

A survey of Canadian gastroenterologists about the management of Barrett's esophagus

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L MacNeil-Covin, AG Casson, D Malatjalian, S Veldhuyzen van Zanten. A survey of Canadian gastroenterologists about the management of Barrett's esophagus. *Can J Gastroenterol* 2003;17(5):313-317.

The aims of the present study were to determine practice patterns of Canadian gastroenterologists for screening patients with Barrett's esophagus and to compare current practice patterns with published guidelines. A secondary goal was to evaluate whether gastroenterologists recommend a 'once in a lifetime' endoscopy for patients with chronic gastroesophageal reflux disease. A structured questionnaire regarding screening for Barrett's esophagus was sent to members of the Canadian Association of Gastroenterology. The overall response rate was 51% (203 of 396). Of the 203 respondents, 165 (81%) performed endoscopies in adults and form the basis of this report. The majority of Canadian gastroenterologists followed published guidelines, with 62% screening patients without dysplasia every two years. Patients with low grade dysplasia were screened more frequently, with 54% of respondents performing endoscopy every six months, and 35% on a yearly basis. Biopsy protocols showed the greatest variation, with 46% of gastroenterologists taking four-quadrant biopsies at 2 cm intervals along the columnar-lined (Barrett's) esophagus. Seventy-six per cent of gastroenterologists agreed that all patients with chronic gastroesophageal reflux should have a 'once in a lifetime' endoscopy to screen for Barrett's esophagus. The majority of Canadian gastroenterologists follow current guidelines for the management of Barrett's esophagus and support the concept of 'once in a lifetime' endoscopy.

Key Words: *Barrett's esophagus; Canada; Dysplasia; Gastroesophageal reflux disease; Screening; Survey*

Barrett's esophagus (BE) is a premalignant condition characterized by replacement of squamous epithelium of the esophagus with specialized intestinal columnar epithelium. The development of BE is associated with chronic gastroesophageal reflux disease (GERD) (1,2). The prevalence of BE is estimated at 22.6 cases in 100,000 population, based on cases detected in patients undergoing esophagogastroscopey (endoscopy) (3). However, the results of 733 unselected autopsies estimated the actual prevalence to be much higher in the general population, at 376 per 100,000 (3). The prevalence of BE is threefold higher in male patients compared with females (4). It is generally accepted that BE carries a small but definite risk of progression to invasive esophageal adenocarcinoma,

Enquête auprès des gastro-entérologues canadiens sur le traitement de l'œsophage de Barrett

Cette enquête visait à déterminer les modèles de pratique des gastro-entérologues canadiens pour le dépistage de l'œsophage de Barrett ainsi qu'à comparer les modèles actuels de pratique avec les lignes directrices publiées. Son objectif secondaire était de déterminer si les gastro-entérologues recommandent une « seule endoscopie à vie » chez les patients qui souffrent de reflux gastro-œsophagien chronique. Un questionnaire structuré sur le dépistage de l'œsophage de Barrett a été envoyé aux membres de l'Association canadienne de gastro-entérologie. Le taux de réponse global a été de 51 % (203 sur 396). Parmi les 203 répondants, 165 (81 %) effectuent des endoscopies chez des adultes et ce sont eux qui ont servi de base à ce rapport. La majorité des gastro-entérologues canadiens respectent les lignes directrices émises, et 62 % d'entre eux effectuent un test de dépistage tous les deux ans chez des patients ne présentant pas de dysplasie. Les patients qui présentent une légère dysplasie sont examinés plus fréquemment; à cet égard, 54 % des répondants prescrivent à ces patients une endoscopie tous les six mois et 35 %, une endoscopie par année. Les protocoles de biopsie ont montré de grandes différences alors que 46 % des gastro-entérologues effectuent des biopsies sur les quatre faces de l'œsophage, à intervalles de 2 cm le long de l'endobranchy-œsophage (œsophage de Barrett). Au total, 76 % des gastro-entérologues reconnaissent que tous les patients souffrant de reflux gastro-œsophagien chronique devrait subir une endoscopie au cours de leur vie dans le but de dépister l'œsophage de Barrett. La majorité des gastro-entérologues suivent les lignes directrices émises pour le traitement de l'œsophage de Barrett et appuient le concept de l'endoscopie une fois dans sa vie.

that is estimated from one in 52 to one in 208 patient years follow-up (5-9) or 0.5% per year (4). However, a recent report suggests a publication bias exists in reporting of cancer risk, consequently overestimating risk (10).

Over the past 30 years the incidence of primary esophageal adenocarcinoma has increased steadily (4), especially in white males (4,11,12). The prognosis for invasive esophageal adenocarcinoma is poor, and despite advances in multimodality therapy, five-year survival generally remains below 10% (13). However, in selected surgical series, overall five-year survival may approach 30% following resection of early stage disease (14,15), or for tumours with favourable biology (16). This observation underlies the rationale for endoscopic surveillance

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Received for publication October 18, 2002. Accepted February 12, 2003

(17), with the hope that early detection will improve long term survival. Currently, there is consensus that patients diagnosed with BE should enter an endoscopic surveillance program. However, the optimal frequency with which endoscopy and biopsy should be repeated is not known.

A number of guidelines for managing BE have been proposed (Table 1), with the following considerations: frequency of surveillance for patients with BE without dysplasia, and for low grade and high grade dysplasia; the timing of surgical referral; the role of alternative therapies; and standardization of biopsy protocols (18-21). None of these guidelines is based on prospective randomized studies.

The aim of the present study was to determine practice patterns of Canadian gastroenterologists for screening patients with BE and to compare those results with the published guidelines. A secondary objective was to determine whether gastroenterologists perform a 'once in a lifetime' endoscopy in patients who have long standing GERD.

METHODS

A two-page survey was developed, pretested using five gastroenterologists, and mailed with a self-addressed return envelope to active members of the Canadian Association of Gastroenterologists (CAG). The survey focused on endoscopic surveillance practices for patients with BE without dysplasia, with low grade dysplasia and with high grade dysplasia. Physicians were also asked about their biopsy techniques and whether they support a 'once in a lifetime' endoscopy for patients with chronic GERD. Surveys were sent out in English only. The survey was anonymous and included the following questions: practice setting (university or community); number of years in practice; and the number of patients seen with high grade dysplasia and esophageal adenocarcinoma. Physicians were asked to complete the survey without having to rely on patient charts. In the analysis the proportion of respondents who followed recommended guidelines is reported.

RESULTS

Surveys were mailed to 476 members of the CAG. From 80 surveys, it could not be determined whether the CAG members were in active clinical practice, which left 396 possible responders. It is estimated that at least 25% of CAG members are nonphysicians but the database does not contain that information. A total of 203 (51%) surveys were returned. One

hundred sixty-five of the 203 responders were practising gastroenterologists, and their responses were used in the analysis. If nonphysician CAG members are excluded the response rate is 65% (203 of 297). Of the 38 excluded from analysis, 18 responders were pediatric gastroenterologists not dealing with BE, eight did not perform endoscopy, seven were retired, three were full-time researchers, one was a radiologist and one was a surgeon who did not perform endoscopy. Of the 165 responders 52 (32%) were from Western Canada (British Columbia, Alberta, Manitoba, Saskatchewan), 67 were from Ontario (41%), 25 were from Quebec (15%), 20 were from Eastern Canada (12%) (Newfoundland, Prince Edward Island, Nova Scotia, New Brunswick) and three (1%) were from an unknown location.

Physician characteristics

The number of years in practice was distributed as follows (Table 2): 31% less than 10 years, 33% 11 to 20 years and 35% greater than 20 years. Fifty per cent of gastroenterologists were in community practice, and the remaining 50% indicated they had either full-time or part-time university-based practices. Most of the respondents (82%) indicated they see more than five patients with BE every year. When asked about the total number of patients with BE with high grade dysplasia seen over the course of their practice, most of the respondents (85%) indicated they had seen less than five cases. Similarly, the number of esophageal adenocarcinomas seen by physicians was also reported to be low. Dividing the estimated number of cancer cases by the number of years in practice, it can be estimated that physicians see on average one patient with esophageal adenocarcinoma each year.

Endoscopic surveillance intervals

Surveillance intervals varied depending on whether patients with BE had no, low grade or high grade dysplasia (Table 3). For patients with BE without dysplasia, 62% of gastroenterologists indicated they would perform endoscopy every two years; 19% indicated they would perform yearly endoscopy and the remaining 19% at intervals every three years or greater. The frequency of surveillance for patients with low grade dysplasia was reported to be six-monthly (55%), yearly (35%), or less than six months (10%). For patients with high grade dysplasia, 56 gastroenterologists reported they would continue surveillance with a frequency of every three months or less (70%), or every six months (30%).

TABLE 1
Current practice guidelines for the screening of Barrett's esophagus

Guidelines (reference)	Date	No dysplasia	Endoscopy intervals		Biopsy protocol*
			Low grade dysplasia	High grade dysplasia	
SFED guidelines (20)	2000	>3 cm: two years <3 cm: three years	every six months for one year	two pathologists confirm, then surgery or alternative therapy	four quadrants: >3 cm, q 2 cm < 3cm, q 1 cm
ACG guidelines (18)	1998	two to three years	six month intervals (twice) then at one year	esophagectomy or alternative therapy	four quadrants: q 2 cm, and abnormalities
Canadian Consensus (19)	1997	two years	three to six months	esophagectomy or three month surveillance	four quadrants, q 2 cm
Provenzale et al (21) Computer cohort	1994	two to three years five years	↑ survival highest quality-adjusted life expectancy ↑ life expectancy similar to common medical intervention		

*Biopsies taken from all 4 quadrants. This technique was repeated every 1 or 2 cm along the length of Barrett's Esophagus (q 1 cm, 2 cm). Symbols (<3 cm, >3 cm) refer to the visible length of Barrett's Esophagus. ACG American College of Gastroenterology; SFED French Society of Digestive Endoscopy. NOTE: The ACG guidelines have recently been updated (27). They do not specify the initial interval of endoscopies after the diagnosis Barrett's esophagus is made. The updated guideline states that the screening interval can be increased to three years after two consecutive endoscopies did not detect dyspepsia

TABLE 2
Characteristics of respondents

Survey question	Number of respondents (%)
Number of years in practice	
< 10	50 of 163 (31)
11-21	50 of 163 (31)
21-30	52 of 163 (32)
>31	11 of 163 (7)
Type of practice	
Community-based	83 of 165 (50)
Full-time university (academic)	56 of 165 (34)
Part-time university	26 of 165 (16)
Number of patients with Barrett's esophagus they see per year	
<5	29 of 165 (18)
6-10	55 of 165 (33)
11-20	42 of 165 (25)
21-30	18 of 165 (11)
>31	11 of 165 (13)
Number of patients ever seen with high grade dysplasia	
<5	140 of 164 (85)
6-10	18 of 164 (11)
>11	6 of 164 (5)
Number of patients ever seen with esophageal adenocarcinoma	
<5	31 of 165 (19)
6-10	22 of 165 (13)
11-20	43 of 165 (26)
21-30	18 of 165 (11)
31-40	20 of 165 (12)
41-50	11 of 165 (7)
>50	20 of 165 (12)

Management of patients with high grade dysplasia

Three selections were given in the survey for the management of patients with high grade dysplasia: continued surveillance, esophageal resection or other (alternative) therapy. As responders were able to check multiple options there is overlap for the following percentages. However, most respondents indicated a preference for esophageal resection (81%), followed by continued surveillance (34%), and other therapies, such as mucosal ablation, laser or photodynamic therapy (32%); 20% would consider all three options.

Endoscopic biopsy techniques

Most gastroenterologists (71%) indicated they used the four-quadrant biopsy technique, but differed on the length of columnar-lined esophagus biopsied (Table 4): 1 cm intervals (13%); 2 cm intervals (46%); greater than 3 cm intervals (7%); and no specified intervals (5%). Fifteen per cent of respondents indicated they did not adhere to a defined biopsy protocol.

TABLE 3
Endoscopic surveillance intervals used in the physicians' practices*

BE with no dysplasia	n (%)	BE with LDG	n (%)	BE with HDG	n (%)
One year	31 of 165 (19)	Less than five months	11 of 152 (7.2)	Less than three months	39 of 56 (70)
Two years	103 of 165 (62)	Six months	83 of 152 (55)	Six months	16 of 56 (28)
Greater than three years	31 of 165 (19)	One year	53 of 152 (35)	Other	1 of 56 (2)
Other	1 of 165 (0.6)	Greater than two years	5 of 152 (3%)		

*Some physicians did not respond to all questions. BE Barrett's esophagus; HGD High grade dysplasia; LGD Low grade dysplasia

'Once in a lifetime' endoscopy for patients with chronic GERD

This component of the survey posed two questions about 'once in a lifetime' endoscopy for patients with chronic GERD (Table 5). Seventy-six per cent of gastroenterologists indicated support for 'once in a lifetime' endoscopy. In response to the second question about criteria used to determine when a person should have the endoscopy, 61% indicated duration of symptoms (greater than five years); 40% said they would use age (greater than 50 years); and 33% indicated other criteria, including medication use.

DISCUSSION

The present survey found that Canadian gastroenterologists regularly perform endoscopic surveillance of patients with BE, and the majority follow published guidelines (18-21). Comparable surveys have been performed in other countries with similar results (22-25). All reported that the majority of physicians follow published guidelines, but found considerable variation with surveillance interval and biopsy protocols.

In the present survey, the majority of respondents (62%) carried out endoscopic surveillance every two years for patients with BE without dysplasia, as recommended by Canadian guidelines (19), although 19% of respondents performed yearly screening. Given the low potential for cancer progression in patients with BE, adhering to the published guidelines would likely result in substantial savings to the Canadian health care system. Furthermore, recent data suggest that the screening interval perhaps can be increased to three years if dysplasia is not seen at two endoscopic intervals (26).

The American College of Gastroenterology (ACG) recommends that surveillance endoscopies are performed in patients in whom a diagnosis of Barrett's esophagus is made (18). However, the guidelines are vague in that they do not state the screening interval. Recently, the ACG guidelines have been updated (27). They still do not specify an initial screening interval after the diagnosis of Barrett's esophagus is made. However, the new guidelines state that the interval can be three years after two consecutive endoscopies that did not find any evidence of dysplasia on histology. The present survey was conducted before the updated guidelines were published. At the moment the recommendations for screening intervals are being evaluated. It seems likely that in the future the screening intervals will increase in patients who have no evidence of dysplasia. It is interesting that the guidelines do not take ethnicity into account. It is well established that especially white males are at the highest risk for developing Barrett's esophagus.

There are no prospective randomized controlled clinical trials to help determine the optimal endoscopic interval. Current guidelines (18-21) base their recommendations on cohort and retrospective studies. Yearly endoscopic screenings

TABLE 4
Endoscopic biopsy protocol used by physicians for patients with Barrett's esophagus*

Biopsies	n of 151 respondents (%)
Four quadrant biopsies taken at	
1 cm intervals	20 (13)
2 cm intervals	69 (46)
Greater than 3 cm intervals	11 (7)
No specified intervals	8 (5)
Random biopsies	5 (3)
No protocol followed	23 (15)
Other	15 (10)

*14 respondents did not answer this question

have not been proven to be more beneficial than every two years. Whether screening patients with BE with regular endoscopy is cost effective is also unproven, although it is the current standard of practice. One recent prospective study (28) evaluated 143 patients with BE undergoing yearly screening over 10 years, and found that only one cancer was detected as a result of the surveillance program. Esophageal adenocarcinomas developed in a total of five individuals, but was detected during an unscheduled endoscopy for worsening symptoms in two patients, and in two patients who had defaulted from the program.

An economic study of endoscopic screening for BE found that yearly endoscopies would cost an estimated US\$62,000 (in 1988) and 78 h of lost work-days to discover one cancer during the screening process (9). The authors recommended screening every two years to reduce cost. A more recent economic modelling study found that yearly surveillance was the best choice if only length of life is considered (21). However, when quality of life and life expectancy were both considered, two to three year intervals were recommended (21).

There is concern that the risk of developing adenocarcinoma has been overestimated and, consequently, the intervals between endoscopies can be increased. A study by Shaheen et al. (10), which looked at 27 publications, found that reporting a higher risk of cancer was related to study size, the definition of BE, and the nature of the study (retrospective versus prospective), supporting publication bias.

Esophageal adenocarcinoma progresses through well defined histological stages, described as the metaplasia-dysplasia-carcinoma sequence (29, 30). The increased risk of developing cancer in patients with low grade dysplasia is reflected in the published guidelines that recommend surveillance increase to every six months. After one year without worsening histology, the surveillance can extend to yearly intervals (18-20). The concern about low grade dysplasia progressing to malignancy is reflected in this survey, with 55% of respondents screening every six months, and 35% performing yearly screening for patients with low grade dysplasia.

The published guidelines recommend that patients with confirmed high grade dysplasia, who are surgically fit, undergo esophageal resection (18-21). Approximately 50% of patients with high grade dysplasia will be found to have unsuspected invasive adenocarcinoma (31,32). Recent studies have suggested that surgery can be delayed in patients with high grade dysplasia although this is not the current standard of care (32,33-36). The majority (81%) of Canadian gastroenterologists indicate that they refer patients with high grade dysplasia for surgery. Although some physicians reported continued surveillance of patients with high grade dysplasia, or alternative therapy, there is overlap with these numbers because 11 of 165 (7%) respondents checked all three options, suggesting that these options are patient-dependent. For example, an elderly person who is medically at high risk for surgery may be referred for endoscopic ablation therapy.

Detection of high grade dysplasia and unsuspected adenocarcinoma are the main reasons for standardized biopsy protocols (36,37). Most guidelines recommend four-quadrant biopsies at 2 cm intervals (18-20). Boyer and Robaszkiewicz (20) recommend 1 cm intervals for BE segments shorter than 3 cm. Biopsy protocols were quite variable in this survey, ranging from four-quadrants every 2 cm (46%) to 15% of respondents who said they did not follow any biopsy protocol. It is likely that this in part is due to patients with short segment BE where a standardized biopsy protocol is not possible.

Although the ACG recommends that patients with chronic GERD should have an endoscopy to screen for BE (18), no timing was specified. This survey demonstrates that Canadian gastroenterologists agreed with this statement, as 76% said they believe in 'once in a lifetime' endoscopy for patients with chronic GERD. They also indicated that criteria for endoscopy

TABLE 5
Physician's opinions of once in a lifetime endoscopies for patients with longstanding gastroesophageal reflux disease

A) Do you believe that in all patients with a convincing history of heartburn and acid regurgitation, endoscopy should be performed to detect Barrett's esophagus?			
Yes	125 of 165 (76)		
No	40 of 165 (24)		
B) If you agree, we would be interested in knowing when this endoscopy should take place and whether you use any criteria to determine that time (ie, age/ duration of symptoms).			
Age	50 of 125 (40)	Duration of symptoms	76 of 125 (60)
Greater than 40 years	14 of 50 (28)	Less than five years	20 of 76 (26)
Greater than 45 years	9 of 50 (18)	Five years	38 of 76 (50)
Greater than 50 years	23 of 50 (46)	10 years	18 of 76 (24)
Other	4 of 50 (8)		
Other criteria	30 of 125 (24)		
Endoscope at time of referral	10 of 30 (33)		
Endoscope if the patient needs constant medications (Proton-pump inhibitors)	6 of 30 (20)		
Other	14 of 30 (47)		

should include duration of symptoms (61%) and age (40%). However, the optimal timing and criteria for 'once in a lifetime' endoscopy warrants further critical study before evidence based recommendations can be given. Large forceps biopsies are recommended to get adequate biopsy samples.

The results of the present survey may not reflect the opinions of all Canadian gastroenterologists as the response was 68%. However, we found that the majority of Canadian gastroenterologists who responded to the survey followed the published guidelines, and indicated support for a 'once in a lifetime' endoscopy. Future advances in understanding the molecular pathogenesis of BE and esophageal adenocarcinoma may further modify endoscopic surveillance for this disease in the future (38).

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