

Chronic GERD and risk of esophageal adenocarcinoma: Should we screen with gastroscopy?

Sander Veldhuyzen van Zanten MD PhD

■ Cite as: *CMAJ* 2020 July 6;192:E781-2. doi: 10.1503/cmaj.200697

See related article at www.cmaj.ca/lookup/doi/10.1503/cmaj.190814

A new guideline by the Canadian Task Force on Preventive Health Care recommends against screening all patients with chronic gastroesophageal reflux disease (GERD) for esophageal adenocarcinoma.¹ Although the guideline was robustly developed, its strong recommendation against gastroscopy screening is based on very low-quality evidence, which warrants discussion.

The guideline developers looked at 3 main outcome measures in the systematic review of esophageal screening studies that informed their recommendations: decrease in mortality, detection of esophageal adenocarcinoma at an earlier stage and detection of treatable precancerous conditions, such as Barrett esophagus or dysplasia, resulting in improved outcomes.

They found a single small retrospective study of 155 patients, which showed that screening was associated with cases of esophageal adenocarcinoma being diagnosed at an earlier stage, but showed no survival benefit.² A second retrospective study of 153 patients did not provide meaningful data on the outcomes of interest.¹

The new guideline's recommendation against gastroscopy screening does not apply to patients with alarm symptoms such as dysphagia, evidence of upper gastrointestinal bleeding, weight loss and vomiting. Nor does it apply to patients who receive a diagnosis of Barrett esophagus, which requires that gastroscopy and histology must have been performed in the past. Such patients are considered to be at higher risk of esophageal adenocarcinoma. Unfortunately, more than 90% of patients given a diagnosis of esophageal adenocarcinoma do not have a previous diagnosis of Barrett esophagus.³ This, despite the belief that most esophageal adenocarcinomas occur on a background of Barrett esophagus, which is a change in the squamous epithelium of the lower esophagus to intestinal metaplasia that develops as a consequence of pathologic acid reflux into the esophagus. Furthermore, Barrett esophagus is detected in only 5%–20% of patients who undergo gastroscopy for GERD symptoms.^{4,5}

Ongoing surveillance gastroscopy is recommended in most patients with Barrett esophagus, with competing comorbidities

KEY POINTS

- Esophageal cancer, including esophageal adenocarcinoma, is uncommon in Canada.
- Having symptoms of chronic gastroesophageal reflux disease (GERD) increases the risk of developing Barrett esophagus and esophageal adenocarcinoma.
- A review undertaken for a new Canadian guideline found no evidence that screening most patients with chronic GERD for Barrett esophagus and esophageal adenocarcinoma improves overall mortality or mortality associated with esophageal adenocarcinoma.
- Screening with gastroscopy should be avoided in patients with chronic GERD who are young (< 50 yr), as the yield of clinically important findings is likely to be low, but it may yet be reasonable to consider screening in older men (> 50 yr) with risk factors such as smoking or central obesity, as waiting for alarm symptoms may mean cancer is diagnosed at an inoperable stage.

and advanced age exceptions.³ Evidence that this leads to better long-term outcomes, such as decrease in mortality associated with esophageal cancer, is scant. Some studies have shown that surveillance gastroscopy for Barrett esophagus can diagnose dysplasia and esophageal adenocarcinoma at an earlier stage.⁶ However, surveillance gastroscopy programs for Barrett esophagus are expensive, and benefits, if any, are few for most patients.

Esophageal cancer in Canada is uncommon, accounting for 1.6% and 0.5% of new cancers diagnosed in men and women, respectively, and an estimated 1689 deaths from cancer in men and 503 in women in 2019.⁷ The 5-year survival of esophageal cancer is dismal, at 17% and 15% in men and women, respectively, because most cancers are diagnosed at an advanced age.⁷ Esophageal adenocarcinoma is now much more common than esophageal squamous cell cancer, which is explained by reduced population levels of smoking. The incidence of esophageal adenocarcinoma did double over the years 1986–2006, but this

increase has levelled off. Overall, in Canada the incidence of esophageal cancer has been decreasing since 2010. The percentage annual change during the period 1984–2015 was 2.4% in men and 0.4% in women.⁷

Conversely, GERD is common in primary care. However, what constitutes a patient with chronic GERD symptoms — the target population for the new guideline — is poorly defined in the literature. Gastroesophageal reflux disease can be diagnosed if a patient has dominant symptoms of heartburn or acid regurgitation or both,⁸ which is usually effectively and safely treated with acid-suppressive therapy, especially proton pump inhibitors (PPIs). However, the symptoms of GERD, peptic ulcer disease and dyspepsia — defined as meal-associated epigastric pain — overlap substantially.⁹ Moreover, because many patients with GERD have recurrent or persistent symptoms after an initial course of acid-suppressive therapy, a large proportion of long-term PPI users is likely to have chronic GERD. Therefore, for family physicians considering whether the new guideline applies to their patients who have taken PPIs for many years for GERD symptom control, the answer is yes.

The guideline acknowledges that there are established risk factors that increase the possibility of developing Barrett esophagus and esophageal adenocarcinoma. These include male gender, age (≥ 50 yr), white race, central obesity, smoking and duration of symptoms.^{3–5} Having GERD symptoms for more than 5 years significantly increases the risk of developing esophageal adenocarcinoma, although the absolute risk remains low. The systematic review that underpins the guideline identified no studies that provided adequate data to support modifying the recommendation to not offer screening for any of these risk factors individually or in combination.¹

“Once in a lifetime” gastroscopy in patients with GERD has not been shown to lead to a decrease in mortality related to esophageal adenocarcinoma or all-cause mortality. However, absence of evidence of benefit — in this case, screening with gastroscopy — does not mean there is evidence of absence of a benefit. Given the high prevalence of GERD, its substantial overlap with dyspepsia (non-GERD upper gastrointestinal symptoms) and the current high usage of gastroscopy, it is unlikely that definitive studies, ideally randomized controlled trials (RCTs), addressing this specific question will ever be conducted.

The task force’s strong recommendation against gastroscopy screening for patients with chronic GERD without alarm symptoms depended in part on the assumption that scarce health resources would need to be expended to implement screening. Although the task force review delved into the potential harms of screening, gastroscopy is really a straightforward, safe and well-tolerated procedure. It also diagnoses more than just esophageal cancer. When we wait until there are alarm symptoms, esophageal adenocarcinoma will often be inoperable. Certainly, performing gastroscopy should be avoided in patients younger than 50 years with chronic GERD symptoms, as the yield of clinically important findings in such patients is very low. If physicians do consider judicious use of gastroscopy for patients with chronic GERD, it should be for patients older than 50 years.

The authors of the task force guideline note that several other published guidelines have qualified their recommendation to not offer screening to all patients with chronic GERD by acknowledg-

ing that certain subgroups of patients are at increased risk of developing Barrett esophagus and, hence, esophageal adenocarcinoma.¹ For example, both the Clinical Guidelines Committee of the American College of Physicians and the American College of Gastroenterology state that screening for Barrett esophagus and esophageal adenocarcinoma may be considered.^{4,5} But this is limited to men aged 50 years or older with chronic (> 5 yr) or frequent symptoms of GERD, who have additional risk factors, such as obesity, smoking or white race.

Furthermore, a recent large RCT, the ASPECT trial, found that in patients with Barrett esophagus greater than 1 cm in length, treatment with a PPI twice daily was superior to once-daily PPI in reducing the composite outcome of mortality, diagnosis of esophageal adenocarcinoma or high-grade dysplasia.¹⁰ Given these findings suggesting that high-dose (twice-daily) PPI could be protective, it is likely that a push to screen for Barrett esophagus, for which the target population is the patient with chronic GERD, will continue. As such, the current task force guideline is unlikely to entirely prevent screening of patients with chronic GERD.

References

- Groulx S, Limburg H, Doull M, et al.; the Canadian Task Force on Preventive Health Care. Guideline on screening for esophageal adenocarcinoma in patients with chronic gastroesophageal reflux disease. *CMAJ* 2020;192:E768-77.
- Rubenstein JH, Sonnenberg A, Davis J, et al. Effect of a prior endoscopy on outcomes of esophageal adenocarcinoma among United States veterans. *Gastrointest Endosc* 2008;68:849-55.
- Spechler SJ, Sharma P, Souza RF, et al. American Gastroenterological Association medical position statement on the management of Barrett’s esophagus. *Gastroenterology* 2011;140:1084-91.
- Shaheen NJ, Weinberg D, Denberg T, et al. Upper endoscopy for gastroesophageal reflux disease: best practice advice from the clinical guidelines committee of the American College of Physicians. *Ann Intern Med* 2012;157:808-16.
- Shaheen NJ, Falk GW, Iyer PG, et al.; American College of Gastroenterology. ACG clinical guideline: diagnosis and management of Barrett’s esophagus. *Am J Gastroenterol* 2016;111:30-50.
- Codipilly DC, Chandar AK, Singh S, et al. The effect of endoscopic surveillance in patients with Barrett’s esophagus: a systematic review and meta-analysis. *Gastroenterology* 2018;154:2068-86.
- Canadian Cancer Statistics Advisory Committee. *Canadian Cancer Statistics 2019*. Toronto: Canadian Cancer Society; 2019. Available: cancer.ca/Canadian-Cancer-Statistics-2019-EN.pdf (accessed 2019 Sept. 15).
- Vakil N, Veldhuyzen van Zanten S, Kahrilas P, et al.; Global Consensus Group. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol* 2006;101:1900-20.
- Veldhuyzen van Zanten SJO, Flook N, Chiba N, et al. An evidence-based approach to the management of uninvestigated dyspepsia in the era of *Helicobacter pylori*. Canadian Dyspepsia Working Group. *CMAJ* 2000;162(Suppl):S3-23.
- Jankowski JAZ, de Caestecker J, Love SB, et al. Esomeprazole and aspirin in Barrett’s esophagus (AspECT): a randomised factorial trial. *Lancet* 2018;392:400-8.

Competing interests: Sander Veldhuyzen van Zanten reports receiving consulting fees from Paladin and speaker fees from Pfizer, and reports being an advisory board member for AbbVie and Allergan, all outside the submitted work.

This article was solicited and has not been peer reviewed.

Affiliation: Division of Gastroenterology, Zeidler Ledcor Centre, Department of Medicine, University of Alberta; Digestive Health Strategic Clinical Network, Alberta Health Services, Edmonton, Alta.

Correspondence to: Sander Veldhuyzen van Zanten, vanzanten@ualberta.ca