

## Effect of a prior endoscopy on outcomes of esophageal adenocarcinoma among United States veterans

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**Background:** The efficacy of screening and surveillance EGD for esophageal adenocarcinoma (EAC) is controversial.

**Objective:** To examine the effect of an EGD before the diagnosis of EAC on survival after the diagnosis of cancer among patients with gastroesophageal reflux (GER).

**Design:** A retrospective, controlled cohort study.

**Subjects:** The national administrative databases of the Veterans Affairs were accessed, and patients diagnosed with EAC, from 1995 through 2003, who had a prior diagnosis consistent with GER were identified. Electronic medical records were then abstracted. Cases were subjects who had an EGD performed between 1 and 5 years before the diagnosis of EAC; controls were those subjects without a prior EGD.

**Results:** A total of 155 subjects with EAC and GER were identified. Cases with a history of an EGD at least 1 year before a diagnosis of EAC ( $n = 25$ ) were diagnosed at earlier stages than those without a prior EGD ( $P = .02$ ) but did not experience a significant improvement in survival (adjusted hazard ratio 0.93 [95% CI, 0.58–1.50]). Cases who had been enrolled in surveillance programs that adhered to published guidelines trended toward improved survival, but long-term survival reverted toward the rate found without any surveillance.

**Conclusions:** A prior EGD was associated with an improved stage at the diagnosis of EAC but did not alter long-term survival. In the absence of prospective, randomized, controlled trials, the benefit of screening and surveillance to decrease mortality from EAC cannot be confirmed. (*Gastrointest Endosc* 2008;68:849-55.)

The incidence of esophageal adenocarcinoma (EAC) is rising faster than that of any other cancer in the United States and many other westernized nations.<sup>1,2</sup> Barrett's esophagus (BE) is the accepted precursor of EAC,<sup>3-5</sup> and gastroesophageal reflux (GER) increases the risk of both BE and EAC.<sup>3,4</sup> It is commonly accepted that GER leads to the development of BE in some individuals, and BE then progresses to low-grade and high-grade dysplasia before developing into invasive cancer in a subset of patients.<sup>4</sup> A number of retrospective studies suggested that a prior EGD among patients with EAC is associated with an earlier

stage of cancer at the time of initial diagnosis and improved survival.<sup>6-11</sup> Therefore, multiple gastroenterology societies recommend screening patients with GER symptoms for BE and EAC, and repeated surveillance of patients who have BE.<sup>4,12-14</sup> Because of the limitations of the previous studies, including potential lead-time bias, length-time bias, and selection bias, the efficacy of screening and surveillance remains controversial and is not uniformly recommended.<sup>15-17</sup>

To warrant the expense of endoscopic surveillance in the population of patients with GER, a strategy of screening and surveillance ought to be clearly effective in improving outcomes from EAC. Our primary hypothesis was that, among patients with GER and EAC, a history of a screening EGD would be associated with a more favorable stage at the time of diagnosis, an increased likelihood of surgical resection, and improved long-term survival after the diagnosis of cancer compared with patients with GER and EAC but with no prior EGD. We also hypothesized that adherence to

*Abbreviations:* ACG, American College of Gastroenterology; BE, Barrett's esophagus; EAC, esophageal adenocarcinoma; GER, gastroesophageal reflux; HR, hazard ratio; ICD, International Classification of Diseases; NPCD, National Patient Care Datasets; OR, odds ratio; VA, United States Department of Veterans Affairs.

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published guidelines for the interval of surveillance would be associated with improved outcomes from EAC among patients with GER and documented BE.

## PATIENTS AND METHODS

### Databases

Subjects were retrospectively identified within the United States Department of Veterans Affairs (VA) National Patient Care Datasets (NPCD). The NPCD is a computerized administrative database that includes all inpatient admissions at any VA hospital throughout the country since 1970 and all outpatient encounters within the VA system since 1990.

### Identification of subjects

Veterans were initially identified who were diagnosed with adenocarcinoma of the distal third of the esophagus or of the gastric cardia (International Classification of Diseases [ICD] 151.0) from 1995 through 2003, and who had gastroesophageal reflux (GER) diagnosed (ICDs 530.10-530.12, 530.81, or 787.1) before the diagnosis of cancer. Potential subjects were excluded if they did not have at least one admission or outpatient encounter in each of the 5 years before the cancer diagnosis. The electronic medical records of each potential subject were accessed via remote Internet access upon approval of the institutional review board of the VA Ann Arbor Healthcare System. The histology and location of the cancer were abstracted based on pathology, surgery, and endoscopy reports. The subjects without EAC (such as gastric cardia adenocarcinoma, which shares the same ICD code as EAC) were excluded based on the review of the electronic medical records. Subjects with dysplasia but no evidence of EAC were excluded. Electronic medical records were also abstracted for the date of pathologic diagnosis, stage at diagnosis, and date of death.

### Comorbidities and upper endoscopies

Comorbid diagnoses during the 1 year before the diagnosis of cancer were collected from the NPCD.<sup>18-20</sup> Diagnostic EGDs that were performed between 5 years and 1 year before the diagnosis of cancer were identified by using the NPCD (Current Procedural Terminology codes: 43200, 43202, 43221, 43222, 43234, 43235, 43239; or ICD-9 procedural codes: 42.23, 42.24, 44.13, 45.13, 45.16). In the primary analysis, cases were defined as eligible subjects who had an EGD between 1 and 5 years before the diagnosis of EAC, and controls were eligible subjects without a prior EGD in that time frame. If available, all prior endoscopic and histologic findings were abstracted from the electronic medical records. Subjects with BE were assessed as nonadherent with the 2002 American College of Gastroenterology (ACG) guidelines for surveillance of BE if they had a prior EGD, but they were overdue for surveillance at the time of cancer diagnosis based on the most recent histologic findings.<sup>4</sup>

### Capsule Summary

#### What is already known on this topic

- Screening and surveillance EGD for esophageal adenocarcinoma (EAC) are not uniformly recommended because of limitations in earlier studies, including potential lead-time bias, length-time bias, and selection bias.

#### What this study adds to our knowledge

- In a retrospective review of 155 subjects with EAC and gastroesophageal reflux, those with a history of EGD at least 1 year before a diagnosis of EAC were identified at earlier stages than those without a prior EGD, but no significant improvement in survival was seen.

## RESULTS

### Subject population with EAC

A total of 311 subjects were identified with GER and a billing diagnosis consistent with EAC and who had been active in the NPCD for each of the 5 years before the diagnostic code of cancer. On review of the electronic medical records, subjects were excluded if their cancer type was other than EAC (133), if they had BE but no documented evidence of cancer (5), if there were insufficient electronic medical records to validate a cancer diagnosis (16), or if the EAC was diagnosed before 1995 (2).

The resulting cohort contained 155 subjects with GER and EAC; 99% were men, 84% were white, 5% were Hispanic, 3% were African American, and 8% were of unknown race or ethnicity. At the time of diagnosis, 15% were stage I, 37% stage II, 22% stage III, and 26% stage IV. Fifty-one percent of these subjects underwent surgical resection. As expected, the stage at diagnosis predicted survival ( $P < .0001$ ). Five-year stage-specific survival (I, 42%; II, 12%; III, 6%; IV, 3%) was at least as good as for male patients with esophageal cancer who were enrolled in the Surveillance Epidemiology and End Results registry (localized, 29%; regional, 13%; distant, 2%).<sup>21</sup> In the survival analysis, when using the Cox proportional hazard model, advancing age (hazard ratio [HR] 1.02 for each year [95% CI, 1.00-1.04]) and increasing number of comorbidities (HR 1.19 for each [95% CI, 1.05-1.36]) were also significant risk factors for death. Subjects who were undergoing surgical resection had improved survival (HR 0.45 [95% CI, 0.32-0.63]) compared with those not undergoing resection.

### Influence of prior EGD on outcomes from EAC

Of the 155 subjects with GER who developed EAC, there were 25 patients (16%) who had undergone EGD between 1 and 5 years before the diagnosis of cancer (Fig. 1). Compared with the 130 controls with no history of a prior EGD, subjects with a prior EGD were older (72.0 vs 68.3 years,

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