HHS Public Access

Author manuscript

Dig Dis Sci. Author manuscript; available in PMC 2019 November 01.

Published in final edited form as:

Dig Dis Sci. 2018 November ; 63(11): 3112–3119. doi:10.1007/s10620-018-5241-y.

Prior diagnosis of Barrett's esophagus is infrequent, but associated with improved esophageal adenocarcinoma survival

Theresa Nguyen Wenker[1], **Mimi C. Tan**[1,2], **Yan Liu**[1], **Hashem B. El-Serag**[1,2], and **Aaron P. Thrift**[3,4]

[1]Section of Gastroenterology and Hepatology, Department of Medicine, Baylor College of Medicine, Houston, TX

[2]Center for Innovations in Quality, Effectiveness and Safety (IQuESt), Michael E DeBakey Veterans Affairs Medical Center, Houston, TX

[3]Section of Epidemiology and Population Sciences, Department of Medicine, Baylor College of Medicine, Houston, TX

[4]Dan L Duncan Comprehensive Cancer Center, Department of Medicine, Baylor College of Medicine, Houston, TX

Abstract

Background: Efforts to reduce mortality from esophageal adenocarcinoma (EA) have focused on screening and surveillance of Barrett's esophagus (BE).

Aims: We sought to determine the frequency of prior diagnosis of BE in patients with EA, and to evaluate the impact of a prior BE diagnosis on mortality in EA patients.

Methods: This was a retrospective cohort study of patients diagnosed with EA in the VA during 2002–2016. We compared the distributions of EA stage and receipt of treatment between EA patients with and without a prior BE diagnosis and used Cox proportional hazards models to compare mortality risk (all-cause and cancer specific) unadjusted and adjusted for stage and treatment to assess their impact on any survival differences.

Results: Among 8564 EA patients, only 4.9% had a prior BE diagnosis. The proportion with prior BE diagnosis increased from 3.2% in EA patients diagnosed during 2005–2007 to 7.0% in those diagnosed during 2014–2016. EA patients with a prior BE diagnosis were more likely to have stage 1 disease and receive any treatment. A prior BE diagnosis was associated with lower all-cause mortality risk (hazard ratio [HR] unadjusted for stage, 0.69; 95% CI, 0.61–0.80), which was largely explained by the earlier stage of EA at the time of diagnosis (HR adjusted for stage, 0.87; 95% CI, 0.75–0.99). There was no evidence of lead time bias or length time bias.

Correspondence: Aaron P. Thrift, Ph.D., Dan L Duncan Comprehensive Cancer Center, Baylor College of Medicine, One Baylor Plaza, Houston, Texas, 77030-3498. Tel: 713-798-9107; Fax: 713-798-3658; aaron.thrift@bcm.edu.

Author's contribution: Study concept and design: APT. Statistical analysis and interpretation of data: TNW, MCT, YL, HES, APT. Acquisition of data and obtained funding: APT. Data preparation: YL. Drafting of the manuscript: TNW, APT. Critical review of the manuscript for important intellectual content: TNW, MCT, YL, HES, APT. Study supervision: APT. All authors read and approved the final version for submission.

Conflict of interest: None.

Conclusions: Prior diagnosis of BE was associated with better survival, largely due to earlier EA stage at diagnosis.

Keywords

esophageal neoplasms; surveillance; incidence; mortality

INTRODUCTION

The incidence of esophageal adenocarcinoma (EA) has increased rapidly in Western populations during the past four decades.[1, 2] In the United States, the incidence of EA has increased almost 10-fold among white men.[3] Once diagnosed, the overall 5-year observed survival rate for individuals with EA remains <20%, with a median survival of approximately 11 months.[4] Barrett's esophagus (BE), a metaplastic columnar epithelium of the distal esophagus, is the only known precursor lesion for EA. The current approach to the prevention of deaths from EA relies on identifying patients with BE from among individuals with frequent symptoms of gastroesophageal reflux disease (GERD), followed by regular endoscopic surveillance of BE to identify patients with neoplastic progression before invasive EA occurs.[5–8] The potential success of this strategy therefore relies on identifying BE in patients prior to their EA diagnosis.

Few population-based studies have examined the fraction of newly diagnosed EA patients with a prior diagnosis of BE. A systematic review and meta-analysis involving 12 studies published prior to 2000, involving 1503 EA patients, found that 4.7% had a prior known or established diagnosis of BE.[9] Three studies using data from persons diagnosed with EA between 1994 and 2011 in the US National Cancer Institute's Surveillance Epidemiology and End Results (SEER)-Medicare database found that 8.1%−13% of EA patients had a diagnosis of BE >6 months prior to their cancer diagnosis date.[10–12] However, the SEER-Medicare population mostly includes persons aged ≥65 years, and is therefore not representative of the >40% of persons with EA in the US that are aged <65 years at diagnosis.[13] Similarly, among 716 EA patients diagnosed between 2003 and 2008 in Northern Ireland, Bhat et al.[14] found that 7.3% had a prior BE diagnosis >6 months prior to their cancer diagnosis date. They also showed that the fraction of EA patients in Northern Ireland with a prior BE diagnosis had not changed over time (6.8% of EA patients diagnosed 2003–2005 vs. 7.7% of those diagnosed 2006–2008) but the time period covered by the study was relatively short.[14] Screening recommendations to identify BE in high-risk individuals started in 2011 in the US.[5] Given the changes in screening and treatment guidelines and modalities in recent years, and as the survival benefit associated with long-term surveillance remains unclear,[15, 16] additional studies are needed in more contemporary cohorts of EA cases to determine the prevalence of prior BE diagnosis and to evaluate the impact of a prior BE diagnosis on EA stage, receipt of treatment, and overall survival.

We therefore conducted a retrospective cohort study to investigate the prevalence of prior established diagnosis of BE in a large national cohort of patients with EA identified in the national Veteran Affairs (VA) databases. Our objective was to examine the overall as well as secular trends in prevalence of established BE in EA patients over time. We also examined

for differences in tumor characteristics, treatment and survival in EA patients with and without a prior diagnosis of BE.

METHODS

Study Population and Design

This was a retrospective cohort study of patients diagnosed with a first primary EA between 2002 and 2016. We identified EA patients in the VA Central Cancer Registry (VACCR) through the VA Corporate Data Warehouse. The VACCR was initiated in 1995 and serves as a national data repository for over 750,000 VA patients with cancer.[17, 18] Cancer registrars at each VA Hospital manually abstract data, conforming to standards set by the North American Association of Central Cancer Registries, and data are then aggregated into the national cancer registry where cases are merged and quality assurance checks are conducted. The VACCR includes information on patient demographics, date of cancer diagnosis, primary site, histology, grade, tumor size, extension, staging, and treatment. This study was approved by the Institutional Review Boards at Baylor College of Medicine and the Michael E. DeBakey VA Medical Center.

We identified patients with EA using International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3) site code C15 (esophagus) in combination with histology codes M8140-M8575. For all EA patients, we identified those with a diagnosis of BE recorded in VA outpatient files between 1 October 1999 and their EA diagnosis date. BE diagnosis was ascertained by the presence of ICD-9-CM code 530.85, combined with at least one esophagogastroduodenoscopy test (CPT codes 43200–43259, excluding 43246) within 12 months of the initial BE code date. We previously validated this algorithm in 400 randomly selected patients in the VA databases (with a 93.3% positive predictive value for correctly identifying BE patients). The date for BE diagnosis was defined by the date of the esophagogastroduodenoscopy occurring within 1 year of the appearance of an ICD-9 code for BE. Consistent with previous studies,[11, 12, 14] patients whose EA was diagnosed within 6 months of their BE diagnosis were assumed to be prevalent cases and were not considered to have a prior BE diagnosis in the primary analysis. For the primary analysis, established prior BE was therefore defined as evidence of ICD and CPT codes as described above, >6 months prior to date of cancer diagnosis.

EA stage and cancer treatment (surgery, chemotherapy and radiotherapy) information were extracted from the VACCR. Cancer specific and all-cause deaths, if any, were identified from the VA Vital Status file. The Vital Status file combines information from Medicare, VA, Social Security, and VA compensation and pension benefits to determine date of death (sensitivity 98.3%; specificity 99.8% relative to National Death Index).[19] Cancer specific deaths were defined as those with underlying cause of death ICD codes 150.0–151.9. Patients were followed up from the date of EA diagnosis to the date of death or 12/31/2016.

Statistical Analysis

Characteristics of EA patients with and without a prior BE diagnosis were compared using chi-square tests for categorical variables and the Student t-test for continuous variables. We

calculated the overall prevalence of prior BE diagnosis, and examined for a trend over time using logistic regression. We examined the association between prior BE diagnosis and early-stage EA (stage 1 vs. stages 2, 3, or 4) or receipt of any cancer treatment (surgery, local ablation and/or resection, chemotherapy or radiation) in separate multivariable logistic regression models. The cumulative risk of mortality following cancer diagnosis was compared among EA patients with and without prior BE diagnosis using the Kaplan-Meier method and log-rank test. We examined the associations between prior BE diagnosis and the risks of cancer specific mortality or all-cause mortality using separate Cox proportional hazards regression models. Several variables were examined as potential confounders, including age at EA diagnosis, sex, race/ethnicity, year of EA diagnosis, year of BE diagnosis, body mass index (BMI, kg/m^2), alcohol use, smoking status, and number of primary care visits and GI visits prior to EA diagnosis. We used forward stepwise regression to reduce the covariables included in the final models; only variables with $p<0.01$ were retained. Adjusted odds ratios (ORs) and hazard ratios (HRs) and their accompanying 95% confidence intervals (CIs) were estimated in the models.

We examined the role of EA stage at time of diagnosis as an explanatory variable for the association between prior BE diagnosis and receipt of cancer treatment, as well as the role of cancer stage and treatment as explanatory variables for the association between prior BE diagnosis and mortality risk. We included these potential explanatory variables in the respective models and evaluated for an attenuation of the effect of prior BE diagnosis on the outcomes. Finally, we examined the associations with prior BE diagnosis stratified by cancer stage and treatment.

We adjusted for estimated lead time bias and length time bias in models comparing mortality risk using the methods described by Duffy et al.[20] To adjust for lead time bias, the sojourn time for EA, the time where the EA is asymptomatic but surveillance detectable in BE patients, was estimated as the difference in mean age at EA diagnosis between patients with and without an established prior BE diagnosis. In the presence of length time bias, cancers detected through screening appear to have longer survival. However, this survival benefit is likely due to the presence of more slowly growing tumors, which are more likely to be detected, but less likely to be fatal. We therefore conducted sensitivity analyses as suggested by Duffy et al.[20] and compared to the unadjusted relative risk (RR) of mortality at 3 years between patients with and without prior BE.

In other sensitivity analyses, we modified the window of time used to define a prior BE diagnosis, using a cut-off of >3 months prior to cancer diagnosis as well as >12 month prior. Furthermore, we also re-defined BE diagnosis as only requiring an ICD-9-CM code 530.85 (*i.e.*, not requiring the concurrent EGD code).

All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC). Statistical significance was determined at $\alpha = 0.05$, and all p-values for statistical significance were two-sided.

RESULTS

We identified 8564 patients diagnosed with EA in the VA between 2002 and 2016 and who met the study's inclusion and exclusion criteria. Overall, 588 patients (6.9%) had evidence of a BE diagnosis. Among these, median time between BE diagnosis date and EA diagnosis date was 2.4 years (range, 0–11 years). A total of 169 (28.7% of all patients with a BE diagnosis) had a BE index date within 6 months of their cancer diagnosis date. Therefore, 419 (4.9% of all EA patients) had a diagnosis of BE >6 months prior to their cancer diagnosis date and were considered in our analysis as having an established prior BE diagnosis. We found similar results when we used only the presence of an ICD code to define prior BE: 9.3% of EA patients with evidence of a BE diagnosis; 31.0% ≤6 months and 69.0% >6 months prior to their cancer diagnosis date.

For the 419 patients with an established prior BE diagnosis, the mean duration between BE index date and EA diagnosis date was 4.3 years (SD, 2.7). Of those with >5 years of administrative data available prior to EA diagnosis, the proportion with a prior diagnosis of BE increased from 3.2% in EA patients diagnosed during 2005–2007 to 7.0% in EA patients diagnosed during 2014–2016 (Table 1). Compared to EA patients diagnosed from 2005–2007, those diagnosed from 2014–2016 were more likely to have a prior BE diagnosis after adjusting for confounders, including frequency of primary care and GI clinic visits (OR, 2.45; 95% CI, 1.66–3.63).

The majority of EA patients in our cohort were male (99.4%) and non-Hispanic white (85.3%). The mean age of EA patients at cancer diagnosis was 67.3 years (SD, 9.6). EA was diagnosed as stage 1 in 12.9% of patients, stage 2 in 17.6%, stage 3 in 19.4%, stage 4 in 34.4%, and missing stage in 15.6% of patients. Any type of treatment was received by 6427 (75.0%) of EA patients. EA patients with and without a prior diagnosis of BE were no different with regards to age at EA diagnosis and sex (Table 1). Compared to EA patients without a prior BE diagnosis, EA patients with a prior BE diagnosis had higher mean BMI, but were less likely to have a history of alcohol and tobacco use. Furthermore, compared to EA patients without a prior BE diagnosis, EA patients with a prior BE diagnosis had greater frequency of primary care (Quartile 4, 56.1% vs. 23.39%) and GI clinic (Quartile 4, 79.5% vs. 22.2%) visits prior to their cancer diagnosis.

EA patients with a prior BE diagnosis had significantly lower stage disease than those without (46.5% vs. 11.2% had stage 1; $p<0.001$). Likewise, EA patients with a prior BE diagnosis were more likely to have received any type of treatment compared to EA patients without a prior BE diagnosis (84.7% vs. 74.6%; $p<0.001$). In multivariable logistic regression analysis adjusting for potential confounders, EA patients with a prior BE diagnosis were over 4-fold more likely to be diagnosed with stage 1 disease compared to EA patients without a prior BE diagnosis (OR, 4.45; 95% CI, 3.47–5.71). There was a weaker, non-significant association between prior BE diagnosis and receipt of any treatment (OR, 1.38; 95% CI, 0.98–1.96).

A total of 7336 (85.7%) patients died during the study period. The median survival time in EA patients without a prior BE diagnosis was 10.3 months and in patients with a prior BE

diagnosis was 37.1 months. Figure 1 shows the Kaplan–Meier survival curves for overall survival in EA patients according to prior BE diagnosis status. In the unadjusted Cox model, a prior BE diagnosis was associated with 59% lower risk of all-cause mortality (HR, 0.41; 95% CI, 0.36–0.47). After adjusting for age at EA diagnosis, race/ethnicity, BMI, alcohol use, smoking status, and number of primary care and GI clinic visits, prior BE diagnosis remained associated with lower all-cause mortality risk (HR, 0.69; 95% CI, 0.61–0.80). This inverse association was attenuated considerably towards the null after additionally adjusting for early EA stage (HR, 0.87; 95% CI, 0.75–0.99) (Table 2). There was no association of prior BE diagnosis with all-cause mortality in analyses stratified by EA stage (among patients with stage 1, HR, 0.98, 95% CI, 0.77–1.25; among patients with stages 2–4, HR, 0.90, 95% CI, 0.74–1.10) (Table 3). Similar results were observed for the association between prior BE diagnosis and risk of cancer specific mortality (Tables 2 and 3). We observed similar findings when we varied the period used to define prior BE (Supplementary Table 1).

Given the similar mean age at EA diagnosis in patients with and without a prior diagnosis of BE, there was no strong lead time bias associated with having a prior BE diagnosis. We attempted to adjust for length time bias by using a suggested range of values[20] for the proportion of patients with length bias affected tumors (ranging from 50% to 90%) together with estimates for the relative rate of fatality in the length bias group (ranging from 0.5 to 0.9). In sensitivity analyses examining the influence of length time bias (Supplementary Table 2), the RR adjusted for length time bias ranged from 0.61 to 0.68, with a median RR of 0.62. Assuming the 38.3% of EA patients in our cohort with low-grade or intermediate-grade tumors are the length bias affected group, the length time bias adjusted RR of death at 3 years was 0.61 (compared to unadjusted RR of 0.60).

DISCUSSION

Within our large VA cohort of newly diagnosed EA patients, 4.9% had a diagnosis of BE at least 6 months prior to their cancer diagnosis. While the fraction of EA patients with prior BE diagnosis has increased over time, only 7.0% of EA patients diagnosed from 2014 to 2016 in the VA had a prior diagnosis of BE. Our analysis found that EA patients with a prior BE diagnosis had over 30% lower risk of all-cause mortality, largely due to a higher frequency of early stage cancers among patients with prior BE diagnosis compared to those without prior BE diagnosis. Lead time bias and length time bias did not explain the observed survival benefit.

Our results are consistent with those of a meta-analysis of 12 studies published prior to 2000 which found that only 4.7% of EA patients had a history of prior BE diagnosis.[9] The fraction of EA patients with prior BE in our cohort was slightly lower than recent studies among EA patients in the SEER-Medicare database (prior BE in 8.1–13% of EA patients).[10–12] However, this likely reflects the slightly younger age structure of our VA-based EA cohort compared with the SEER-Medicare dataset that includes EA patients aged >65 years. The average age of our EA cohort was also lower than that of the Northern Ireland study, which found 7.3% of EA patients with prior BE.[14]

We showed that, on average, EA patients with a prior diagnosis of BE had lower risks of all-cause and cancer specific mortality compared to EA patients without a prior BE diagnosis. Four prior studies have compared all-cause mortality between EA patients with and without a prior BE diagnosis. Three of these studies used data from SEER-Medicare, and each showed lower risk of mortality associated with a prior diagnosis of BE.[10–12] Likewise, in the other study, conducted in Northern Ireland, a prior diagnosis of BE was associated with lower risk of mortality.[14] Together, these data provide evidence for a survival benefit associated with prior diagnosed BE. When we adjusted for stage, the effect estimates were attenuated towards the null. Consistent with prior studies,[12,14] we found little evidence for an effect of length time bias on the observed survival benefit associated with having an established prior BE diagnosis.

Whether or not the survival benefit associated with having a prior BE diagnosis is explained by lead time bias remains unclear. In our study, since age at EA diagnosis was similar for patients with and without a prior BE diagnosis, lead time bias did not impact our results. This is consistent with our prior study, whereby we performed extensive chart reviews in a small cohort of EA patients in the VA and defined EA patients diagnosed by surveillance vs. non-surveillance endoscopy; surveillance endoscopy was associated with improved survival after adjusting for lead time bias.[16] Likewise, Cook et al.[11] in their analysis of data from EA patients aged ≥68 years in SEER-Medicare found no differences in age at EA diagnosis and little evidence for lead time bias. Conversely, in another study using the SEER-Medicare database, EA patients with a prior BE diagnosis were older on average than EA patients without prior BE diagnosis and adjusting for lead time bias significantly attenuated the inverse association between prior BE diagnosis and mortality risk.[12] In the Northern Ireland study, where EA patients with a prior BE diagnosis were younger on average than EA patients without prior BE diagnosis, the survival benefit associated with prior BE diagnosis was not explained by lead time bias.[14]

This study has multiple strengths. We identified all possible newly diagnosed EA patients using an expanded search strategy of automated data, which resulted in a large cohort of EA patients with sufficient follow-up time to determine receipt of treatment and death. Another strength of our study was the completeness of our cancer staging data; which far exceeded that of prior studies and enabled investigation of stage as a potential explanation for the survival advantage in EA patients with a prior BE diagnosis. There are several limitations to our study. Since our cohort consisted of predominantly White males with EA and was conducted among the VA population, our cohort is less reflective of the underlying population than the prior Irish[14] and SEER-Medicare database[10–12] studies, and the results may not be generalizable to the general population. However, while our results may not be generalizable to women and non-veterans, because EA and BE disproportionately affects men and whites, the veteran population is adequate to study risk factors and outcomes for BE and EA. Furthermore, our findings are consistent with previously published results from EA studies conducted in the US and Northern Ireland. We potentially misclassified any EA patients who were diagnosed with BE prior to 1 October 1999 when the VA Corporate Data Warehouse became available. However, in these missed patients, lack of diagnosis codes from 1 October 1999 to their EA diagnosis date represents lack of surveillance so would not affect the overall effect on survival. We may have underestimated the prevalence of prior BE

if EA patients were diagnosed with BE during an endoscopy at a non-VA facility. Also, veterans diagnosed with EA but not registered in the VACCR were not included in the current study. It is unclear how this may have affected the findings of our study. Cancer-specific deaths were defined using diagnosis codes, which under-estimates true deaths attributable to cancer (e.g., sepsis or organ dysfunction due to underlying cancer would not be captured). This method only assigned 55% of all deaths as cancer specific; therefore, all-cause mortality may be better to examine impact on death. Finally, although we attempted to control for potential confounders, residual confounding by unknown or unmeasured factors could still have influenced our results.

In summary, we found that the fraction of EA patients with prior BE diagnosis remains low. Nonetheless, a prior BE diagnosis was associated with lower mortality risk. While a higher prevalence of earlier stage cancers among EA patients with prior BE diagnosis explained a large fraction of the observed survival benefit, we found no evidence that the survival benefit was due to lead time bias and/or length time bias. Assuming BE surveillance does confer a survival benefit, at the population-level, given the continued low prevalence of prior BE diagnosis in the EA patient population, current practice will continue to only improve outcomes in a minority of EA patients and further focus should be on increasing screening for BE detection.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding: This work was supported in part by National Institutes of Health grant P30 DK056338 (Study Design and Clinical Research Core), which supports the Texas Medical Center Digestive Diseases Center. Hashem El-Serag is also supported by NIDDK K24–04-107. This research was supported in part with resources at the VA HSR&D Center for Innovations in Quality, Effectiveness and Safety (#CIN 13–413), at the Michael E. DeBakey VA Medical Center, Houston, TX. The opinions expressed reflect those of the authors and not necessarily those of the Department of Veterans Affairs, the US government or Baylor College of Medicine.

Abbreviations:

BE	Barrett’s esophagus
CI	confidence interval
EA	esophageal adenocarcinoma
GERD	gastroesophageal reflux disease
HR	hazard ratio
OR	odds ratio

REFERENCES

1. Thrift AP, Whiteman DC. The incidence of esophageal adenocarcinoma continues to rise: analysis of period and birth cohort effects on recent trends. Ann Oncol 2012;23:3155–3162. [PubMed: 22847812]
2. Hur C, Miller M, Kong CY, et al. Trends in esophageal adenocarcinoma incidence and mortality. Cancer 2013;119:1149–58. [PubMed: 23303625]
3. Vaughan TL, Fitzgerald RC. Precision prevention of oesophageal adenocarcinoma. Nature Reviews Gastroenterology and Hepatology 2015;12:243–248. [PubMed: 25666644]
4. Thrift AP. The epidemic of oesophageal carcinoma: Where are we now? Cancer Epidemiol 2016;41:88–95. [PubMed: 26851752]
5. Spechler SJ, Sharma P, Souza RF, et al. American Gastroenterological Association technical review on the management of Barrett's esophagus. Gastroenterology 2011;140:e18–52 [PubMed: 21376939]
6. Shaheen NJ, Falk GW, Iyer PG, et al. ACG Clinical Guideline: Diagnosis and management of Barrett's esophagus. Am J Gastroenterol 2016;111:30–50. [PubMed: 26526079]
7. Fitzgerald RC, di Pietro M, Ragunath K, et al. British Society of Gastroenterology guidelines on the diagnosis and management of Barrett's oesophagus. Gut 2014;63:7–42. [PubMed: 24165758]
8. Whiteman DC, Appleyard M, Bahin FF, et al. Australian clinical practice guidelines for the diagnosis and management of Barrett's esophagus and early esophageal adenocarcinoma. J Gastroenterol Hepatol 2015;30:804–20. [PubMed: 25612140]
9. Dulai GS, Guha S, Kahn KL, et al. Preoperative prevalence of Barrett's esophagus in esophageal adenocarcinoma: a systematic review. Gastroenterology 2002;122:26–33. [PubMed: 11781277]
10. Cooper GS, Kou TD, Chak A. Receipt of previous diagnoses and endoscopy and outcome from esophageal adenocarcinoma: a population-based study with temporal trends. Am J Gastroenterol 2009;104:1356–62. [PubMed: 19491849]
11. Cook MB, Drahos J, Wood S, et al. Pathogenesis and progression of oesophageal adenocarcinoma varies by prior diagnosis of Barrett's oesophagus. Br J Cancer 2016;115:1383–1390. [PubMed: 27780192]
12. Tramontano AC, Sheehan DF, Yeh JM, et al. The Impact of a Prior Diagnosis of Barrett's Esophagus on Esophageal Adenocarcinoma Survival. Am J Gastroenterol 2017;112:1256–1264. [PubMed: 28374815]
13. SEER. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 9 Regs Research Data, Nov 2016 Sub (1973–2014) <Katrina/Rita Population Adjustment> - Linked To County Attributes - Total U.S., 1969–2015 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2017, based on the November 2016 submission.
14. Bhat SK, McManus DT, Coleman HG, et al. Oesophageal adenocarcinoma and prior diagnosis of Barrett's oesophagus: a population-based study. Gut 2015;64:20–25. [PubMed: 24700439]
15. Corley DA, Mehtani K, Quesenberry C, et al. Impact of endoscopic surveillance on mortality from Barrett's esophagus-associated esophageal adenocarcinomas. Gastroenterology 2013;145:312–9. [PubMed: 23673354]
16. El-Serag HB, Naik AD, Duan Z, et al. Surveillance endoscopy is associated with improved outcomes of oesophageal adenocarcinoma detected in patients with Barrett's oesophagus. Gut 2016;65:1252–60. [PubMed: 26311716]
17. Zullig LL, Jackson GL, Dorn RA, et al. Cancer incidence among patients of the U.S. Veterans Affairs Health Care System. Mil Med 2012;177:693–701. [PubMed: 22730846]
18. Jackson GL, Melton LD, Abbott DH, et al. Quality of nonmetastatic colorectal cancer care in the Department of Veterans Affairs. J Clin Oncol 2010;28:3176–81. [PubMed: 20516431]
19. Sohn MW, Arnold N, Maynard C, et al. Accuracy and completeness of mortality data in the Department of Veterans Affairs. Popul Health Metr 2006;4:2. [PubMed: 16606453]
20. Duffy SW, Nagtegaal ID, Wallis M, et al. Correcting for lead time and length bias in estimating the effect of screen detection on cancer survival. Am J Epidemiol 2008;168:98–104. [PubMed: 18504245]

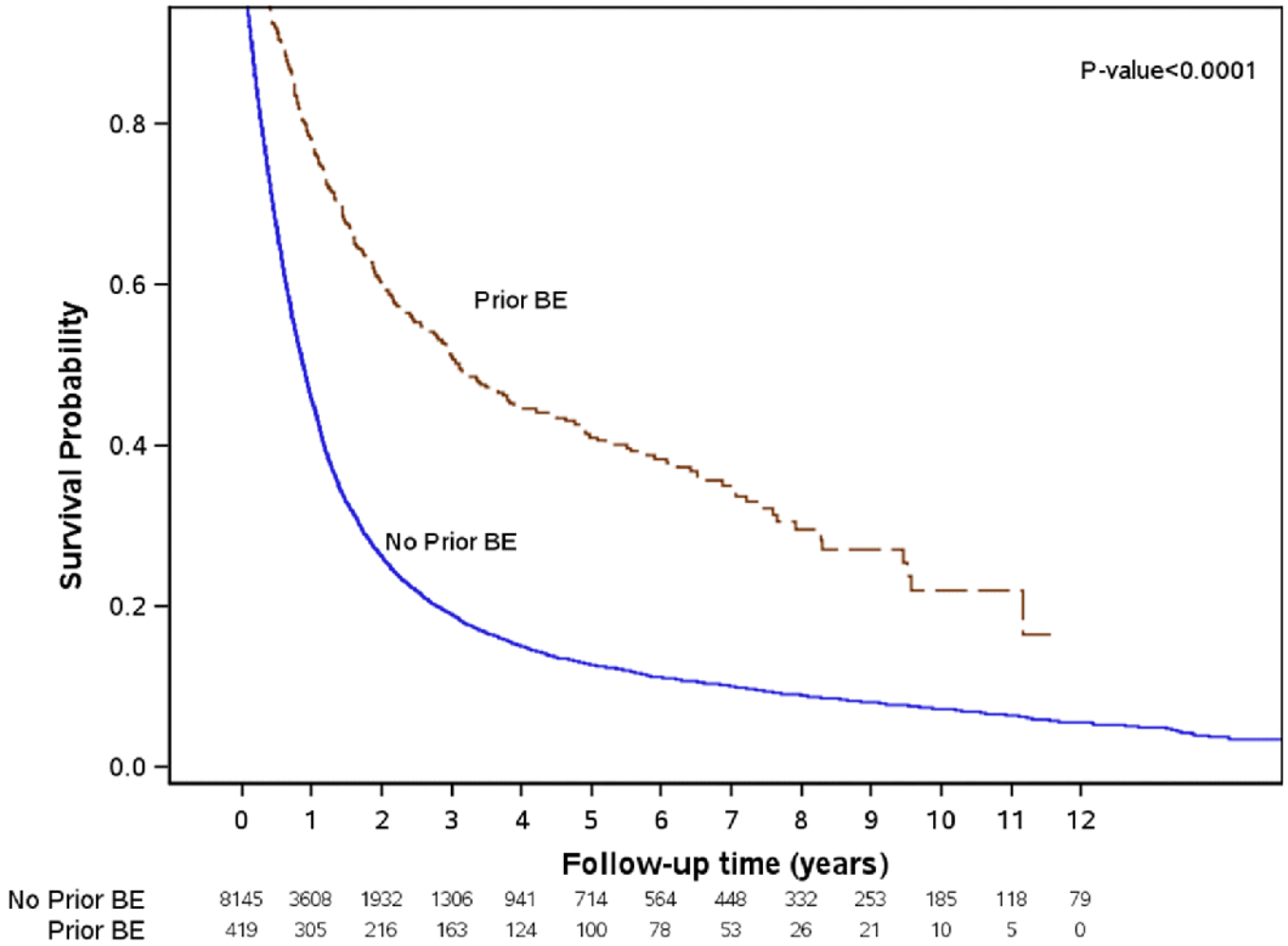

Figure 1.

Kaplan-Meier curve comparing overall survival of esophageal adenocarcinoma patients with and without a prior diagnosis of Barrett's esophagus.

Table 1

Characteristics of patients with esophageal adenocarcinoma stratified by prior diagnosis of Barrett's esophagus

	Patients with no prior BE diagnosis (n=8145)	Patients with a prior BE diagnosis (n=419)	*p*-value*
Age at EA diagnosis, mean (SD)	67.3 (9.6)	67.9 (8.8)	0.14
Male, n (%)	8093 (99.4)	418 (99.8)	0.25
BMI, mean (SD)	26.6 (5.9)	28.1 (6.1)	<0.001
Race/ethnicity, n (%)			<0.001
Non-Hispanic white	6934 (85.1)	374 (89.3)	
Hispanic	228 (2.8)	11 (2.6)	
Black	333 (4.1)	13 (3.1)	
Other	94 (1.2)	7 (1.7)	
Missing	556 (6.8)	14 (3.3)	
Alcohol use, n (%)			0.01
Never	2231 (27.4)	145 (34.6)	
Former	1992 (24.5)	93 (22.2)	
Current	2942 (36.1)	135 (32.2)	
Missing	980 (12.0)	46 (11.0)	
Smoking status, n (%)			0.001
Never	1020 (12.5)	77 (18.4)	
Ever	6876 (84.4)	340 (81.1)	
Missing	249 (3.1)	2 (0.5)	
Cancer stage, n (%)			<0.001
Stage 1	914 (11.2)	195 (46.5)	
Stage 2	1435 (17.6)	71 (17.0)	
Stage 3	1627 (20.0)	34 (8.1)	
Stage 4	2910 (35.7)	38 (9.1)	
Missing	1259 (15.5)	81 (19.3)	
Cancer treatment, n (%)			<0.001
No	1762 (21.6)	43 (10.3)	
Yes	6072 (74.6)	355 (84.7)	
Missing	311 (3.8)	21(5.0)	
Year of EA diagnosis, n (%)			<0.001
2002–2004	1442 (17.7)	4 (1.0)	
2005–2007	1613 (19.8)	54 (12.9)	
2008–2010	1902 (23.4)	119 (28.4)	
2011–2013	1767 (21.7)	135 (32.2)	
2014–2016	1421 (17.4)	107 (25.5)	

BMI, body mass index; EA, esophageal adenocarcinoma; SD, standard deviation.

Cancer treatment: receipt of surgery, chemotherapy and/or radiotherapy.

* Patients with missing values were excluded from comparisons.

Table 2

Effect of a prior diagnosis of Barrett's esophagus on mortality risk for patients with esophageal adenocarcinoma

Prior BE diagnosis vs. No prior BE diagnosis	HR (95% CI)
All-cause mortality	
Unadjusted	0.41 (0.36–0.47)
Adjusted * (without stage or treatment)	0.69 (0.61–0.80)
Adjusted * (including stage)	0.87 (0.75–0.99)
Adjusted * (including stage and treatment)	0.84 (0.73–0.96)
Cancer specific mortality	
Unadjusted	0.28 (0.23–0.35)
Adjusted * (without stage or treatment)	0.51 (0.41–0.64)
Adjusted * (including stage)	0.70 (0.56–0.87)
Adjusted * (including stage and treatment)	0.67 (0.53–0.84)

BE, Barrett's esophagus; CI, confidence interval; HR, hazard ratio.

*Adjusted for age, race/ethnicity, body mass index, alcohol use, smoking status, number of primary care visits, and number of GI clinic visits.

Table 3

Effect of a prior diagnosis of Barrett's esophagus on mortality risk for patients with esophageal adenocarcinoma, stratified by stage and treatment

Prior BE diagnosis vs. No prior BE diagnosis		HR* (95% CI)
All-cause mortality		
Stage		
	Stage 1	0.98 (0.77–1.25)
	Stages 2–4	0.90 (0.74–1.10)
Any treatment		
	No	0.43 (0.30–0.63)
	Yes	0.77 (0.66–0.89)
Cancer specific mortality		
Stage		
	Stage 1	0.79 (0.50–1.25)
	Stages 2–4	0.78 (0.59–1.03)
Any treatment		
	No	0.27 (0.15–0.50)
	Yes	0.60 (0.47–0.77)

BE, Barrett's esophagus; CI, confidence interval; HR, hazard ratio.

*Adjusted for age, race/ethnicity, body mass index, alcohol use, smoking status, number of primary care visits, and number of GI clinic visits.

Cancer treatment: receipt of surgery, chemotherapy and/or radiotherapy