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Temporal trends of esophageal disorders by age in the Cerner Health Facts® Database

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Abstract

PURPOSE—Esophageal adenocarcinoma (EA) incidence has increased approximately 600% over the last four decades in the US. Little research has been conducted on the temporal trends of gastroesophageal reflux disease (GERD) and Barrett's esophagus (BE), yet it is important to establish whether these conditions have also increased with time or differ by age.

METHODS—The Cerner Health Facts® database contains information on 35 million patients between 2001 and 2010. GERD, BE, and EC cases were defined using ICD-9 codes. We calculated age-adjusted rates and 95% confidence intervals for GERD, BE, and EC.

RESULTS—In this population, the overall, all-age rate per 100,000 encounters for GERD was 711.9, BE was 21.6, and EC was 6.1. During 2001–2010, GERD rates increased by approximately 50% and EC rates more than doubled, but BE rates declined by approximately 40%. Trends were similar by age, and all rates were higher in Caucasians and males.

CONCLUSIONS—These data indirectly support the idea that increased incidence of EC may be partially due to GERD, and raise the provocative hypothesis that BE rates may be decreasing possibly as a forerunner of continued stabilization of EA rates and a possible subsequent decline.

INTRODUCTION

In 2014, approximately half of the 18,170 anticipated incident esophageal cancers (EC) in the United States (US) were expected to be adenocarcinomas [1]. Esophageal adenocarcinoma (EA) incidence has increased approximately 600% over the last four decades in the US [2, 3]. Gastroesophageal reflux disease (GERD) is characterized by reflux of gastric contents into the esophagus [4]. It is a common condition that is estimated to affect 10–20% of adults in Western countries, and can cause loss of the native squamous

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epithelium, followed by development of Barrett's epithelium (BE) [5]. While it is not known if BE is a necessary precursor of EA [6], the dominant paradigm is that individuals may transition from GERD to BE and then to EA. However, studies have shown that GERD in the absence of BE appears to be a risk factor for EA as well [7]. Little research has been conducted on the temporal trends of GERD and BE, yet it is important to establish whether these conditions mirror EA secular changes, particularly by age. Therefore, we analyzed the overall and annual rates of GERD, BE, and EC in the Cerner Health Facts® Database [8]. We also examined sex-, age-, and race-specific rates of these conditions and annual rates stratified by age.

METHODS

Data Source

The data for this study is from the Cerner Health Facts® Database [8], with utilizes an automated electronic medical record system to capture hospital procedures (e.g., endoscopy), diagnostic information (e.g., diagnosis of esophageal disorders), demographics, medical history, admission, discharge, drug prescriptions, and laboratory tests over time [9]. A total of 152 hospitals contributed de-identified information on 35 million patients seen between January 1, 2001 and December 31, 2010. The Cerner Health Facts® Database is a HIPAA compliant, de-identified, longitudinal collection of individual level information generated from the Cerner® electronic medical record system which is utilized by both community and academic facilities across the United States. Due to the de-identified nature of the datasets obtained, this study was not considered human subjects research and was considered exempt from review by the Virginia Commonwealth University Institutional Review Board and the National Institutes of Health Office of Human Subjects Research.

Study Cohort

All patient encounters that occurred within the Cerner Health Facts® Database were utilized, yielding 81,392,956 inpatient and outpatient encounters. All instances of endoscopy were identified, utilizing International Classification of Diseases ninth edition clinical modification (ICD-9-CM) procedure codes. ICD-9-CM codes (42.23, 42.24, 42.33, 43.41, 44.13, 44.14, 44.22, 44.43, 45.13, 45.14, 45.30, 46.32, 51.10, 51.14, 51.84, 51.85, 51.87, 51.88, 52.13, 52.14, and 52.93) identified 167,185 endoscopies.

Outcomes

Esophageal disorders were identified utilizing ICD-9-CM diagnosis codes. Esophageal disorders included in this study were gastroesophageal reflux disease (ICD-9-CM 530.81 and 787.1), Barrett's esophagus (ICD-9-CM 530.85, and ICD-9-CM 530.2 prior to 2004), esophageal cancer (ICD-9-CM 150.0–150.9), esophagitis (ICD-9-CM 530.10–530.13 and 530.19), and reflux esophagitis (ICD-9-CM 530.11). Due to the unavailability of histology codes in this database, we were unable to distinguish between esophageal adenocarcinoma and esophageal squamous cell carcinoma. Thus, we analyzed all esophageal cancer cases together. There were 809,076 gastroesophageal reflux, 32,325 Barrett's esophagus, 10,934 esophageal cancer, 100,552 esophagitis, and 38,623 reflux esophagitis cases included. For the main analyses, GERD and esophagitis outcomes were allowed to repeat in an individual

due to possible disease recurrence, whereas BE and EC diagnoses were each separately restricted to first ("incident") diagnoses only.

Statistical Methods

We calculated rates and 95% confidence intervals (CI) for any recorded diagnosis of GERD or esophagitis and any initial diagnosis of BE and EC per 100,000 encounters with age-adjustment to the World Standard Population. We also used the number of endoscopies to crudely adjust the annual rates for increasing use of endoscopy during the time period. Thus, using years 2001–2002 as the referent, we divided the subsequent number of endoscopies per year by the referent to calculate an endoscopy ratio. Then, we divided the rates and 95% CI by the endoscopy ratio. Stratified analyses were conducted by sex, race (Caucasian, African-American, other), age (10 year age groups; 0–9, 10–19, ..., 70–79, 80+) and calendar year (2 year groups; 2001–2002, ..., 2009–2010). We also calculated the rate of esophageal disorders by age group and individual calendar year for graphical representation of temporal trends by age. Finally, we calculated the age-adjusted rate ratio of men:women by individual year for graphical representation.

As sensitivity analyses, we 1) computed the rates for individuals with at least two diagnostic codes for each BE and EC; 2) calculated a measure of person-years by allowing only one encounter per year per individual, and 3) computed the rates for only hospitals that contributed data in every year. All analyses were conducted using SAS version 9.3 (SAS Institute, Cary, NC).

RESULTS

In this population, the overall, all-age prevalence of GERD was approximately 1%, BE was 0.04%, and EC was 0.01%. As shown in **Table 1 and Figure 1A**, the rates of GERD per 100,000 encounters have increased by about 50% and EC rates more than doubled between 2001 and 2010. However, the rates of BE have been declining since the mid-2000s—the recent time period of 2009–2010 showed a 40% decline in rates when compared with 2001–2002. The same trends in BE rates were seen when examined per 100,000 endoscopies, instead of encounters, and restricted to diagnoses that were concurrent with an endoscopy procedure (**Supplementary Table 1**), yet it is noteworthy that the increase in EC rates dramatically subsided in this sensitivity analysis. Similar to BE, rates of esophagitis and reflux esophagitis have decreased by 30–40% during this time period (**Supplementary Tables 2–3**).

The trends of increasing annual rates of GERD and decreasing annual rates of BE and esophagitis were observed for all ages (**Figure 1B–C and Supplementary Figure 1A–B**). For EC, rates increased substantially between 2001 and 2010 (**Figure 1D**). Rates for all three esophageal disorders were higher in Caucasians and males (**Table 1**), and the sex rate ratios remained stable overtime (**Supplementary Figure 2**). Additionally, rates increased with increasing age (**Table 1 and Figure 1B–D**).

While rates of esophageal disorders varied in the sensitivity analyses, the trends seen were consistent regardless of the definition for the esophageal disorders (**Supplementary Table**

5), estimated denominator (**Supplementary Table 6**), or hospital population (**Supplementary Table 7**).

CONCLUSIONS

The overall rates of BE [10, 11] and EC [1] are similar to previously reported estimates for US populations. However, the prevalence of GERD in this population is notably lower than previous US estimates of 20–30% for GERD symptoms in adults [12, 13]. As the current study is exclusively based on ICD-9 codes for a GERD diagnosis, we are likely only to capture severe cases of GERD. Regardless of the comparability of this population with prior survey-based prevalence estimates, the underlying trends of the severe GERD cases we have likely captured are valid and provide interesting results from which inferences can be made.

A limitation of this study is that the full patient history is unavailable. Thus, we were unable to distinguish individuals with newly diagnosed BE, which would require an endoscopy, from individuals with existing BE. For example, as shown in **Supplementary Table 4**, only eight percent of individuals that had a first-observed ("incident") BE ICD-9 code during an encounter also had a concurrent endoscopy—however, when we restricted the BE analysis to this subpopulation, the temporal trend was unaltered (**Supplementary Table 4 versus Table 1**). This is likely a conservative underestimate, as the ICD code for BE may not be utilized until after the receipt of the pathology report in follow-up visit – possibly weeks or months post-endoscopy. We examined an alternative definition of concurrent endoscopy – up to six months prior to BE diagnosis, but this did not substantially change the number of individuals with a BE diagnosis that had an endoscopy recorded (data not shown). Referral from a "non-Cerner" specialist to a "Cerner tertiary center" is likely a primary reason why many of the Cerner BE diagnoses lack concurrent endoscopy. Another potential limitation is that hospitals contributed electronic medical record data to the Cerner Health Facts® Database for varying lengths of time. This could potentially explain the rapid decrease in cases of GERD and BE in the 2009–2010 timeframe. However, when we compared analyses of hospitals that contributed data to the entire study period with hospitals that contributed data only during the final years of the study period, we received similar results (data not shown). We also conducted an analysis only using outpatient encounters, and results were similar (data not shown).

The large increase in EC rates in the primary analysis may reflect increased overdiagnosis of indolent cancers due to expansion of gastroenterology services in some of the Cerner centers. The fact that the increasing EC trend was less apparent when adjustment was made for number of endoscopies offers support for this interpretation. Although EC rates have not dramatically increased in SEER registry data over the last decade, it is likely that the Cerner population is less representative of the total US population. Lastly, primary reason for endoscopy was not available, thus we were unable to assess EC trends by symptom which may have provided further insight into EC trends.

While this data has noted limitations, the size of the Cerner Health Facts® Database is extremely large, with over 81 million encounters captured during the study period. This allowed our study to examine these three esophageal disorders by both year and age to

determine if rates of these conditions were increasing or decreasing in similar ways overtime and by age.

In summary, GERD rates increased, plateaued and then decreased slightly, BE rates decreased by approximately 40%, and EC rates increased. These patterns were fairly consistent when stratified by age. Additionally, we report higher rates of all three disorders among Caucasians and among males. These data indirectly support the idea that increased incidence of EC may be partially due to GERD, and raise the provocative idea that BE rates may be decreasing possibly as a forerunner of continued stabilization—and possible subsequent decline—of esophageal adenocarcinoma rates.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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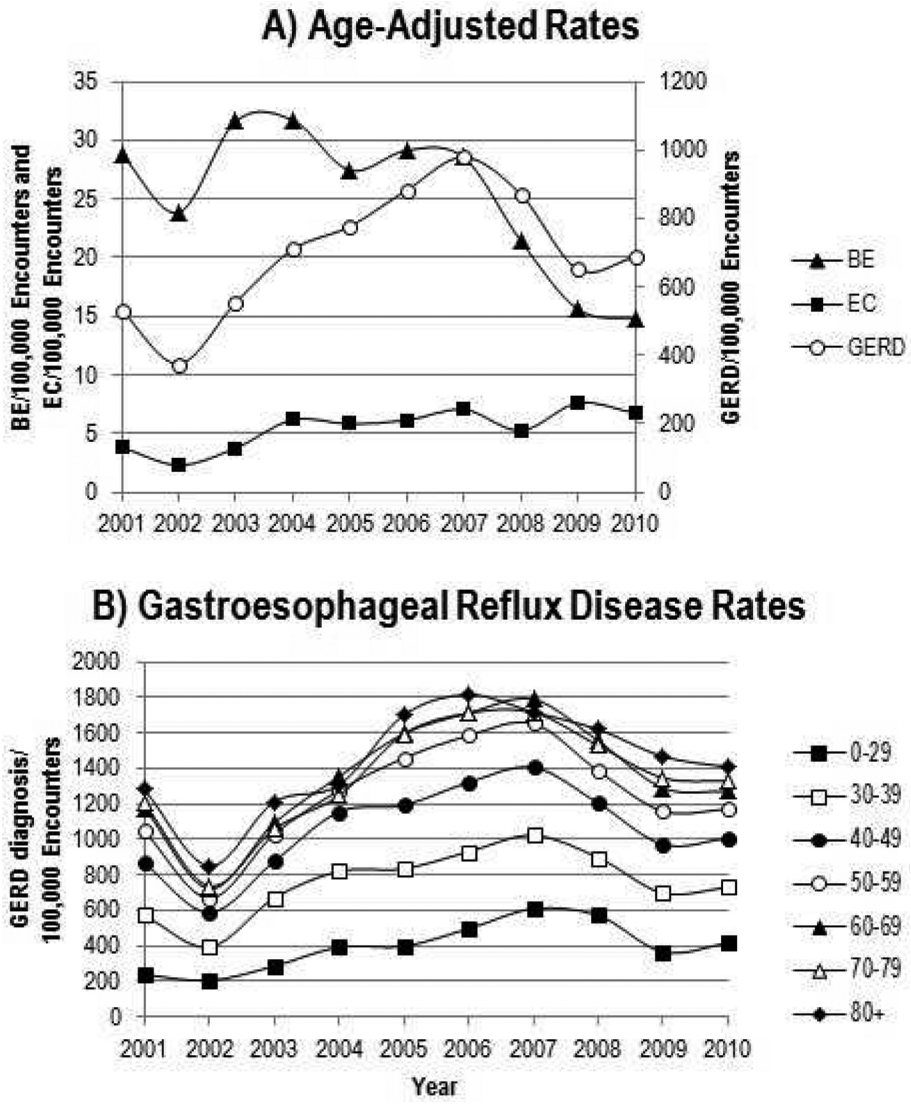

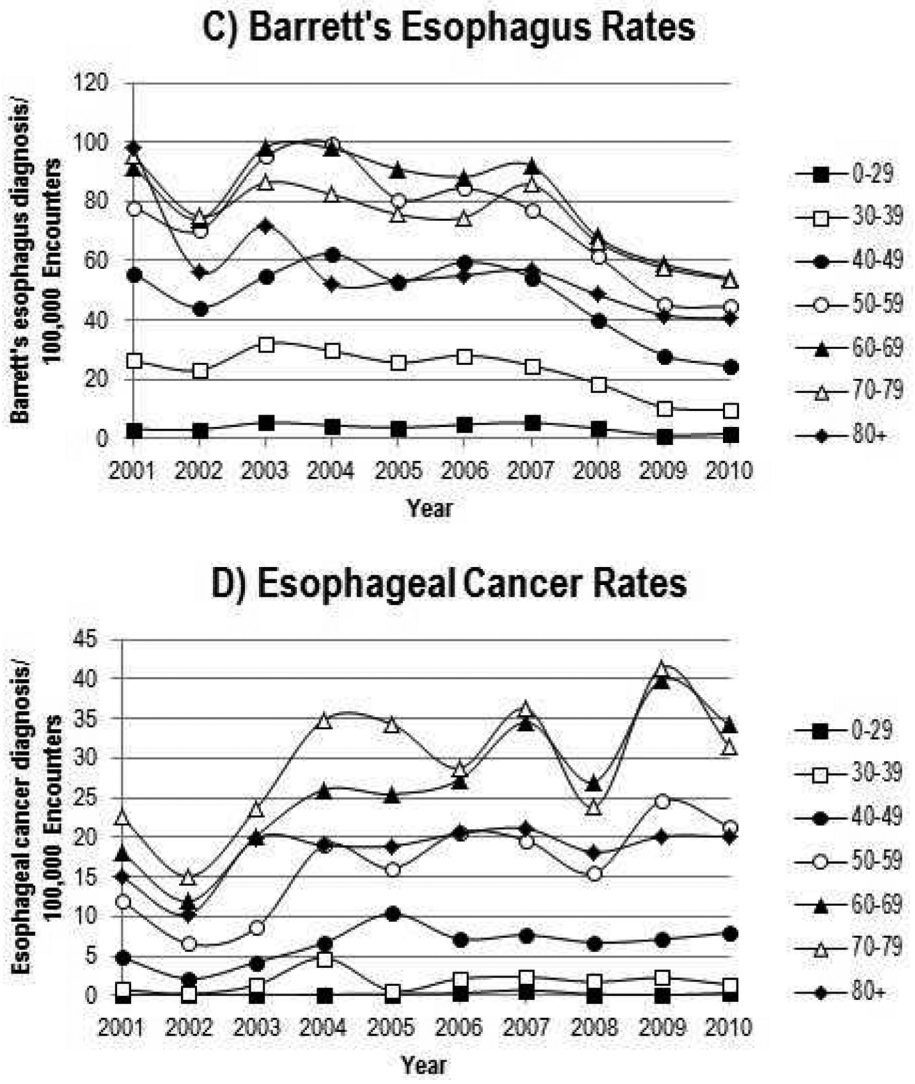

Figure 1.

Temporal trends of gastroesophageal reflux, Barrett's esophagus and esophageal cancer overall (A), and by age (B–D), Cerner Health Facts® Database, 2001–2010.

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Table 1

Age-adjusted rates of gastroesophageal reflux, Barrett's esophagus, and esophageal cancer per 100,000 encounters, Cerner Health Facts® Database, 2001–2010.

				Gastroesophageal Reflux/ 100,000 encounters		Barrett's esophagus/ 100,000 encounters		Esophageal cancer/ 100,000 encounters	
	Encounter N	Endoscopies N	Endoscopy Ratio	GERD N	Rate (95% CI)	BE N	Rate (95% CI)	EC N	Rate (95% CI)
Overall	81,392,956	167,185		809,076	711.9 (709.9, 713.9)	32,325	21.6 (21.3, 21.9)	10,934	6.1 (6.0, 6.3)
Years									
2001-2002	8,892,780	22,143		59,101	452.9 (448.3, 457.5)	4,293	26.3 (25.4, 27.2)	623	3.1 (2.8, 3.3)
2003-2004	7,923,607	24,727		73,052	631.5 (625.3, 637.6)	4,613	31.7 (30.6, 32.8)	952	5.0 (4.6, 5.3)
2005-2006	10,090,055	28,956		122,509	834.4 (828.1, 840.7)	5,154	28.4 (27.5, 29.3)	1,369	6.0 (5.6, 6.4)
2007-2008	16,535,982	41,641		201,474	916.4 (911.3, 921.6)	7,292	24.4 (23.8, 25.1)	2,158	6.0 (5.7, 6.3)
2009-2010	37,950,532	49,718		352,940	669.2 (666.5, 672.0)	10,973	15.2 (14.9, 15.5)	5,832	7.2 (7.0, 7.4)
Years, adjusted for number of endoscopies performed									
2001-2002	8,892,780	22,143	1	59,101	452.9 (448.3, 457.5)	4,293	26.3 (25.4, 27.2)	623	3.1 (2.8, 3.3)
2003-2004	7,923,607	24,727	1.1	73,052	565.5 (559.9, 571.0)	4,613	28.4 (27.4, 29.3)	952	4.5 (4.1, 4.8)
2005-2006	10,090,055	28,956	1.3	122,509	638.0 (633.2, 642.9)	5,154	21.7 (21.0, 22.4)	1,369	4.6 (4.3, 4.9)
2007-2008	16,535,982	41,641	1.9	201,474	487.3 (484.6, 490.1)	7,292	13.0 (12.7, 13.3)	2,158	3.2 (3.0, 3.4)
2009-2010	37,950,532	49,718	2.2	352,940	298.1 (296.8, 299.3)	10,973	6.8 (6.6, 6.9)	5,832	3.2 (3.1, 3.3)
Sex									
Male	31,423,289	74,152		288,389	693.2 (690.0, 696.4)	18,611	33.3 (32.7, 33.9)	7,899	11.3 (11.0, 11.6)
Female	49,969,667	93,033		455,421	629.9 (627.5, 632.3)	12,513	13.4 (13.1, 13.6)	2,054	1.8 (1.7, 1.9)
Age									
0-9	7,651,027	1,755		38,882	508.2 (503.1, 513.2)	26	0.3 (0.2, 0.5)	12	0.2 (0.1, 0.2)
10-19	6,103,494	2,549		16,694	273.5 (269.4, 277.7)	111	1.8 (1.5, 2.2)	10	0.2 (0.1, 0.3)
20-29	8,150,478	6,802		35,270	432.7 (428.2, 437.3)	471	5.8 (5.3, 6.3)	22	0.3 (0.2, 0.4)
30-39	8,576,937	11,681		65,034	758.2 (752.4, 764.1)	1,578	18.4 (17.5, 19.3)	150	1.7 (1.5, 2.0)
40-49	11,292,051	21,404		119,444	1057.8 (1051.8, 1063.8)	4,570	40.5 (39.3, 41.6)	777	6.9 (6.4, 7.4)
50-59	12,748,553	30,389		158,954	1246.8 (1240.7, 1253.0)	7,987	62.7 (61.3, 64.0)	2,414	18.9 (18.2, 19.7)
60-69	10,949,149	30,520		149,475	1365.2 (1358.3, 1372.1)	7,823	71.4 (69.9, 73.0)	3,378	30.9 (29.8, 31.9)
70-79	9,211,490	32,755		126,376	1371.9 (1364.4, 1379.5)	6,346	68.9 (67.2, 70.6)	2,890	31.4 (30.2, 32.5)
80+	6,709,777	29,330		98,947	1474.7 (1465.5, 1483.9)	3,413	50.9 (49.2, 52.6)	1,281	19.1 (18.0, 20.1)

	Encounter N	Endoscopies N	Endoscopy Ratio	Gastroesophageal Reflux/ 100,000 encounters		Barrett's esophagus/ 100,000 encounters		Esophageal cancer/ 100,000 encounters	
				GERD N	Rate (95% CI)	BE N	Rate (95% CI)	EC N	Rate (95% CI)
Race									
Caucasian	63,582,557	139,755		617,716	680.2 (677.9, 682.6)	29,367	24.1 (23.8, 24.5)	8,624	5.8 (5.6, 5.9)
African-American	11,554,043	18,472		93,399	650.4 (645.9, 654.9)	832	4.9 (4.5, 5.2)	992	5.4 (5.1, 5.7)
Other	6,256,356	8,958		32,695	450.6 (445.5, 455.7)	925	11.6 (10.8, 12.4)	337	3.9 (3.5, 4.3)