected cancer.

Description of prediction guide: The CDT combined preendoscopic serologic testing (tissue transglutaminase [TTG] antibody) and assessment of symptoms to identify patients at high or low risk for celiac disease. The CDT was modified in the validation cohort to include duodenal biopsy for all high-risk patients. Patients were at high risk if they had indications for weight loss, anemia (hemoglobin level < 120 g/L in women or < 130 g/L in men), or diarrhea (bowel movement frequency > 3 times/d). Patients were at low risk if they had atypical symptoms for celiac disease, including abdominal pain, reflux, dyspepsia, vomiting or nausea, or chest pain.

Outcomes: Diagnosis of celiac disease.

MAIN RESULTS

61 (4.2%) patients in the derivation cohort and 77 (3.9%) patients in the validation cohort were newly diagnosed with celiac disease. In the validation cohort, 739 (37%) patients were categorized as high risk and 1261 (63%) were categorized as low risk; the prevalence of celiac disease was 9.6% in the high-risk group and 0.5% in the low-risk group. The CDT with preendoscopic serologic testing and duodenal biopsy in high-risk patients had higher sensitivity but lower specificity than did the CDT with preendoscopic serologic testing only (Table). The likelihood ratios are in the Table.

CONCLUSION

A clinical decision tool based on preendoscopic serologic testing combined with duodenal biopsy for high-risk patients diagnosed all cases of celiac disease.

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Derivation and validation of a clinical decision tool to diagnose celiac disease in patients referred for gastroscopy*

Clinical decision tool	Cohort	Sensitivity (95% CI)	Specificity (CI)	+LR	–LR
Preendoscopic serologic testing (PST) only	DER	94%	97%	31	0.06
	VAL	91%	91%	10	0.1
PST + duodenal biopsy for high-risk group	VAL	100% (95 to 100)	61% (59 to 63)	2.6	0

*DER = derivation; VAL = validation. Diagnostic terms defined in Glossary. LRs calculated from data in article.

COMMENTARY

Serologic testing has shown a high prevalence of celiac disease (approximately 1%) in many areas, including North America, where it was previously thought to be uncommon. It has also facilitated diagnosis. However, the protean clinical manifestations of celiac disease mean that the disease has to be included in the differential diagnosis for many patients. Unfortunately, current serologic tests are neither sufficiently sensitive nor specific to be used alone as screening tests in all clinical settings (1).

The categorization of patients into high- and low-risk groups according to the CDT by Hopper and colleagues is pragmatic: Important groups, such as patients with a family history or those with conditions associated with celiac disease, were not considered. In addition, the quantitative element of the TTG assay has been ignored. The pragmatic categorization resulted in more than one third of patients being considered as high risk for celiac disease and therefore requiring duodenal biopsy irrespective of the results of the TTG assay. Consequently, in the validation cohort, 739 patients in the high-risk group proceeded to upper gastrointestinal endoscopy to diagnose 71 cases of celiac disease, including 7 cases in 585 high-risk patients with normal results on the TTG test.

Although Hopper and colleagues maintain that their CDT would be cost-effective in reducing the numbers of patients needing duodenal biopsies by 40%, this presupposes that celiac disease was being considered in the differential diagnosis for these low-risk patients. What is clear is that the specificity of the TTG assay alone is poor (90.9%), with the positive predictive value in the high-risk group being only 28.6%. Relying on the TTG assay alone will result in a considerable number of patients needing duodenal biopsies.

Nevertheless, the study is an important contribution to improving the diagnosis of celiac disease: It confirms that in patients at low risk for the condition, a negative result on the TTG assay is sufficient to rule out the diagnosis of celiac disease.

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Reference

1. **Lewis NR, Scott BB.** Systematic review: the use of serology to exclude or diagnose coeliac disease (a comparison of the endomysial and tissue transglutaminase antibody tests). Aliment Pharmacol Ther. 2006;24:47-54.